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Research article

A mathematical model of *Clostridioides difficile* transmission in long-term care facilities

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Abstract: *Clostridioides difficile*, also known as *C. difficile*, is a prevalent cause of infectious diarrhea in United States healthcare facilities. Spread through the fecal-oral route and often through contact with spores on contaminated surfaces, *C. difficile* can cause severe diarrhea, stomach pain, and colitis. Most individuals can mount an effective immune response, but older populations, immunocompromised individuals, and those taking antibiotics have a higher risk of being colonized by *C. difficile*. While extensive research has been conducted in hospital-based settings to improve understanding of the transmission of this bacteria, few studies apply mathematical models in the context of long-term care facilities. This work introduced a mathematical model using a system of ordinary differential equations to represent *C. difficile* transmission dynamics in assisted living facilities, with their interactive nature and high risk factors. The equations included four resident classes (susceptible, colonized, diseased, and isolated) and three pathogen-carrying classes (high-traffic areas, low-traffic areas, and healthcare workers' hands) to simultaneously capture the movement between classes and track spore density on environmental reservoirs and healthcare workers' hands, including their contributions to

disease spread. Parameter estimation using data from the Emerging Infections Program at the Centers for Disease Control and Prevention was completed and was followed by sensitivity analyses to quantify the impact of varying these parameters and their impact on incidence. Mitigation strategies, including frequent disinfection, increased healthcare worker hand hygiene compliance, a lower ratio between residents and healthcare workers, and increased resident screening had the greatest impact on reducing the incidence of *C. difficile*.

Keywords: *Clostridioides difficile*; ordinary differential equations; environmental transmission; colony-forming units; sensitivity analysis; parameter estimation; mathematical model

1. Introduction

Clostridioides difficile (*C. difficile*) is a gram-positive, anaerobic bacteria that spreads through the fecal-oral route. Inactive spores can survive for months on surfaces before an individual comes in contact with the contaminated surface and picks up the spores. Once ingested, *C. difficile* becomes active in the intestines and can cause symptoms including diarrhea, nausea, stomach tenderness, and colitis [1]. Causing almost 500,000 infection cases and 30,000 deaths annually, *C. difficile* remains a pressing concern in healthcare settings with an estimated burden of five billion dollars annually for inpatient care [2]. In United States healthcare facilities, including long-term care facilities (LTCFs), *C. difficile* accounts for a direct cost of approximately $647 million [3].

"Long-term care" is a broad term that encompasses a wide variety of services designed to meet an individual's health or personal care needs when they can no longer address those needs unassisted [4]. There are many types of LTCFs that provide varying levels of care, including independent living, adult day care, assisted living facilities, nursing homes, and residential care communities [5]. For our purposes, we will use "LTCFs" to refer to a specific type of residential care community with individual bedrooms and bathrooms for residents and shared common spaces where residents tend to interact frequently during daily activities such as meals and social gatherings. Residents in LTCFs may require some healthcare worker (HCW) assistance with daily activities but are generally not bedridden and can interact with other residents regularly. We classify "HCWs" to include registered nurses, certified nursing assistants, and nurse practitioners; these individuals come in close, regular contact with residents each day. These three categories make up the majority of the healthcare workforce in LTCFs [6]. Some tasks and services provided by HCWs for residents include assistance with toileting, bathing, dressing, and medication management [7].

While most individuals can mount an effective immune response to *C. difficile* and prevent an infection [1], older populations, immunocompromised individuals, and those taking antibiotics have a higher risk of being colonized by *C. difficile*. Upon colonization, some individuals remain asymptomatic and eventually clear the bacteria over the course of several weeks or months. If a colonized individual begins to exhibit symptoms, they may be diagnosed with a *C. difficile* infection (CDI). Symptomatic CDI is defined as having three or more unformed stools in 24 hours as well as a positive culture in a laboratory test [8].

Environmental surfaces and cleaning protocols play a crucial role in *C. difficile* transmission in healthcare settings. Both asymptomatically- and symptomatically-infected LTCF residents shed inactive spores onto their surroundings, allowing other susceptible residents to potentially contract the disease even without direct interaction with an infected individual. These inactive spores can live for months on various surfaces, and once ingested, *C. difficile* becomes active in the large intestine [1]. While many spores can exist within the environment, the particular spores that can cause infection are commonly measured in colony-forming units (CFUs) [9]. *C. difficile* also has a high resistance to many alcohol-based disinfectants [10], which are commonly used for disinfecting hands and surfaces in healthcare settings. Comparatively, soap and water eliminate 90% of *C. difficile* spores while alcohol-based hand rubs (ABHRs) remove only 20% [11]. Note also the distinction between cleaning, decontamination, and disinfection in our parameters: *cleaning* typically refers to removal of debris [12], while *decontamination* aims to reduce contamination to safe levels [13]. *Disinfection*, which terminates most pathogens lying on the surface, is a subset of decontamination [13].

Many studies have investigated *C. difficile* transmission in hospital settings through agent-based or compartmental models, most of which include susceptible, colonized, and diseased/infected classes. Some studies focus on the impact of mitigation strategies, such as screening upon admission and isolation [14], while others assess the impact of particular treatments, including vaccinations and fecal microbiota transplantation [15]. Models involving HCWs, doctors, and visitors operate on the underlying assumption that they are not susceptible to colonization and instead treat them as vectors of disease transmission [16–18].

A number of agent-based models (ABMs) consider the environmental impact of agents interacting with their surroundings, sometimes treating the environment as binary (either contaminated or uncontaminated) [17]. Other ABMs model environmental impact through the probability of transmission during interaction; Barker et al. [16] considers the role of handwashing and disinfection (both routine and terminal/final disinfection after contamination). However, these ABMs do not differentiate between different areas in the hospital (e.g., low-traffic versus high-traffic) and instead designate different probabilities of spore transfer between an agent class, such as a nurse, doctor, or resident, and the environment. Bintz et al. [19] incorporates antibiotic heterogeneity and its impact on transmission of *C. difficile*, while Stephenson et al. [20] also includes the impact of these antibiotic heterogeneities together with vaccinations, environmental cleaning, and explicit hand hygiene compliance from HCWs. We define hand hygiene compliance as the percent of time in which HCWs comply with associated protocols. This includes cleaning hands before and after interacting with a patient, whether using ABHR or washing hands with soap and water.

Compartmental models are a common type of model that focus on assessing the effectiveness of various mitigation strategies. Lanzas et al. [21] used an ordinary differential equation (ODE) model to evaluate *C. difficile* transmission contributions from both symptomatic and asymptomatic patients in a hospital setting. Li et al. [22] developed both a deterministic ODE model and a stochastic Markovian compartmental model to quantify environmental disease transmission, and Wolkewitz et al. [23] used an ODE model and stochastic simulations to predict the effect of hygiene interventions during a vancomycin-resistant enterococci outbreak in a hospital. In particular, Stephenson et al. [24] used an ODE model to target the impact of vaccinations on *C. difficile* transmission while also performing optimal control to consider cost-effectiveness. Furthermore, Sulyok and Fox et al. [12] specified a

distinction between high- and low-touch surfaces within their ODE model to quantify their impact on the dynamics of *C. difficile* spread in a hospital setting.

While mathematical models of *C. difficile* have primarily been developed for hospital and acute-care settings, research analyzing its transmission in LTCFs remains limited [25]. Some studies in LTCFs focus on other infectious diseases, such as methicillin-resistant *Staphylococcus aureus* (MRSA), scabies, norovirus, and more recently, coronavirus disease (COVID-19) [26–28]. Both compartmental and agent-based frameworks have been used for these. Chamchod et al. [27] considered uncontaminated and contaminated HCW classes in addition to susceptible and colonized resident classes in their ODE model of MRSA transmission. Assab et al. [26] also included HCWs in their stochastic norovirus model to observe the impact of hand hygiene, with HCWs considered susceptible to the virus as well, and Chen et al. [29] used a compartmental ODE model to examine the spread of COVID-19 in LTCFs. Specifically for *C. difficile* spread, Durham et al. [30] explored a stochastic compartmental transmission model that broadened the scope of *C. difficile* to the community level and included dynamics between LTCFs and hospitals, and Rhea et al. [31, 32] developed an ABM of *C. difficile* transmission in a major regional healthcare network in North Carolina, with a focus on antibiotic stewardship in the network. Although these models go beyond the typical healthcare facility spread of *C. difficile*, to our knowledge, no studies have quantified the impact of *C. difficile* in the context of an individual LTCF, as has been previously done with individual hospital settings.

Typically, LTCFs assist fewer individuals than hospitals, with an average of 39 beds in LTCFs [33] compared to an average of 168 beds in a hospital [34]. In addition to facility size, the frequency and dynamics of contact between patients in hospitals and residents in LTCFs differs as a result of the distinct layout of each facility type. Communal spaces found in LTCFs such as cafeterias and lounges increase the potential for *C. difficile* transmission mediated by resident interaction. However, hospital patients interact with a median of 5.5 persons each hour [35] while LTCF residents were found to have an average of 17.3 distinct contacts over a study period of 21 days [36]. Furthermore, hospitals have a high turnover rate and shorter length of stay; in 2022, the average length of stay was six days for acute care [37]. Meanwhile, residents of LTCFs stay for a longer period, with an average duration of 20.3 months [38]. Lastly, the size of the healthcare staff and rigor of cleaning protocols tend to differ from that of hospitals. With the daily interactions between HCWs and residents for various assistance needs, *C. difficile* spores can transfer from and to HCW hands through physical contact. HCWs in LTCFs have a 17% rate of handwashing compliance [39] compared to a range of 40%–60% in hospitals [40], which also heightens the risk of transmission. The vast differences in cleanliness, facility geometry, resident or patient density, and frequency of interaction all create substantial differences in transmission dynamics between LTCFs and hospitals.

Our model uses a system of ODEs and attempts to fill the gap in literature by building off the deterministic compartmental model introduced by Sulyok and Fox et al. [12] and applying the ideas from their hospital dynamical system to an LTCF. In particular, we incorporate components that differ between hospital and LTCF settings, with the inclusion of an isolated resident class, HCW pathogen-carrying class, and interactions between residents as a source of transmission. Our model also introduces a different categorization of environmental reservoirs as low- versus high-traffic areas instead of low- and high-touch surfaces. For our purposes, "high-traffic" refers to communal or shared spaces in the LTCF where residents are more likely to interact with each other, such as a cafeteria or lounge area.

"Low-traffic" refers to areas with a smaller number of unique visitors, such as a resident's individual room or bathroom. Additionally, compared to acute healthcare settings, the HCW staffing numbers and behaviors differ in LTCFs due to the nature of the service. As previously mentioned, LTCF services range from assistance with bathing and toileting to social and recreational activities [7]. Therefore, there are many instances of contact both between residents and between residents and HCWs. To capture these dynamics, we also include HCWs as a vector of disease transmission by considering the spore density on their hands. We aim to measure the interactions between residents, HCWs, and the environment in LTCFs to provide further insight into potential mitigation strategies to reduce the incidence of *C. difficile* colonizations and infections in LTCFs.

2. Methods

Our mathematical model quantifies the transmission of *C. difficile* in an LTCF through four resident and three pathogen-carrying classes as described in Table 1. This model extends previous work done by Sulyok and Fox et al. [12] in hospitals and adapts their model to describe dynamics in LTCFs. Transmission among these seven classes is described in Figure 1 and represented by seven nonlinear ODEs (2.1).

Table 1. Resident and pathogen-carrying classes.

Variable	Description (*Units*)
S	Susceptible residents (*individuals*)
C	Colonized residents (*individuals*)
D	Diseased residents (*individuals*)
Q	Quarantined residents (residents in isolation) (*individuals*)
P_H	*C. difficile* spore density in high-traffic areas ($CFUs \cdot cm^{-2}$)
P_L	*C. difficile* spore density in low-traffic areas ($CFUs \cdot cm^{-2}$)
P_W	*C. difficile* spore density on HCW hands ($CFUs \cdot cm^{-2}$)

The four resident classes are measured in units of *individuals*. Advanced age is a significant risk factor for *C. difficile*, so any residents who are not colonized, diseased, or isolated are in the susceptible class S. The colonized class C contains residents asymptomatically infected with *C. difficile*, meaning their gut microbiomes have been colonized by *C. difficile*, but they are not exhibiting symptoms. Diseased individuals D are symptomatically infected with *C. difficile* but are still moving about the facility. The final resident class Q represents individuals infected with *C. difficile* who have been moved into isolation or quarantine, which we will refer to as the isolated class. This model assumes perfect isolation, so once individuals are in this class, they are no longer a source of *C. difficile* transmission since they cannot interact with other residents or the environment.

The three pathogen-carrying classes measure spore density in units of $CFUs \cdot cm^{-2}$. The class P_H represents spore density in high-traffic areas, which are defined to be shared spaces such as common rooms, dining halls, communal bathrooms, and fitness areas. Analogously, P_L represents spore density in low-traffic areas such as individual resident rooms and bathrooms. The final pathogen-carrying class P_W represents the spore density on the hands of HCWs. As HCWs interact with residents and

move around the facility, the density of spores on their hands can cause transmission. The interactions among all classes is described by our system of ODEs in (2.1) below with a full list of accompanying model parameters, descriptions, and sources given in Table 2.

$$\begin{aligned}
\frac{dS}{dt} &= a_S\delta(t)N + \alpha C + \lambda Q - kS \\
&\quad - \beta\left(\omega\frac{P_H}{P_H+K_F} + \frac{P_L}{P_L+K_F} + \tau(1-n)\frac{P_W}{P_W+K_W} + \varepsilon(1-f)C + \theta(1-f)D\right)S \\
\frac{dC}{dt} &= a_C\delta(t)N - (\alpha+\varphi+k)C \\
&\quad + \beta\left(\omega\frac{P_H}{P_H+K_F} + \frac{P_L}{P_L+K_F} + \tau(1-n)\frac{P_W}{P_W+K_W} + \varepsilon(1-f)C + \theta(1-f)D\right)S \\
\frac{dD}{dt} &= \varphi C - (\psi+k_D)D \\
\frac{dQ}{dt} &= \psi D - (\lambda+k_D)Q \\
\frac{dP_H}{dt} &= \rho_{CH}C + \rho_{DH}D - \mu\sigma P_H + \rho_{HW}T_1(t) - z_H\frac{P_H}{P_H+K_F}S \\
\frac{dP_L}{dt} &= \rho_{CL}C + \rho_{DL}D - \sigma P_L + \rho_{LW}T_2(t) - z_L\frac{P_L}{P_L+K_F}S \\
\frac{dP_W}{dt} &= \rho_{CW}C + \rho_{DW}D - (\eta+\ell)P_W - \rho_{HW}T_1(t) - \rho_{LW}T_2(t) - z_W\frac{P_W}{P_W+K_W}S
\end{aligned} \tag{2.1}$$

where

$$\delta(t)N = k(S+C) + k_D(D+Q) \tag{2.2}$$

represents the number of residents being discharged from the facility at a given time. Since our model assumes a fixed population size $N = S+C+D+Q$, representative of an LTCF operating at full capacity, the sum of the four ODEs representing the change in the patient classes must sum to zero. Residents can be admitted into either the susceptible or colonized classes and discharged from any of the four resident classes. We assume residents are only admitted to the S and C classes since individuals who are exhibiting symptoms or are in isolation will likely be in a hospital for treatment and not admitted into an LTCF. Thus, the proportions of residents admitted into the susceptible and colonized classes a_S and a_C sum to one.

Resident movement from susceptible to colonized is governed by the sum of influence of susceptible interaction with pathogen-carrying classes and interactions with colonized and diseased residents. In-flow into the susceptible class comes from newly admitted residents ($a_S\delta(t)N$), colonized residents who have recovered at rate α, and residents who have been successfully treated and released from isolation at rate λ. Residents are either colonized at admission or become colonized within the LTCF based on the sum of interactions with environmental reservoirs and other colonized or diseased residents. Once colonized, residents either recover at rate α, develop symptoms and move to the diseased class at rate φ, or are discharged at rate k. Diseased residents are either moved to the isolation class at

rate ψ or are discharged at rate k_D. From there, the isolated residents either recover and move back into the susceptible class at rate λ or are discharged at rate k_D due to death or hospitalization.

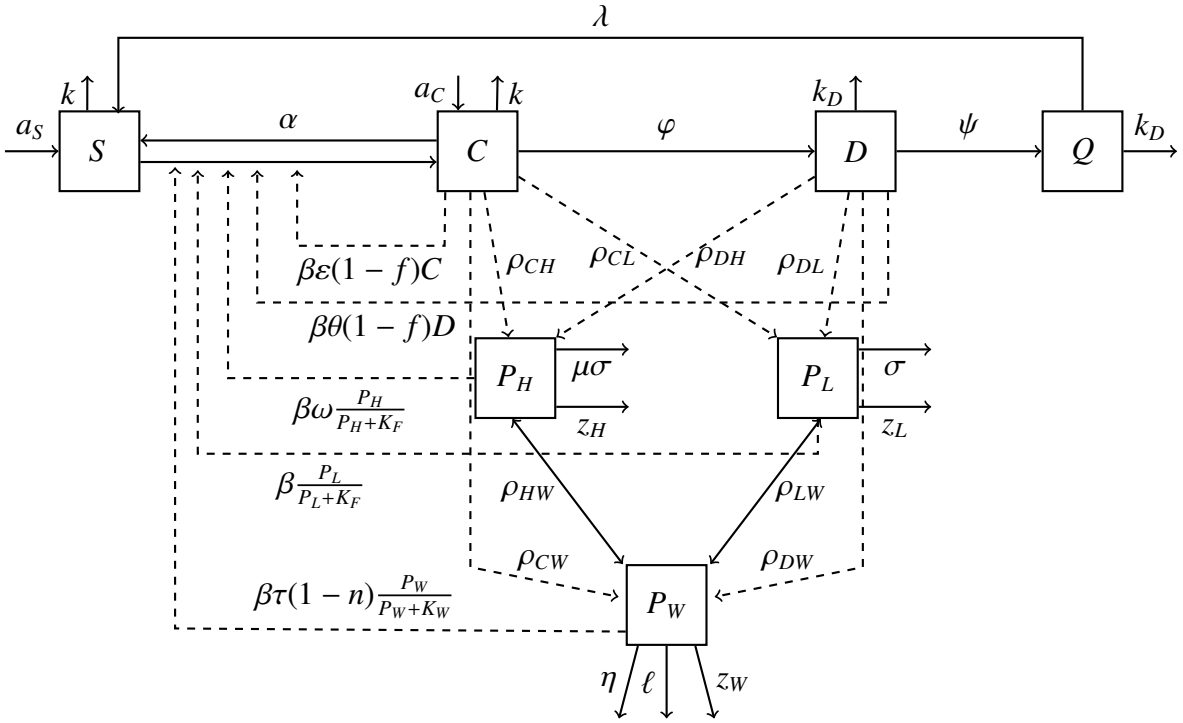

Figure 1. Schematic of *C. difficile* transmission in an LTCF. Solid lines indicate transfer between the classes while dotted lines represent interaction between classes without explicit movement between them. The double-sided arrows between the pathogen-carrying classes represent a one-directional spore transfer that depends on the value of each class (measured in $CFUs \cdot cm^{-2}$).

The equations for the three pathogen-carrying classes, P_H, P_L, and P_W, are primarily governed by a set of eight spore-shedding and transfer rates. Six of the rates represent the shedding of spores from colonized or diseased residents onto high-traffic areas (ρ_{CH}, ρ_{DH}), low-traffic areas (ρ_{CL}, ρ_{DL}), and HCW hands (ρ_{CW}, ρ_{DW}). The other two spore transfer rates, ρ_{HW} and ρ_{LW}, represent the transfer of spores between HCW hands and environmental reservoirs. Our model assumes that when an HCW interacts with a contaminated surface, there is a net transfer of *C. difficile* spores (i.e., one surface has an increase in spore density and the other a corresponding decrease). In order to model this behavior, we utilize the Heaviside function:

$$H(x) = \begin{cases} 1, & x > 0 \\ 0, & x \leq 0 \end{cases}.$$

The Heaviside functions applied to the pathogen-carrying classes in Eq (2.3) are used to represent a one-directional spore transfer between P_H or P_L and P_W, respectively. In particular, the value of $T_1(t)$ will be either P_W or $-P_H$ at any time step and, likewise, $T_2(t)$ will be either P_W or $-P_L$. These equations appear in the model (2.1) in $\frac{dP_H}{dt}$, $\frac{dP_L}{dt}$, and $\frac{dP_W}{dt}$. Spores will either transfer from the HCW hands to the surfaces or from the surfaces to the HCW hands. In order to keep the model tractable and to capture the

average effect of surface-mediated transmission without introducing additional parameters where data is currently limited, we make the following assumption: the pathogen-carrying class with the greater spore density will transfer spores to the class with lower density based on the appropriate rate of spore transfer. The transfer functions are given by the following:

$$\begin{aligned} T_1(t) =& H(P_W - P_H)P_W - H(P_H - P_W)P_H \\ T_2(t) =& H(P_W - P_L)P_W - H(P_L - P_W)P_L \end{aligned}. \tag{2.3}$$

The proportion of spores removed from P_H and P_L due to disinfection is represented by σ, with an additional weighting constant μ in high-traffic areas to signify the extra cleaning of surfaces within these areas. The rates at which susceptible residents pick up CFUs when they come in contact with a pathogen-carrying class are denoted by z_H, z_L, and z_W. This type of interaction decreases the spore density on any pathogen-carrying class. Spore pick-up rates are multiplied by the proportion of spores transferred from that compartment to the resident upon contact, written in the form $\frac{P_i}{P_i+K_j}$, where $i = H, L, W$ and $j = F, W$. The half-saturation constant K_F indicates the spore density in high- and low-traffic areas needed to colonize 50% of the population; similarly, K_W is the half-saturation constant for spore density on HCW hands.

Table 2. Model parameters.

Parameter	Description (*Units*)	Value	Source
a_S	Proportion of individuals admitted into S (*dimensionless*)	0.911	[41]
a_C	Proportion of individuals admitted into C (*dimensionless*)	0.089	[41]
k	Discharge rate for S and C ($days^{-1}$)	0.0016	[38]
k_D	Discharge rate for D and Q ($days^{-1}$)	0.0021	[38,42]
λ	Successful treatment rate for Q ($days^{-1}$)	0.0729	[1,43]
α	Recovery rate for C ($days^{-1}$)	0.01285	[44]
β	Colonization rate upon transfer of spores ($days^{-1}$)	0.0081	Estimated
ε	Weighting constant for interactions with C ($individuals^{-1}$)	0.0484	[36,45,46]
θ	Weighting constant for interactions with D ($individuals^{-1}$)	0.2053	[30,36,46,47]
ω	Weighting constant for interactions with P_H (*dimensionless*)	1.94	[46]
τ	Weighting constant for interactions with P_W (*dimensionless*)	2.185	[36,46]
μ	Weighting constant for increased cleaning of P_H (*dimensionless*)	2.5	[48–50]
f	Proportion of time residents are socially inactive (*dimensionless*)	0.479	[51]
n	Ratio of HCWs to residents (*dimensionless*)	0.145	[52]
φ	Disease rate with insufficient immune response ($days^{-1}$)	0.0021	Estimated
ψ	Isolation rate ($days^{-1}$)	0.111	[8,53–55]
σ	Proportion of P_H and P_L spores removed by disinfecting ($days^{-1}$)	0.375	[48,50]
z_H	Pickup rate of P_H ($CFUs \cdot cm^{-2} \cdot individuals^{-1} \cdot days^{-1}$)	0.139	[46,56,57]
z_L	Pickup rate of P_L ($CFUs \cdot cm^{-2} \cdot individuals^{-1} \cdot days^{-1}$)	0.0357	[46,56,57]
z_W	Pickup rate of P_W ($CFUs \cdot cm^{-2} \cdot individuals^{-1} \cdot days^{-1}$)	0.008	[36,57,58]
ρ_{CH}	Shedding rate of C onto P_H ($CFUs \cdot cm^{-2} \cdot individuals^{-1} \cdot days^{-1}$)	0.034	[56,59]
ρ_{CL}	Shedding rate of C onto P_L ($CFUs \cdot cm^{-2} \cdot individuals^{-1} \cdot days^{-1}$)	0.018	[56,59]
ρ_{CW}	Shedding rate of C onto P_W ($CFUs \cdot cm^{-2} \cdot individuals^{-1} \cdot days^{-1}$)	0.047	[36,59,60]
ρ_{DH}	Shedding rate of D onto P_H ($CFUs \cdot cm^{-2} \cdot individuals^{-1} \cdot days^{-1}$)	0.0867	[56,59]
ρ_{DL}	Shedding rate of D onto P_L ($CFUs \cdot cm^{-2} \cdot individuals^{-1} \cdot days^{-1}$)	0.045	[56,59]
ρ_{DW}	Shedding rate of D onto P_W ($CFUs \cdot cm^{-2} \cdot individuals^{-1} \cdot days^{-1}$)	0.1037	[36,60]
ρ_{HW}	Spore transfer rate between P_H and P_W ($CFUs \cdot cm^{-2} \cdot individuals^{-1} \cdot days^{-1}$)	0.698	[46,56]
ρ_{LW}	Spore transfer rate between P_L and P_W ($CFUs \cdot cm^{-2} \cdot individuals^{-1} \cdot days^{-1}$)	0.204	[46,56]
η	HCW hand hygiene decontamination rate ($days^{-1}$)	6.102	[11,39,61]
ℓ	Shift-end decontamination rate ($days^{-1}$)	1	[62]
K_F	Half-saturation constant for surfaces ($CFUS \cdot cm^{-2}$)	2.78	[63]
K_W	Half-saturation constant for HCWs hands ($CFUS \cdot cm^{-2}$)	1.39	[63]

2.1. Parameter estimation

While the transmission rate of *C. difficile* is well established in hospital settings [25], the variable conditions in LTCFs and the sparsity of associated literature make the transmission rate more challenging to determine. As such, we estimated β, the colonization rate upon transfer of spores, using the method of ordinary least squares (OLS) and data from the Centers for Disease Control and Prevention (CDC). Furthermore, although we were able to find some literature on a potential disease rate φ [44], the information failed to fit our model and reproduce values that reflected real-world incidence rates. As such, we also included φ in our OLS estimation. The method of OLS involves fitting the model to a dataset of interest by comparing model output at each time step to observed data and minimizing the error between the two by using the squared residuals. Assume j indexes the values in the dataset so that $j = \{1, 2, \ldots, n\}$, where n is the sample size. In practice, if $x(t_j; \theta)$ is the model output at time t_j under parameter set θ, and y_j is the corresponding value from the dataset, OLS minimizes the sum of $[y_j - x(t_j; \theta)]^2$ for each j. In particular, OLS finds the optimal parameter combination $\hat{\theta}_{OLS}$ by solving

$$\hat{\theta}_{OLS} = \text{argmin}_{\theta \in \Theta} \sum_{j=1}^{n} [y_j - x(t_j; \theta)]^2,$$

where the parameter set θ is constrained by a reasonable region defined by Θ. Refer to Brauer et al. [64] for more detailed information on the method.

For our parameter estimation, we utilized data from the CDC that details CDI incidence in eight geographic areas across the United States as part of the Emerging Infections Program (EIP) [65, 66]. From 2011 to 2022, the total number of LTCF-onset *C. difficile* incidence cases across all eight areas was recorded monthly. An incident CDI case was counted when a person at least one year old had a positive stool test (toxin or molecular assay) and had not tested positive in the previous eight weeks. Cases were identified through active, population-based surveillance of clinical laboratories, which reported results directly to EIP staff. To ensure complete reporting, laboratories were regularly audited. The dataset also included a total population count across all regions stratified by age group. Considering the typical LTCF age demographic, we only considered those individuals older than 65. Due to the data constraints and the magnitude of the model, we scaled the incidence cases to match an average-sized LTCF of roughly 39 beds [33], which we rounded to 40 residents.

Using available World Health Organization data between the years 2011 to 2022, we calculated the average percent of individuals in LTCFs to be 2.475% of all those 65 and older [67]. With this percentage, we approximated the population of individuals in long-term care in this study by multiplying the CDC-provided older than 65 population by 2.475%. This allowed us to convert monthly observed CDI across the study to expected incidence of CDI in a 40-person LTCF each month. Due to the substantial decrease in cases of *C. difficile* in LTCFs over the years 2011 to 2022, we fit our model's predicted diseased values to the incidence of cases each month in 2022. The large variability in incidence between years necessitates a different transmission rate β each year for the best accuracy.

To obtain disease incidence as representative of the CDC data, we estimated both the transmission rate β and the disease rate of colonized residents φ. We completed our analysis in MATLAB using the `fmincon` function in the Optimization Toolbox with the sequential quadratic programming (SQP) algorithm. SQP is a notably effective method for solving nonlinearly constrained optimization prob-

lems iteratively [68]. With the use of `fmincon` through SQP, we are able to obtain the minimum of a nonlinear multivariable function subject to constraints (linear or nonlinear). MATLAB permits the estimation of multiple parameters simultaneously, but as is the case with most local optimizers, it is very sensitive to the values of initial conditions as it can fail to escape a local minimum instead of achieving a global minimum. In order to find the true minimum, we tested over 40 combinations of β and φ initial guesses, varying β from 0.005 to 0.01 in increments of 0.0025 and φ from 0.001 to 0.004 in increments of 0.0015. These bounds were chosen as they captured the range of plausible values for both β and φ based on CDC data (i.e., values that would allow our model to emulate the scaled monthly incidence as closely as possible). Due to the inconsistent shape of the data, our goal was to find parameters that provided the best average fit across an entire year. Across all of the values of β and φ generated by testing different initial conditions, only one combination of β and φ led to a steady state. Hence, we chose values $\beta = 0.0081$ and $\varphi = 0.0021$ as baseline for our model.

2.2. Incidence rates

With these estimated parameters, our model also replicates incidence rates documented in LTCFs. As is common for facility-level rates, we report incidence as the count of diagnosed CDIs per 10,000 *resident-days* (comparable to *patient-days* for hospitals). Donskey [69] reported that asymptomatic cases outnumber symptomatic cases of CDI by 7:1 in LTCFs, a ratio our model reflects for baseline incidence values.

Table 3. Estimated transmission rate β values when varying the antisocialization parameter f, which measures social interaction between residents. The bold row with $f = 0.479$ represents baseline parameter values from Table 2. Incidence is reported per 10,000 resident-days.

Value of f	Value of β	Incidence of C	Incidence of D
0.179	0.0062	9.18	1.29
0.229	0.0065	9.37	1.31
0.279	0.0068	9.47	1.32
0.329	0.0071	9.48	1.32
0.379	0.0074	9.39	1.31
0.429	0.0077	9.20	1.29
0.479	**0.0081**	**9.23**	**1.29**
0.529	0.0086	9.43	1.31
0.579	0.0091	9.48	1.32
0.629	0.0096	9.36	1.31
0.679	0.0102	9.34	1.30
0.729	0.0109	9.36	1.31
0.779	0.0117	9.38	1.31

Since the socialization of residents in an LTCF varies greatly among facilities, we also explored the impact of our antisocial parameter f on transmission rate β and resulting incidence rates. Table 3 shows the different estimated β values when the antisocialization parameter f is varied; note that the

disease rate φ was held constant at $\varphi = 0.0021$ for this analysis. We observed that the incidence of diseased individuals remained fairly consistent across all runs as both f and β were simultaneously varied. There was a slight increase in the incidence of colonized residents as β increased, but the incidence of diseased for each f value was within 0.03 individuals per 10,000 resident-days. This analysis provided a range of β values for different levels of socialization that produce incidence that still replicates the CDC data and a 7:1 ratio of asymptomatic to symptomatic individuals. As results shifted minimally throughout testing, we moved forward in our model simulations with our baseline value of f listed in Table 2.

2.3. Sensitivity analysis

To assess which parameters in our model cause significant changes in the incidence of colonized and diseased residents, we conducted a global sensitivity analysis following the procedure outlined in Marino et al. [70]. First, we used Latin hypercube sampling to select a random set of parameter values from a uniformly distributed sample range. We then measured the strength of the association between parameters and outputs with partial rank correlation coefficients (PRCCs). PRCC values range from -1 to $+1$, with a PRCC value close to -1 representing a strong negative correlation between that parameter and the associated output, and a value close to $+1$ indicating a strong positive correlation. PRCC values near 0 indicate little to no correlation.

We observed how varying the parameters affected six main outputs related to incidence by including all possible routes of colonization and infection incorporated in the model. Specifically, we considered the incidence of residents through the following pathways:

1) Colonized due to contact with surfaces in high-traffic areas,
2) Colonized due to contact with surfaces in low-traffic areas,
3) Colonized due to contact with contaminated hands of HCWs,
4) Colonized from interaction with colonized residents,
5) Colonized from interaction with diseased residents, and
6) Diseased (symptomatic).

In order to appropriately interpret the PRCC values, the relationship between the sampled parameter values and the corresponding output must be monotonic. Unless otherwise noted, our parameters were sampled from a range of 50% below to 50% above the baseline values given in Table 2. Parameters that were non-monotonic across this range either required sampling from a smaller range or omission from analysis. In particular, ω, α, ρ_{LW}, and σ necessitated restricted sampling ranges due to non-monotonicity with respect to incidence of colonizations due to other residents (both C and D). Similarly, due to non-monotonocity with respect to the incidence of colonizations due to HCWs, we also restricted the sampling range for φ. The adjusted sampling bounds for these parameters along with their descriptions are provided in Table 4. Additionally, the parameters K_F (the half-saturation constant for high- and low-traffic areas) and ρ_{HW} (spore transfer between high-traffic areas and HCW hands) were non-monotonic with respect to the incidence of colonizations due to interactions with colonized residents, and were removed from analysis. Asterisks in Table 5 indicate that the parameters

were removed from analysis due to non-monotonicity with respect to that incidence. Lastly, note that the admission parameters a_S and a_C were not included in the analysis as they are proportions that must sum to one.

Table 4. Adjusted ranges for select parameters to achieve monotonicity with respect to desired outputs.

Parameter	Description	Lower bound	Upper bound
σ	Proportion of P_H and P_L spores removed by disinfecting	0.1319	0.5069
ω	Weighting constant for interactions with P_H	1.2131	2.6660
ρ_{LW}	Spore transfer rate between P_L and P_W	0.1164	0.2916
α	Recovery rate for C	0.0084	0.0173
φ	Disease rate with insufficient immune response	0.0015	0.0027

We conducted our sensitivity analysis with 2000 distinct parameter sets. Each PRCC value is coupled with a p-value; p-values less than 0.05 indicate that the associated PRCC value is significant. Significant PRCC values are provided in Table 5. Blank cells indicate that a parameter was not found to be significant with respect to that output.

As expected, the colonization rate β has a high positive PRCC value across all incidence types, meaning that as its value increases, so do the incidences in all six pathways. The disease rate for individuals with an insufficient immune response φ has negative PRCC values for the incidence of colonizations due to all pathogen-carrying classes, but has high, positive PRCCs for incidence of colonizations due to interactions with other residents (both C and D). Since φ is the rate at which asymptomatic infections become symptomatic, the large impact it has upon colonized and diseased interactions is sensible. The rate of isolation ψ has no significance with respect to incidence of colonizations due to the pathogen-carrying classes, but has high negative PRCCs in the incidence of colonizations due to other residents (both C and D). This highlights the fact that isolation of infected residents primarily reduces the transfer of spores between individuals.

The spores removed due to disinfecting σ has a negative PRCC value with respect to incidence of colonizations due to all pathogen-carrying classes as well as the incidence of diseased. However, the PRCC value for σ is not significant with respect to the incidence of colonizations due to other colonized residents and has a small positive PRCC value with respect to incidence of colonizations due to other diseased residents. This is likely the case because the spore shedding rate from diseased individuals is so large that increased disinfection is not as impactful. It is also important to note that the additional cleaning of high-traffic areas μ is not as impactful here.

The weighting constant on interaction with colonized individuals ε is only significant for the incidence of colonizations due to the pathogen-carrying classes. In contrast, the weighting constant on interactions with diseased individuals θ is only significant with respect to the incidence of colonizations due to other residents (both C and D). The weighting constants for both high-traffic areas ω and for HCW hands τ have positive PRCC values with respect to incidence of colonizations due to all pathogen-carrying classes, but they have negative values for the incidence of colonizations due to other residents (both C and D).

Table 5. Significant PRCC values across six incidence rates. Blank cells indicate that a parameter was not found to be significant with respect to that output. Asterisks indicate that the parameters were removed from analysis due to non-monotonicity with respect to that incidence.

Parameter	Incidence of C due to P_H	Incidence of C due to P_L	Incidence of C due to P_W	Incidence of C due to C	Incidence of C due to D	Incidence of D
λ	–	–	–	0.050	0.049	–
α	−0.608	−0.574	−0.563	–	0.123	−0.567
β	0.740	0.737	0.723	0.862	0.859	0.722
ε	0.165	0.175	0.126	–	–	0.148
θ	–	–	–	0.875	0.870	–
ω	0.320	0.247	0.282	−0.054	−0.054	0.284
τ	0.245	0.177	0.197	−0.052	−0.083	0.172
μ	−0.210	−0.163	−0.181	–	–	−0.151
f	−0.149	−0.151	−0.150	−0.844	−0.840	−0.149
n	–	–	–	−0.055	–	–
φ	−0.149	−0.113	−0.141	0.867	0.865	−0.131
ψ	–	–	–	−0.828	−0.829	–
σ	−0.914	−0.909	−0.901	–	0.054	−0.905
z_H	−0.086	−0.060	−0.104	–	–	−0.047
z_L	−0.051	−0.068	–	–	−0.056	−0.063
z_W	–	−0.078	−0.049	–	–	–
ρ_{CL}	–	–	–	–	−0.058	–
ρ_{CW}	0.416	0.409	0.371	–	–	0.366
ρ_{DH}	0.052	–	0.055	–	–	–
ρ_{DL}	–	0.060	–	–	–	0.060
ρ_{DW}	0.703	0.692	0.674	–	–	0.687
ρ_{HW}	0.818	0.800	0.797	*	*	0.801
ρ_{LW}	0.289	0.272	0.253	–	–	0.234
η	−0.849	−0.843	−0.834	–	–	−0.832
ℓ	−0.267	−0.219	−0.252	–	–	−0.221
K_F	−0.162	−0.144	−0.131	*	*	−0.116
K_W	−0.110	−0.128	−0.090	–	–	−0.087

The HCW handwashing decontamination rate η has high negative PRCC values for the incidence of colonizations due to all pathogen-carrying classes. Given the frequency of contact between HCWs and residents, these results indicate that an increase in handwashing is particularly effective at limiting spore shed from HCW hands and thereby limiting the transmission of *C. difficile*. Note that the parameter ρ_{HW}, which represents HCW contact with high-traffic areas, was found to be more impactful than ρ_{LW}, which represents HCW contact with low-traffic areas, likely due to the higher number of interactions of residents with high-traffic areas. Spore shed from diseased residents onto HCWs, ρ_{DW}, has larger PRCC values than spore shed from colonized residents onto HCWs, from colonized residents onto low-traffic areas, from diseased residents onto low-traffic areas, and from diseased residents onto high-traffic areas (ρ_{CW}, ρ_{CL},ρ_{DL}, and ρ_{DH}, respectively). This further suggests that spores shed onto HCWs are particularly important for limiting transmission of *C. difficile*.

To determine which of the significant parameters are most influential on each incidence pathway, we used pairwise Z-tests to compare PRCC values in order to assess if two PRCC values were significantly different from one another. We then formed an ordered ranking from these Z-tests in Tables 6 and 7. If a parameter is listed under the side of + PRCC, this indicates a positive correlation, and if placed under − PRCC, a negative correlation. Parameter values placed on the same line had PRCC

values that were not significantly different from one another.

According to the pairwise Z-test, the top five most significant PRCC values across incidence of colonizations due to our pathogen-carrying classes (P_H, P_L, and P_W), as well as the incidence of diseased, were the spores removed due to disinfecting σ, the handwashing decontamination rate η, the spore transfer rate between high-traffic areas and HCWs ρ_{HW}, the colonization rate upon transfer of spores from a surface β, the shedding rate of diseased residents onto HCWs ρ_{DW}, and the recovery rate for asymptomatically colonized residents α.

Table 6. Pairwise Z-test rankings of a parameter's PRCC value listed from most significant to least significant for incidences of colonization due to the three pathogen-carrying classes: P_H, P_L, and P_W.

Incidence of C due to P_H		Incidence of C due to P_L		Incidence of C due to P_W	
+ PRCC	− PRCC	+ PRCC	− PRCC	+ PRCC	− PRCC
	σ		σ		σ
	η		η		η
ρ_{HW}		ρ_{HW}		ρ_{HW}	
β, ρ_{DW}		β, ρ_{DW}		β, ρ_{DW}	
	α		α		α
ρ_{CW}		ρ_{CW}		ρ_{CW}	
ρ_{LW}, ω	ℓ	ρ_{LW}, ω	ℓ	ρ_{LW}, ω	ℓ
$\varepsilon, \theta, \rho_{DL}, \tau$	$f, \mu, \varphi, K_F, K_W, z_H, z_L$	$\varepsilon, \rho_{DL}, \tau$	$f, \mu, \varphi, K_F, K_W, z_W, z_H, z_L$	ε, τ	$f, \mu, \varphi, K_F, K_W, z_H, z_W$

Table 7. Pairwise Z-test rankings of a parameter's PRCC value listed from most significant to least significant for incidences of colonization due to colonized residents C or diseased residents D, as well as incidence of diseased.

Incidence of C due to C		Incidence of C due to D		Incidence of D	
+ PRCC	− PRCC	+ PRCC	− PRCC	+ PRCC	− PRCC
θ, φ, β		θ, φ, β		ρ_{HW}	σ
	f, ψ		f, ψ	β, ρ_{DW}	η
λ	n, ω, τ	α, σ, λ	$\tau, \rho_{CL}, z_L, \omega$	ρ_{CW}	α
				ω, ρ_{LW}, τ	$\mu, K_W, z_H, K_F, \varphi, z_L$
				$\varepsilon, \rho_{DL}, \theta$	$f, \mu, \varphi, K_F, K_W, z_H, z_L$

The parameter ranking with respect to incidence of colonizations due to other residents (both C and D) differs substantially from the incidence of colonization from the pathogen-carrying classes and the incidence of diseased, as shown in Table 7. In order, the most impactful parameters in this case were the weighting constant for interactions with diseased individuals θ, the disease rate of individuals with insufficient immune response φ, the colonization rate β, the proportion of time residents are socially inactive f, and the isolation rate ψ.

The pairwise Z-test emphasizes how the significant parameters for the pathogen-carrying and interactive classes differ greatly. In the pathogen-carrying classes, σ, η, the HCW-related parameters, and α have the greatest impact on incidence. However, θ, φ, f, and ψ have the greatest impact with respect to incidence from interactions with other residents. The colonization rate β remains significant for all classes, and significant parameters in incidence of diseased exhibit the most similarity to the pathogen-carrying classes. These results are consistent with our expectations and suggest that the

impact of different vectors of transmission varies depending upon the setting.

3. Results

The numerical solution to our system with the baseline parameters provided in Table 2 and initial conditions of $S_0 = 36$, $C_0 = 4$, $D_0 = 0$, $Q_0 = 0$, and $P_{H0} = P_{L0} = P_{W0} = 0.01$ is plotted in Figure 2 with corresponding incidence rates, measured per 10,000 resident-days, provided in Table 8. Observe that the values of all four resident and three pathogen-carrying classes quickly approach a steady state. This suggests a possible equilibrium under this parameter regime with constant low levels of transmission and contamination.* We see that initial conditions for the susceptible and colonized classes are very close to the equilibrium values, so the slope of the curve is almost 0. The diseased and isolated classes approach steady-state values of approximately 0.07 and 0.11 individuals, respectively, whereas the pathogen-carrying classes approach $P_H = 0.04$, $P_L = 0.07$, and $P_W = 0.03$ $CFUs \cdot cm^2$.

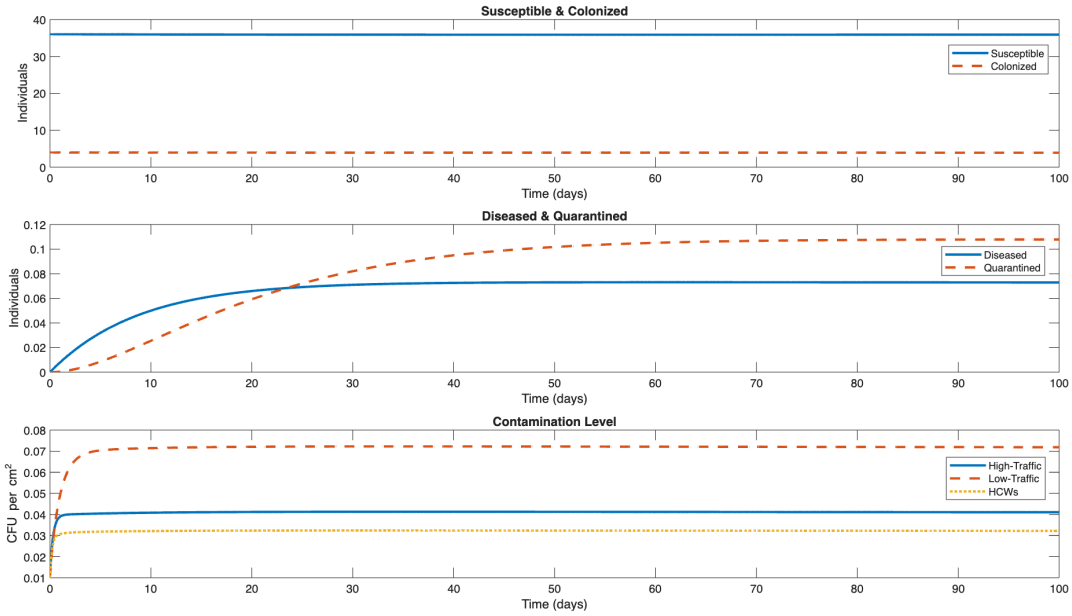

Figure 2. Baseline simulation for ODE model over 100 days. Low levels of transmission are present and all values quickly reach steady states of approximately $S = 35.89$, $C = 3.94$, $D = 0.07$, $Q = 0.11$, $P_H = 0.04$, $P_L = 0.07$, and $P_W = 0.03$.

The baseline incidence values in Table 8 replicated the approximate 7:1 ratio of colonized to diseased residents in LTCFs [69] as previously discussed. The model suggests that interaction with asymptomatic individuals and interaction with HCWs are the two largest contributors to the incidence of colonization. High-traffic areas contributed to roughly 1.5% more cases than low-traffic areas despite being cleaned more frequently; this is likely due to the increased volume of residents in high-traffic areas.

*We attempted to derive a closed-form equilibrium; however, the model's inherent complexity rendered such a solution infeasible.

Table 8. Baseline incidence results per 10,000 *resident-days* with parameters from Table 2.

	Baseline
Incidence of C	9.23
due to high-traffic areas	1.29 (13.98%)
due to low-traffic areas	1.15 (12.46%)
due to HCWs	1.93 (20.91%)
due to colonized interaction	4.52 (48.97%)
due to diseased interaction	0.35 (3.79%)
Incidence of D	1.29

3.1. Mitigation strategies

To assess the most effectual mitigation strategies, we considered 14 different scenarios by increasing and/or decreasing corresponding parameters to determine their effect on the six incidence pathways. Due to their high ranking in the sensitivity analysis results and their relevance to policy modifications in LTCFs, we considered the handwashing decontamination rate η, the proportion of time residents were socially inactive f, the ratio of HCWs to residents n, the weighting constant for increased cleaning of high-traffic areas μ, and the proportion of P_H and P_L spores removed by disinfection σ for mitigation strategies.

3.1.1. Hand hygiene of HCWs

We first considered the effect of the decontamination rate of HCWs η. This parameter was calculated using the hand hygiene compliance rate, the proportion of soap and water use versus the use of ABHRs, and the proportion of spores removed for each method. In particular, we estimated effective hand hygiene by multiplying nursing home hand hygiene compliance with the average number of daily handwashes [61]. To distinguish between soap and water versus ABHR use, we weighted each by its observed proportion of handwashes and corresponding spore removal efficacy [11] and then summed the contributions. A more detailed explanation of our calculations can be found in Supplementary Materials A. The distinction between ABHR and soap/water use is crucial as the proportion of spores removed by these methods differs drastically, with ABHR only eliminating 20% of spores, while soap and water effectively remove 90% [11]. As such, in order to quantify the impact of hand hygiene, there are two considerations:

1) **100% soap and water use:** Since soap and water is more effective in removing *C. difficile* spores than ABHRs, one strategy would be to remove the option of ABHRs and replace it with 100% soap and water use in the calculation for η. As shown in Table 9, removing ABHR use entirely from hand hygiene reduced the incidence of colonizations by roughly 31.64% from baseline. The impact of HCWs on colonization was also substantially reduced, contributing the least out of all the pathogen-carrying classes. At baseline, HCWs accounted for roughly 20.91% of incidence of colonizations while in all soap usage, only 8.56% was traced back to HCWs.

2) **Increased compliance:** Another strategy would be to consider increasing compliance levels of hand hygiene from the baseline 17%. Compliance in this context refers to the extent to which HCWs follow recommended guidelines, protocols, or policies when it comes to hand hygiene

compliance. Simply increasing compliance by 50% had less of an impact compared to the previous scenario, reducing the incidence of colonizations from 9.23 at baseline to 7.80, which showcased a 15.49% decrease. While the reduction is only about half of that seen for all soap usage, the percentage of total incidence of colonizations from HCW contributions also decreased from 20.91% to 15.77%. It is important to note that while HCWs contribute less compared to baseline, it remains the largest pathogen-carrying source for incidence of colonizations in this scenario.

Table 9. Incidence of HCW handwashing mitigation strategies compared to baseline incidence (measured in 10,000 *resident-days*).

	Baseline	All soap usage	Increased compliance
Incidence of C	9.23	6.31	7.80
due to high-traffic areas	1.29 (13.98%)	1.01	1.15
due to low-traffic areas	1.15 (12.46%)	0.90	1.03
due to HCW hands	1.93 (20.91%)	0.54	1.23
due to colonized interaction	4.52 (48.97%)	3.58	4.07
due to diseased interaction	0.35 (3.79%)	0.28	0.31
Incidence of D	1.29	1.00	1.15

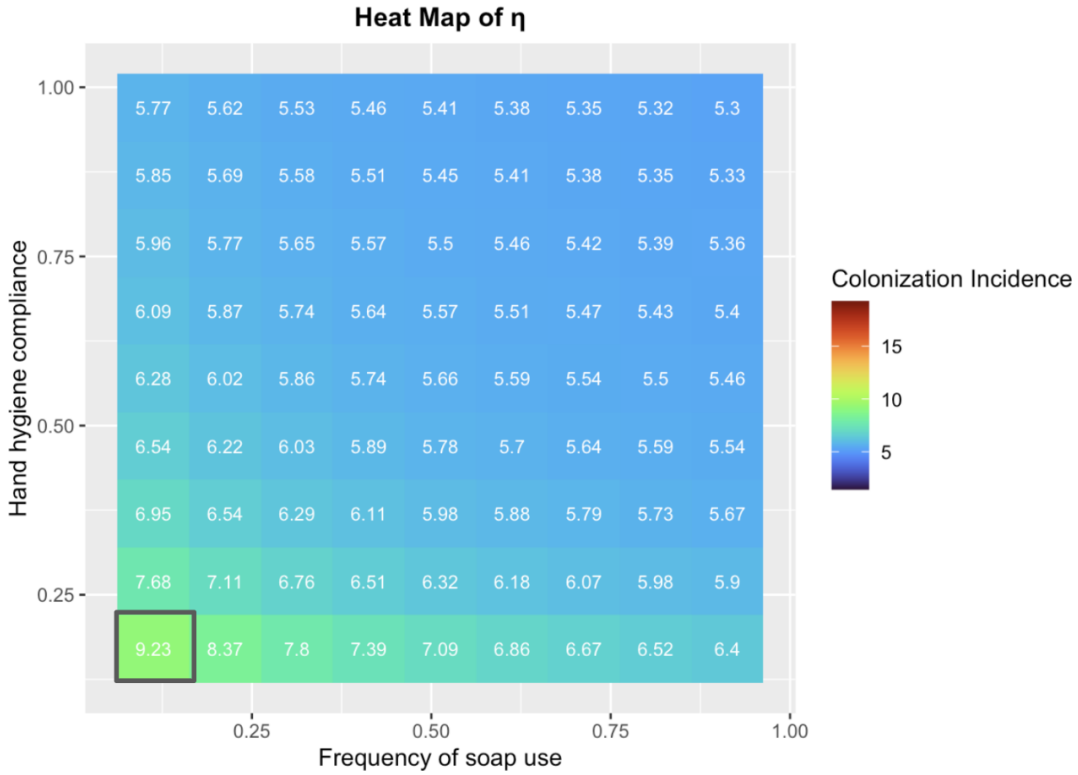

Figure 3. Heat map showcasing the relationship between soap and water use by HCWs and HCW hand hygiene compliance, with the corresponding incidence of colonization (measured in 10,000 resident-days) on each square. The bottom left-hand corner represents baseline.

Both scenarios illustrate the positive impact of HCW hand hygiene on reducing the incidence of colonized and diseased residents in LTCFs, but to further understand the impact of η on colonizations, we simultaneously varied the percentage of compliance and the proportion of soap and water use for hand hygiene while tracking incidence to determine which has the greater impact on reducing incidence. The results are illustrated in the heat map shown in Figure 3, where the bottom left-hand corner represents baseline. Warmer values indicate higher incidence of colonization. As expected, a combination of higher compliance overall and soap and water use were associated with lower incidence of colonization. We see 97% compliance and 91.28% of handwashing using soap and water reduce cases to roughly 5.3 colonized individuals per 10,000 resident-days compared to a baseline of 9.23, a reduction of 42.58%. While Table 9 indicates that 100% soap usage causes a greater reduction in the incidence of colonizations than only a 50% increase in overall compliance, the heat map shows that, in general, increased hand hygiene compliance has a greater impact than higher frequency of soap and water use. This conclusion suggests that simply increasing the frequency of decontamination may be more beneficial than focusing on the method of decontamination.

3.1.2. Length of HCW shifts

In addition to improving hand hygiene of HCWs, we can also consider the impact of the shift-end decontamination by HCWs ℓ. Details about the calculation of ℓ can be found in Appendix A. An increased value of ℓ corresponds to more frequent shift changes and, thereby, increased decontamination. Resulting incidence per 10,000 resident-days for increased and decreased ℓ by 50% are given in Table 10. As expected, increasing shift-end decontamination decreases the incidence of both colonizations and infections. Examining the parameter ℓ, we observe that increasing the length of HCW shifts (decreasing ℓ) has a greater impact upon incidence than decreasing the length of shifts (increasing ℓ). Generally, alterations to the shift length of HCWs does not impact incidence as greatly as improving HCW hand hygiene compliance (discussed in Table 9).

Table 10. Incidence results for shift-end decontamination for HCWs.

	Baseline	Increased ℓ	Decreased ℓ
Incidence of C	9.23	8.91	9.62
due to high-traffic areas	1.29 (13.98%)	1.26	1.32
due to low-traffic areas	1.15 (12.46%)	1.12	1.18
due to HCW hands	1.93 (20.91%)	1.77	2.12
due to colonized interaction	4.52 (48.97%)	4.42	4.64
due to diseased interaction	0.35 (3.79%)	0.33	0.36
Incidence of D	1.29	1.26	1.33

3.1.3. Disinfection of environment

C. difficile often spreads through contact with inactive spores on surfaces, and the risk of contraction in LTCFs is heightened due to their interactive, communal nature, where residents and HCWs come in continued contact in shared spaces. Environmental contribution to incidence cases is represented by the environmental reservoir classes P_H and P_L in our model. As a mitigation strategy, we vary the proportion of spores in both high- and low-traffic areas removed by disinfection σ. To bet-

ter quantify its impact, we increased and decreased the values separately by 50%, with corresponding results presented in Table 11.

1) **Increased σ by 50%:** Increasing the proportion of spores in both high- and low-traffic areas removed by disinfecting had a small impact on decreasing the total colonization incidence, reducing the number of colonizations per 10,000 resident-days by 10.51%. As expected, increasing σ decreased the contribution of both high- and low-traffic areas on the incidence of colonizations. In this scenario, low-traffic areas contributed to 11.02% of the total incidence of colonizations compared to 12.46% at baseline, while high-traffic areas were responsible for 12.71% compared to 13.98% at baseline.

2) **Decreased σ by 50%:** As expected, decreasing σ increases the incidence of colonizations to 10.75 per 10,000 resident-days, a 16.47% increase from baseline. The change increased the contribution of high- and low-traffic areas to 15.35% and 14.42%, respectively. It is worthwhile to note that decreasing the disinfection rate has a greater impact on incidence than increasing it.

Table 11. Incidence results for spore removal from disinfection.

	Baseline	Increased σ	Decreased σ
Incidence of C	9.23	8.26	10.75
due to high-traffic areas	1.29 (13.98%)	1.05	1.65
due to low-traffic areas	1.15 (12.46%)	0.91	1.55
due to HCW hands	1.93 (20.91%)	1.76	2.19
due to colonized interaction	4.52 (48.97%)	4.22	4.98
due to diseased interaction	0.35 (3.79%)	0.32	0.38
Incidence of D	1.29	1.20	1.44

Another parameter of interest in relation to environmental contamination is the weighting constant for increased cleaning of high-traffic areas μ. As can be seen across cases, high-traffic areas contribute more to incidence of colonizations than low-traffic areas at baseline. Similarly to σ, we increased and decreased the baseline value of μ by 50% to explore its impact on incidence of colonizations (Table 12):

1) **Increased μ by 50%:** Increasing the weighting constant for cleaning of high-traffic areas results in a 5.2% decrease in the incidence of colonizations from 9.23 at baseline to 8.75 colonizations per 10,000 resident-days. While this value is smaller than the percentage decrease seen with σ, there was a 15.50% decrease in incidence due to high-traffic areas, which was the largest decrease out of all the sources. This result matches our expectations for this weighting constant, as a larger value for μ involves more cleaning of high-traffic areas. On the other hand, while colonizations in low-traffic areas only decreased by 3.48%, they still accounted for 11.02% of incidence of colonizations compared to 12.45% at baseline. The slight increase in value from 1.11 to 1.20 is likely due to reduced contribution from high-traffic areas. The other sub-incidences of colonizations experienced a decrease roughly between 2.86% and 4.66%. Interactions with colonized individuals still remained the largest source for incidence of colonizations.

2) **Decreased μ by 50%:** As expected, decreasing the weighting constant for increased cleaning of

high-traffic areas resulted in an increase in incidence of colonizations by 7.37%. Note that this had a larger impact than increasing μ by 50%. Furthermore, the incidence of colonizations from high-traffic areas increased by almost 21%, accounting for roughly 15.74% of the total incidence of colonizations. The incidence of colonizations increased across all *C. difficile* sources. While the incidence from HCW hands increased by 6.74%, this contributed to 20.79% of incidence of colonizations compared to 20.91% at baseline, keeping the distribution relatively the same. Incidence of colonizations from interactions with colonized individuals experienced a slight decrease, as it accounted for 47.73% of the total incidence as compared to 48.97% at baseline. Lastly, the incidence of infections increased by the 5.43%, a larger impact than when increasing μ.

Table 12. Incidence results for high-traffic areas P_H with varying weighting constant for cleaning.

	Baseline	Increased μ	Decreased μ
Incidence of *C*	9.23	8.75	9.91
due to high-traffic areas	1.29 (13.98%)	1.09	1.56
due to low-traffic areas	1.15 (12.46%)	1.11	1.20
due to HCW hands	1.93 (20.91%)	1.84	2.06
due to colonized interaction	4.52 (48.97%)	4.37	4.73
due to diseased interaction	0.35 (3.79%)	0.34	0.36
Incidence of *D*	1.29	1.24	1.36

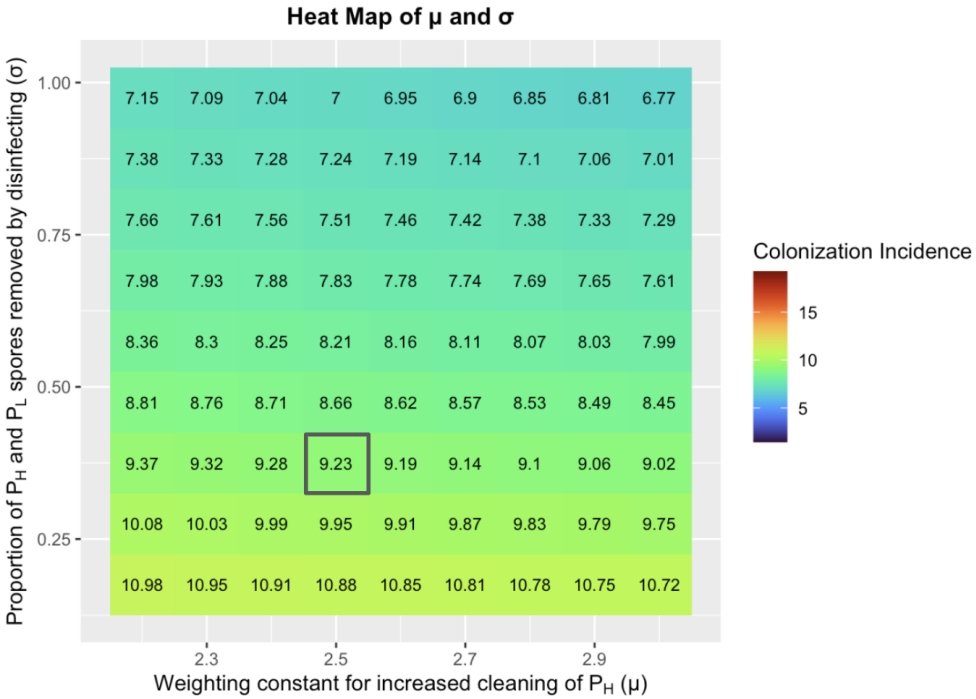

Figure 4. Heat map showcasing the relationship between the weighting constant for increased cleaning of high-traffic areas P_H (μ) and the proportion of P_H and P_L spores removed by disinfecting (σ), with the corresponding incidence of colonization (measured in 10,000 resident-days) on each square. The gray box indicates baseline.

To further explore the environmental contribution on the incidence of colonization, we also simultaneously altered values of σ (the proportion of environmental spores removed by disinfection) and μ (the weighting constant for increased cleaning of high-traffic areas) to better quantify the relationship between these two parameters. The results are showcased in the heat map in Figure 4. The baseline incidence of colonizations is marked with the gray box. Both σ and μ were increased and decreased by 0.10 from their baseline values. Lighter colors of green indicate an increased incidence of colonization. In general, increasing σ and μ decreased the incidence, matching our previous finding when incrementing these parameters by 50% separately. However, it can be seen that increasing σ has a larger impact on reducing the incidence of colonization as seen with the clear gradient along the columns, with μ decreasing incidence more gradually.

3.1.4. Admission proportions

The first parameter we explored related to resident classes was the admission proportion into the colonized class a_C. Individuals can enter from the community or hospital settings and subsequently carry *C. difficile* into the LTCF. As previously discussed, our model assumes only admission into either the susceptible or colonized classes, as individuals symptomatic with *C. difficile* will likely remain in the hospital and not be admitted into an LTCF. Observe that whenever a_C is increased, a_S must decrease correspondingly and vice versa since they must sum to one. The resulting incidences for the scenarios below are detailed in Table 13.

1) **Increased a_C by 50%:** Increasing the number of residents entering as colonized subsequently increased the incidence of colonizations to 9.99 per 10,000 resident-days compared to 9.23 at baseline (an 8.23% increase). The admission proportion of those entering the LTCF as colonized a_C had little impact on the distribution of colonizations from various transmission pathways.

2) **Decreased a_C by 50%:** Decreasing the admission rate of colonized individuals lowered the incidence of colonizations to 8.43 per 10,000 resident-days, showcasing an 8.67% decrease from baseline. The distribution of the sub-incidences remained relatively similar to that at baseline.

Table 13. Incidence results for changes to admissions rates.

	Baseline	Increased a_C	Decreased a_C
Incidence of *C*	9.23	9.99	8.43
due to high-traffic areas	1.29 (13.98%)	1.40	1.17
due to low-traffic areas	1.15 (12.46%)	1.24	1.05
due to HCWs	1.93 (20.91%)	2.08	1.76
due to colonized interaction	4.52 (48.97%)	4.89	4.13
due to diseased interaction	0.35 (3.79%)	0.37	0.32
Incidence of *D*	1.29	1.35	1.17

3.1.5. Resident isolation

With respect to residents, facilities are able to control their rate of isolation once a resident becomes symptomatic with a CDI, denoted by ψ in our model. We considered the impact of both increasing and decreasing this rate by 50%, with detailed results given in Table 14:

1) **Increased ψ by 50%:** Increasing ψ only decreased the incidence of colonizations by 4.77%, and the distribution of the sources remained relatively similar aside from the incidence of colonizations due to interactions with symptomatic patients. Compared to an incidence of 0.35 per 10,000 resident-days at baseline, increasing ψ reduced the incidence from interaction with infected residents from 3.79% to 2.62%. This decrease in contribution from D is expected since increasing ψ moves symptomatic patients out of the infected class more quickly.

2) **Decreased ψ by 50%:** Decreasing the rate of isolation had a larger impact on the baseline incidence, raising the incidence of colonizations from 9.23 per 10,000 resident-days to 10.52 (an increase of 13.98%). Furthermore, interaction with diseased residents accounts for roughly 6.84% of colonized cases compared to 3.79% at baseline, a substantial difference compared to the previous scenario of increasing ψ.

Table 14. Incidence results for isolation mitigation strategies.

	Baseline	Increased ψ	Decreased ψ
Incidence of C	9.23	8.79	10.52
due to high-traffic areas	1.29 (13.98%)	1.23	1.46
due to low-traffic areas	1.15 (12.46%)	1.10	1.29
due to HCWs	1.93 (20.91%)	1.85	2.16
due to colonized interaction	4.52 (48.97%)	4.39	4.89
due to diseased interaction	0.35 (3.79%)	0.23	0.72
Incidence of D	1.29	1.25	1.42

3.1.6. Resident socialization

The proportion of time residents are socially inactive f was ranked highly in our sensitivity analysis, and this sensitivity is reflected in the incidences resulting from increasing and decreasing f by 50% as shown in Table 15. Increasing f by 50% decreased colonization incidence by 50%, which led us to further explore the impact of socialization in LTCFs. Social and community events are a big point of differentiation in LTCFs when compared to hospital settings. Specifically, we explored the relationship between f and n, the ratio of HCWs to residents. Unlike in Section 2.2, where f and β were both varying, we are holding β constant for analyses presented in this section. Results are illustrated in the heat map in Figure 5 with varying levels of socialization and ratio of HCWs to residents. Similar to the previous heat map analysis, f and n were both incremented by 0.1, but f was also decreased by 0.1 to observe more social communities compared to the baseline. The baseline value is outlined in gray.

From Figure 5, we see across all levels of social activity, a higher proportion of HCWs to residents reduces the incidence of colonizations. More social communities tend to have a higher level of transmission, so they benefit substantially from a higher ratio of HCWs to residents. In particular, an LTCF with the f proportion equal to 0.179 experiences a decrease in colonizations from approximately 19.26 per 10,000 resident-days to 12.29, a reduction of about 36.19%. The clear stratification between each column of Figure 5 suggests that the antisocial level has a strong impact on reducing cases, with $n = 0.145$ experiencing a reduction from 19.26 per 10,000 resident-days to 2.79, an 85.51% decrease.

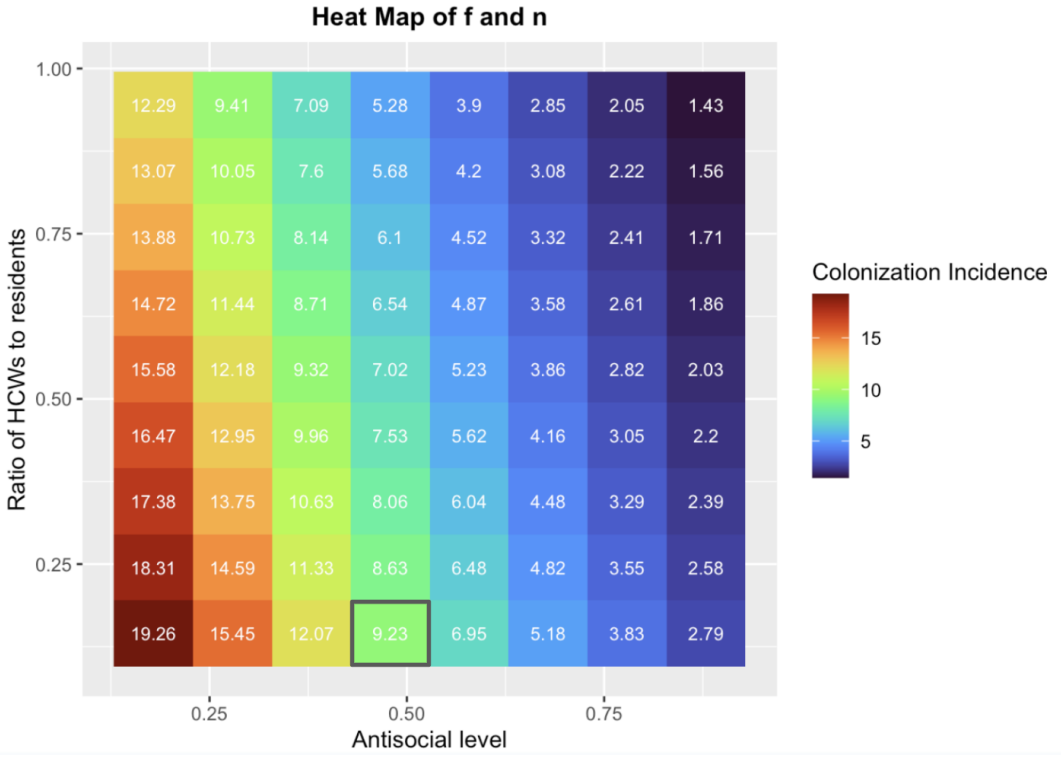

Figure 5. Heat map showcasing the relationship between socialization of residents and ratio of HCWs to residents, with the corresponding incidence of colonization (measured in 10,000 resident-days) on each square. The gray box indicates baseline.

However, we understand that eliminating all social interaction would contradict the nature of these residential communities and instead recommend to consider temporarily reducing the number of interactions, particularly in communal spaces, during severe outbreaks.

Table 15. Incidence results for socialization mitigation strategies.

	Baseline	Increased f	Decreased f
Incidence of C	9.23	4.60	16.91
due to high-traffic areas	1.29 (13.98%)	0.84	1.95
due to low-traffic areas	1.15 (12.46%)	0.75	1.72
due to HCWs	1.93 (20.91%)	1.28	2.82
due to colonized interaction	4.52 (48.97%)	1.61	9.69
due to diseased interaction	0.35 (3.79%)	0.12	0.74
Incidence of D	1.29	0.82	2.05

3.2. Screening of asymptomatic residents

Considering the influence of social behavior on transmission, we also explored the impact of screening residents in order to isolate asymptomatic residents in addition to symptomatic residents. Based on a review of current *C. difficile* screening accuracies, we chose the Toxin EIA A/B test (an

enzyme immunoassay that detects toxins A and B produced by *C. difficile*), as it is low-cost and not labor intensive, detecting *C. difficile* with about 77.5% accuracy. Our baseline value for screening q assumes that screening is completed once per week [71]. We considered the effect of both 100% site-wide screening and randomly sampling five residents. The results are described in Table 16.

Table 16. Incidence results for screening mitigation strategies. Screenings take place weekly.

	Baseline	Sample of 5 tested	100% Site-wide testing
Incidence of C	9.23	7.28	2.30
due to high-traffic areas	1.29 (13.98%)	1.01	0.31
due to low-traffic areas	1.15 (12.46%)	0.90	0.28
due to HCWs	1.93 (20.91%)	1.53	0.48
due to colonized interaction	4.52 (48.97%)	3.57	1.13
due to diseased interaction	0.35 (3.79%)	0.28	0.09
Incidence of D	1.29	1.00	0.31
Incidence of Q	1.24	0.96	0.30

Results indicate that isolating asymptomatically colonized residents has a high impact on overall incidence and all sub-incidence classes. Screening a random sample of five and isolating asymptomatic residents will reduce colonizations by 21.12%, while weekly site-wide screening reduces colonization by 75.08%. Given the high sensitivity of the social inactivity parameter f to transmission as well as the need to provide social community, this strategy could offer a directed way to mitigate *C. difficile* transmission while targeting incidence from resident interaction.

4. Discussion and conclusions

The lack of research on the transmission of *C. difficile* in LTCFs, where there is frequent interaction between residents, HCWs, and the environment, makes it difficult to identify effective strategies that best reduce incidence of colonization and infection within these communities. As such, our model attempts to illustrate the dynamics of transmission by considering the impact of person-to-person transmission as well as contact with the pathogen-carrying classes of high-traffic areas, low-traffic areas, and the contaminated hands of HCWs. While multiple models have extensively described transmission of *C. difficile* in hospital settings, this model is novel due to its application to an LTCF.

Results indicate that, across nearly all scenarios, including baseline, interaction with a colonized, asymptomatic individual accounts for around 50% of incidence cases in LTCFs, regardless of mitigation strategies. The main exceptions are when the proportion of spores in both high- and low-traffic areas removed by disinfecting, the isolation rate, and socialization are decreased, which led to approximately 46.33%, 46.48%, and 35% of colonizations being traced back to interactions with colonized individuals, respectively. Conversely, while interaction with colonized individuals contributed the most to incidence cases, interactions with symptomatic CDI residents contributed the least, accounting for 3.79% of incidence cases. Furthermore, only when the handwashing decontamination rate was recalculated to assume all soap and water usage rather than ABHR, did the contribution of transmission from HCWs drop to 8.56%, which became the smallest out of all the pathogen-carrying reservoirs. Our results indicated that high-traffic areas contribute more to the spread of spores than their low-traffic

counterparts, even when additional cleaning is implemented. The larger contribution of high-traffic areas is consistent with the fact that *C. difficile* spreads through spore transfer on surfaces; higher traffic increases opportunities for interactions with a wider group of residents and for shedding from various individuals. As such, our model reaffirms the necessity of cleaning communal areas, and the findings align with the study by Sulyok and Fox et al. [12], which found high-touch surfaces to contribute more than low-touch surfaces for incidences in hospital settings.

Disinfecting high- and low-traffic areas on a regular basis reduces transmission of *C. difficile*, but we recommend that increased cleaning is accompanied by programs to encourage hand hygiene among HCWs. Our model confirms the importance of various hygiene practices, with an emphasis on increased compliance and frequent disinfection of spaces around the community, particularly low-traffic areas. Increased disinfection and shift-end decontamination for HCWs both had an impact in reducing the incidence, but these changes were much smaller in magnitude compared to compliance. We recommend LTCFs introduce programs for HCWs to encourage more hand hygiene compliance, along with promoting the use of soap and water instead of ABHR, ideally focusing on the former if the conditions prevent an LTCF from pursuing both suggestions simultaneously. These programs may involve reviewing standard protocols and implementing more hand decontamination stations around the facility to increase convenience.

While smaller in impact compared to the other scenarios, we still recommend LTCFs implement *C. difficile* testing upon admission to reduce the number of colonized individuals entering the system. Decreasing admission rates in the colonized class, which would involve more frequent testing and faster turn around for *C. difficile* tests, reduced incidence of colonizations by roughly 8.79%. Given the difference in impact between incrementing and reducing isolation rates, we strongly advise LTCFs to avoid reducing testing for *C. difficile* to determine isolation status. Rather, it would be more beneficial to keep a consistent rate or, if possible, test routinely and opt for a test that has a faster turn-around rate. A higher ratio of HCWs to residents also decreased incidence of colonizations. As such, we recommend LTCFs increase the number of employed HCWs when possible to reduce their workloads. Socialization level had the strongest impact on incidence cases, resulting in extreme swings in colonization incidence between increasing and decreasing the antisocialization parameter in our model. Finally, though screening for colonized individuals was not part of our original model parameters, the results of randomly sampling for colonized individuals as well as site-wide testing provide promising results, resulting in large reductions of colonizations.

As with any mathematical model, various assumptions and generalization were made, and the subsequent results may be sensitive to these decisions. It is important to note that the current model remains incomplete in reflecting all possible interactions and possible vectors of *C. difficile* in LTCFs. In particular, while the model includes HCWs, it does not consider the impact of visitors frequenting these spaces. Furthermore, due to the lack of literature on *C. difficile* in LTCFs, some parameters required the use of hospital estimates in combination with LTCF values; these included pickup rates (z_H, z_L, z_W), shedding rates ($\rho_{DH}, \rho_{CH}, \rho_{DL}, \rho_{CL}, \rho_{DW}, \rho_{CW}$), isolation rate ($\psi$), and weighting constants (ε, τ, ω). Additionally, as more data becomes available, relaxing the simplifying assumption that spore transfer occurs strictly in proportion to prior surface density may allow the model to better capture the mechanisms of surface contamination and interactions.

The accuracy of our parameter estimation was inhibited by the level of granularity in the data we used. As the dataset provided month-by-month totals across the group of facilities, we had to convert the data to include daily totals and scale the data down to model a single 40-person facility based on an estimated total population in LTCFs. Furthermore, as information about the facilities included in the dataset was not available, we generalized socialization levels to better replicate real world interactions. Having access to more granular data that records incidence of *C. difficile* at an individual facility level would allow for more accurate transmission models. Generally, the presence of studies that examine more closely the frequency, duration, and types of interactions within LTCFs would be immensely beneficial. Information regarding how often residents spend in different rooms, how many surfaces they come in contact with, and how many other individuals are in the room with them would lead to more accurate parameterization of *C. difficile* models.

If the aforementioned studies were conducted, future work would include updating parameter values to reflect new and potentially more accurate literature. Comparison of this model with an agent-based model would assess the impact of individual behaviors and stochasticity upon models of *C. difficile* transmission. In the future, we aim to expand the number of environmental reservoir classes. This could include separating the HCW class to distinguish workers with varying types of interactions with residents or modeling visitors as another "mobile" reservoir, especially since visitors may come in more close contact for shorter durations. Ultimately, our study stresses the need for more data and studies on *C. difficile* in LTCF settings to better understand the transmission of the bacteria in a dynamic, lively community.

Authors contribution

- Doran, Hayashida, Joyner, and Moberg: Formal analysis, methodology, software, visualization, and writing - original draft, review and editing.
- Hayashida and Moberg: Data curation.
- Kind and Senese: Methodology, software, supervision, writing - review and editing.
- Stephenson and Sulyok: Conceptualization, data curation, funding acquisition, methodology, project administration, resources, supervision, writing - review and editing.

Use of AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

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Conflict of interest

All authors declare no conflicts of interest in this paper.

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Appendix

A. Parameter calculations

A.1. Resident-related parameters

The recovery rate of colonized residents to susceptible residents α was calculated using data from Simor et al. [72], who found that 70% of residents that had isolated *C. difficile* samples continued to carry the bacteria for less than two months, 7% were asymptomatic for three to six months, and 12% continued to carry it for more than six months. In our conservative estimate, we took the upper and lower bounds and averaged the interval to get 4.5 months. Subsequently, we divided the proportion by the number of days with the following equations, $\frac{0.7}{2\cdot 30\ days} + \frac{0.07}{4.5\cdot 30\ days} + \frac{0.12}{6\cdot 30\ days}$, to get $\alpha \approx 0.01285$.

The rate of isolation ψ was estimated using the assumption that the standard requirements before testing an individual for CDI is three or more unformed stools in 24 hours and a positive toxigenic *C. difficile* result [8]. Fridkin et al. [53] determined that 35% of patients in hospitals actually get tested for *C. difficile* if they have diarrhea. The data showed how characteristics such as age can impact the likelihood of someone receiving an actual test for CDI. Then, assuming those tests are submitted as soon as the criteria is met, a preferred cytotoxin test [55] can take one to three days with a sensitivity of 95% and specificity of 90%–95% [54]. Thus, we computed it as the number of days until test result after beginning symptoms multiplied by both the proportion of individuals with diarrhea that get tested

and the sensitivity of the cytotoxin test.

The rate of release from isolation λ was approximated by dividing the proportion of successful treatments, 0.857 [43], by the typical total days for treatment completion, which was calculated by adding the recommended period of ten days and two days post-symptom [1].

The discharge rate for susceptible and colonized populations k was calculated based on the average 20.3 month length of stay in LTCFs [38]. This was converted into a daily discharge rate, accounting for discharge to the community, another facility, hospital, death, or other reason. In calculating the discharge rate for diseased and isolated populations k_D, we instead considered the rate of hospitalization and death for *C. difficile* listed in [42]. Over the course of their study, there were 70 hospitalizations in 425 cases, giving a discharge rate of 0.00045 $days^{-1}$.

The proportion of individuals who are admitted into the colonized class a_C came from [41], where the estimated colonization rate at admission was 0.089. Analogously, the proportion of individuals admitted into the susceptible class a_S is 0.911.

Separate from the physical movement of residents between the classes, the pickup rates, z_H and z_L, were calculated by multiplying the spore density per contact by the number of contacts per day with the specific pathogen-carrying class. Combined with the lack of literature on high- and low-traffic areas in LTCFs, our model assumes that high-traffic areas function similarly to high-touch surfaces in a hospital setting as communal, high-traffic spaces tend to be cleaned more compared to their low-traffic counterparts. Accordingly, many values from studies of spore shed onto high- and low-touch surfaces in hospitals were used as an approximation for spore shed onto high- and low-traffic areas in LTCFs. To calculate the number of contacts per day between residents and high- and low-traffic areas, spore shed in CFUs onto to high-touch and low-touch surfaces in a hospital from Guerrero et al. [56] were subsequently divided by the average hand area of 540 cm^2 [57] to calculate the spore density. The number of contacts per day for high- and low-traffic were 9.368 and 4.818, respectively [46].

The shedding rates ρ_{CH}, ρ_{CL}, ρ_{DH}, and ρ_{DL} were calculated by approximating contacts with high- and low-traffic areas in LTCFs using contacts with high- and low-touch surfaces in hospitals and multiplying these figures by the number of CFUs on the hands of colonized and diseased residents. Contact rates were taken from [46, 56, 59]. To determine the number of *contacts per day per individual*, we summed the number of contacts with high-touch and low-touch objects recorded in Guerrero et al. [56] to reflect a "contacts per day per individual" rate. Shedding rates were found by multiplying the number of CFUs on the hand for diseased or colonized classes, as found in Figure 4 of Sethi et al. [59], with contact rates for high- and low-touch objects. Then, we divided by 540 cm^2, the surface area of the hand.

The proportion of time residents in LTCFs are socially inactive f was found in [51]. The data in the article had shown that 47.9% residents had chosen to spend the majority of their time on their own, so the proportion of time spent without social contact is 0.479.

Assuming that β is the baseline transmission rate, there is a weighting constant ε on the interaction term between the susceptible and colonized populations. The number of contacts with low-traffic areas is assumed to be the baseline, so ε is scaled accordingly. To calculate ε, the number of resident-resident contacts [36] is multiplied by a_C, the proportion of admissions to the colonized class. Then, that

quantity is divided by the number of contacts with low-touch areas from hospitals as an approximation for contacts with low-traffic areas in LTCFs per day [46]. Finally, this value is multiplied by 0.046, the probability of *C. difficile* transmission based on contact with a colonized individual [45].

The weighing constant for interaction between the diseased class and the susceptible θ was calculated using ε. The main difference between θ and ε was how much more infectious a diseased resident is than a colonized resident. In [30], they estimated that the communicability of *C. difficile* was 15 times greater in diseased patients than the communicability of colonized patients [47].

A.2. HCW-related parameters

The shedding and pickup rates associated with the HCWs were calculated in a similar manner to the values for the residents. For z_W, the spore density was found from Landelle et al. [58] by multiplying the mean of two CFUs on HCWs hands by the percentage of positive samples before dividing by the average hand area. Lastly, the number of contacts per day between HCWs and residents was roughly nine [36].

The parameters ρ_{CW} and ρ_{DW} are shedding rates from colonized and diseased classes onto the HCW hands. As 43% of assisted living residents require assistance toileting and the genital area produces significantly more CFUs than any other area, the proportion of HCWs' interactions with residents that involved incontinence was estimated from Schnelle et al. [60] to inform our shedding rate. Staff normally change residents 1.34 times every 12 hours and assist with toileting 0.5 times every 12 hours. Combining these rates and assuming no nighttime interaction, we approximate this value to be 1.84 times per 12 hour period. From Champredon et al. [36], the median HCW-resident interaction is nine per day, so the proportion of interactions that can contact the genital area is 0.204. These proportions were multiplied by the corresponding average number of CFUs transferred following skin contact, which was documented by Sethi et al. [59]. The sum of these products were finally multiplied by the contacts per day between HCWs and residents [36] and subsequently divided by average hand area [57].

Finally, transfer rates describe how HCWs transfer CFUs from gloves to high- and low-traffic surfaces. Denoted by ρ_{HW} and ρ_{LW}, these parameters were found based on the number of contacts between HCWs and high- and low-traffic areas. Cheng et al. [46] estimated that HCWs in hospitals come in contact with high-touch surfaces 47.12 times per day and low-touch 27.55 times per day. Furthermore, according to Guerrero et al. [56], HCWs acquire eight CFUs from high-touch objects and four from contact with low-touch objects. Since high- and low-touch surfaces in hospitals are comparable to high- and low-traffic areas in LTCFs, we utilize these values to calculate ρ_{HW} and ρ_{LW}. As such, in a similar fashion as outlined previously for ρ_{CW} and ρ_{DW}, the number of contacts with high- and low-traffic areas were multiplied by the corresponding CFU acquisition values and finally divided by the average hand area.

To calculate the hand hygiene decontamination rate η, we found the product of hand hygiene compliance at nursing homes, which was 17% [39], and the number of hand washes per day, which was calculated by summing the total observations over a 91 hour period [61]. To account for the difference in soap and water use versus ABHR, we multiplied the proportion of handwashes that used soap or ABHR with the percentage of spores eliminated by soap and ABHR, which were 0.90 and 0.20

respectively [11], and summed these values together.

Across states and facilities, the ratio of HCWs to residents varies greatly as a result of different levels of care and statutes. A study of staffing in LTCFs from 2000 reported ideal ratios between staff and residents as low as 1:5 and as high as 1:23 [52]. As such, the ratio of staff to residents n was calculated as an average value.

Lastly, the weighting constant for HCWs τ was defined as the total number of contacts between HCWs and residents [36] divided by the number of resident contacts with low-touch surfaces [46], and this value was subsequently divided by one minus the average ratio of residents to HCWs in a typical assisted living facility [52].

A.3. Environmental

Since we assume high-touch and low-touch surfaces are comparable to high-traffic and low-traffic areas, we utilized findings in [62] to estimate the shift-end decontamination rate ℓ to be 1. Saeb et al. [62] states that the frequency of cleaning high-touch and low-touch surfaces was shown to have a general consensus of one cleaning per day, which we assumed to be during shift change.

The average proportion of *C. difficile* CFUs removed in LTCF rooms with routine cleaning is 89.3% [50]. This value was multiplied by 42%, the average proportion of surfaces cleaned per day in an LTCF room [48] to calculate σ, the proportion of CFUs removed by disinfection of P_H and P_L every day. The weighting constant for additional cleaning of high-traffic areas was set as $\mu = 2.5$ [49].

The weighting constant for high-traffic areas ω was obtained by dividing the number of contacts a resident has with high-touch surfaces by the number of contacts with low-touch surfaces [46], with contacts with high- and low-touch surfaces serving as estimates for contacts with high- and low-traffic areas. Half-saturation constants for surfaces were calculated from a study by Lawley et al. [63], which found that ten pure spores or five fecal spores were required to infect half of the population. These numbers were then converted into CFUs using a result from Shafaat and Ponce [73] that found an average 27.8% of spores produced CFUs.

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