Mathematically Modeling the Interactions of Community- and Hospital-Acquired *C. difficile* Infections

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Background

- *Clostridioides difficile* (*C. difficile*) - bacteria spread among humans via fecal-oral route
- Colonized in large intestine and treated with antibiotics
- Can cause illnesses including diarrhea, colon perforation, emergency colectomy, and death
- Symptomatic and asymptomatic patients shed spores
- Spores are an inactive form and have protective coating that allows them to live months and years on surfaces and in food, water, and soil
- Spread by touching a contaminated surface
- Greatest increase in cases is in hospital, but discharged patients can spread the disease in the community

Parameters

Parameter	Description [*Units*]	Reference Value
a_R	proportion of individuals admitted into R [*dimensionless*]	0.75
a_S	proportion of individuals admitted into S [*dimensionless*]	0.09
a_C	proportion of individuals admitted into C [*dimensionless*]	0.15
a_D	proportion of individuals admitted into D [*dimensionless*]	0.01
k_R	discharge rate of R [day^{-1}]	0.33
k	discharge rate of S and C [day^{-1}]	0.15
k_D	discharge rate of D [day^{-1}]	0.068
α	antibiotic prescription rate [day^{-1}]	0.5
θ	gut restoration of colonization resistance rate [day^{-1}]	0.033
ε	successful treatment of infection rate [day^{-1}]	0.08
ϕ	disease rate of colonized individuals with insufficient immune response [day^{-1}]	0.024
ρ_{CH}	shedding rate of C into P_H [$spores \cdot cm^{-2} \cdot individuals^{-1} \cdot day^{-1}$]	0.057
ρ_{CL}	shedding rate of C into P_L [$spores \cdot cm^{-2} \cdot individuals^{-1} \cdot day^{-1}$]	0.029
ρ_{DH}	shedding rate of D into P_H [$spores \cdot cm^{-2} \cdot individuals^{-1} \cdot day^{-1}$]	0.123
ρ_{DL}	shedding rate of D into P_L [$spores \cdot cm^{-2} \cdot individuals^{-1} \cdot day^{-1}$]	0.063
σ	proportion of P_H and P_L spores killed due to disinfection upon discharge [$individuals^{-1}$]	0.83
μ	rate of P_H spores killed due to extra cleaning [day^{-1}]	0.66
K	half-saturation constant [$spores \cdot cm^{-2}$]	7.5
β	colonization rate upon transfer of spores from a fomite [day^{-1}]	0.338
ω	weighting constant for high-touch fomites [*dimensionless*]	1.96
α_C	antibiotic prescription rate in the community [day^{-1}]	0.0086
β_C	colonization rate upon transfer of spores in a community [day^{-1}]	0.0012
γ	contamination rate of food [day^{-1}]	0.04 – 0.30
ρ_{CC}	shedding rate of C into P_C [$spores \cdot cm^{-2} \cdot individuals^{-1} \cdot day^{-1}$]	0.84
ρ_{DC}	shedding rate of D into P_C [$spores \cdot cm^{-2} \cdot individuals^{-1} \cdot day^{-1}$]	1.82
K_F	carrying capacity of F [*proportion*]	1

Variables and Schematic

R_H = resistant individuals in hospital (no recent antibiotics)

S_H = susceptible individuals in hospital (recent antibiotics)

C_H = colonized individuals in hospital (asymptomatic)

D_H = diseased individuals in hospital (symptomatic)

P_H = *C. difficile* spores on high-touch frequency surfaces in hospital

P_L = *C. difficile* spores on low-touch frequency surfaces in hospital

R_C = resistant individuals in community

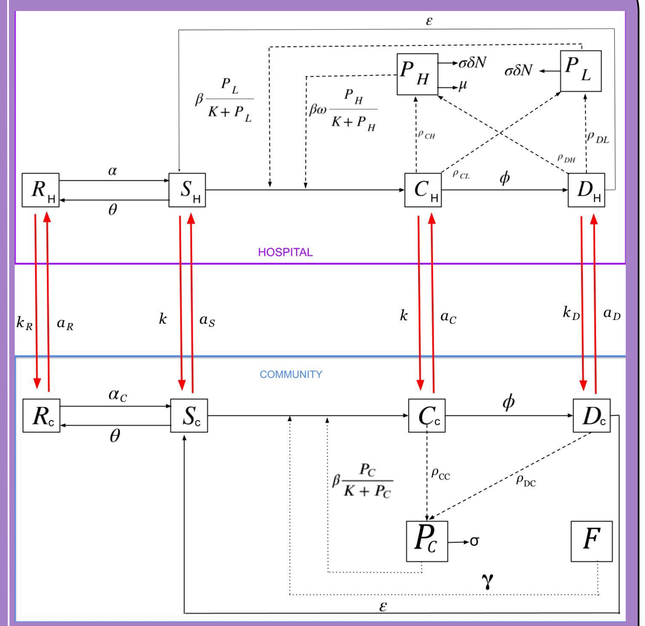
S_C = susceptible individuals in community

C_C = colonized individuals in community

D_C = diseased individuals in community

P_C = *C. difficile* spores on surfaces in community

F = *C. difficile* in food and water sources



System of Differential Equations

$$
\begin{aligned}
R_H' &= a_R\delta(t)N - (k_R+\alpha)R_H + \theta S_H \\
S_H' &= a_S\delta(t)N + \alpha R_H - (k+\theta)S_H - \beta\left(\omega\frac{P_H}{K+P_H} + \frac{P_L}{K+P_L}\right)S_H + \varepsilon D_H \\
C_H' &= a_C\delta(t)N + \beta\left(\omega\frac{P_H}{K+P_H} + \frac{P_L}{K+P_L}\right)S_H - (k+\phi)C_H \\
D_H' &= a_D\delta(t)N + \phi C_H - (k_D+\varepsilon)D_H \\
P_H' &= \rho_{CH}C_H + \rho_{DH}D_H - (\sigma\delta(t)N+\mu)P_H \\
P_L' &= \rho_{CL}C_H + \rho_{DL}D_H - \sigma\delta(t)NP_L
\end{aligned}
\qquad \text{HOSPITAL}
$$

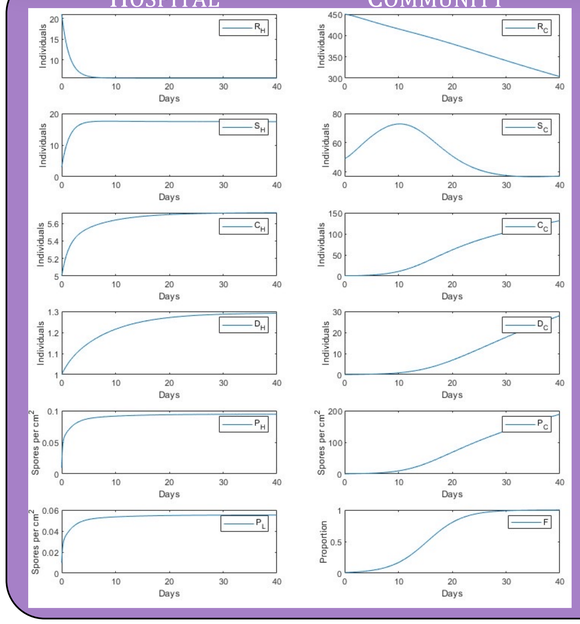
$$
\begin{aligned}
R_C' &= -\alpha_C R_C + \theta S_C - a_R\delta(t)N + k_R R_H \\
S_C' &= -\theta S_C + \alpha_C R_C - a_S\delta(t)N + kS_H + \varepsilon D_C - \beta_C\left(\frac{P_C}{K+P_C}\right)S_C - \gamma\left(\frac{F}{K_F+F}\right)S_C \\
C_C' &= \beta_C\left(\frac{P_C}{K+P_C}\right)S_C + \gamma\left(\frac{F}{K_F+F}\right)S_C - \phi C_C + kC_H - a_C\delta(t)N \\
D_C' &= \phi C_C - \varepsilon D_C + k_D D_H - a_D\delta(t)N \\
P_C' &= \rho_{CC}C_C + \rho_{DC}D_C - \sigma P_C \\
F' &= \gamma F\left(1 - \frac{F}{K_F}\right)
\end{aligned}
\qquad \text{COMMUNITY} \qquad (1)
$$

where

$$\delta(t)N = k_R R_H(t) + k\left(S_H(t) + C_H(t)\right) + k_D D_H(t). \qquad (2)$$

Model Simulations and Results

Hospital



Community

Initial Conditions

$R_H = 21$

$S_H = 3$

$C_H = 5$

$D_H = 1$

$P_H = P_L = 0.01$

$R_C = 450$

$S_C = 49$

$C_C = 1$

$D_C = 0$

$P_C = 0.01$

$F = 0.01$

Incidence Rates

Hospital	
Incidence of C	32.13
due to high-touch	24.73
due to low-touch	7.40
Incidence of D	24.67

Community	
Incidence of C	0.0104
due to fomites	0.0001
due to food	0.0103
Incidence of D	0.0036

Future Work

- Include a testing and removal term for contaminated food and water
- Explore strategies to mitigate *C. difficile* spread in the hospital and community
- Identify potential factors that could lead to a *C. difficile* outbreak in the community

Selected References

[1] Durham, et al. *Emerging Infectious Diseases*, 2016.

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