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Introduction

- **Prolonged hospitalization** is a risk factor for colonization with pathogens such as **carbapenem-resistant Enterobacteriaceae (CRE)**^{4,11,12,15}, which has limited treatment options + high mortality
- **Long-stay patients are at higher risk** for hospital-acquired infections^{1,2,4,17} than short-stay patients, but **the impact of long-stay patients on other patients** in the same unit is unclear
- This **mathematical model of in-hospital pathogen transmission** seeks to answer the question, "How does a single long-stay patient affect the probability that any *other* patient leaves the unit colonized with a pathogen?"

Mathematical Model

Two variants of a discrete-state/continuous-time Markov model (13-bed hospital unit):

Fig 1a: Regular-turnover model - patients enter and exit [vertical hashes] a hospital unit with a given average length of stay

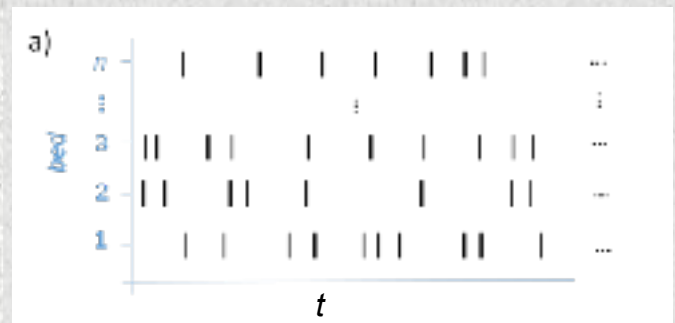
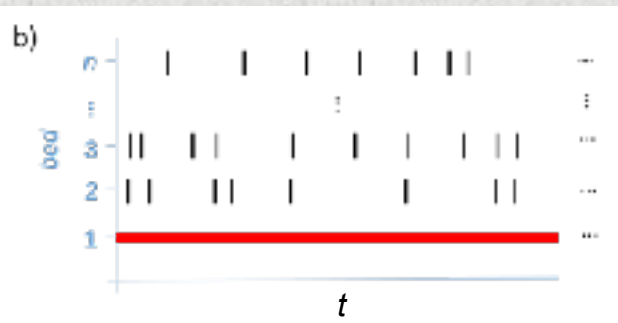


Fig 1b: Long-stay colonized patient model - one patient is colonized [red bar] with an indefinite length of stay.



The state of the unit is the number of positive patients (i), which can increase / decrease:

Fig 2: State Transitions



(a) regular turnover (b) with long-stay colonized patient

Three mechanisms of colonization:

- **pre-existing colonization (ϕ):** endemic within the community¹⁰
- **prior-to-new patient transmission (ψ):** via contaminated bed linens or fomite transmission from the immediate surroundings¹¹
- **patient-patient transmission (γ):** via healthcare providers or other vectors¹⁶

State Transition Equations

Rate of Increase (state $i \rightarrow i+1$)

$$f_i = \underbrace{\gamma i(n-i)}_{\text{patient-patient transmission rate per colonized patient per day}} + \underbrace{\beta(n-i)\phi}_{\text{pre-existing colonization probability}} + \underbrace{\psi(n-i)}_{\text{prior-to-new colonization probability}}$$

Rate of Decrease (state $i \rightarrow i-1$)

$$g_i = \beta i(1-\phi)(1-\psi)$$

Annotations: γ is patient-patient transmission rate per colonized patient per day; β is turnover rate per day; ϕ is pre-existing colonization probability; ψ is prior-to-new colonization probability.

Model Comparison

Equations	Regular Turnover Model	Long-Stay Colonized Patient Model
Rate of increase ($i \rightarrow i+1$)	f_i	$f_i^{LC} = f_i$
Rate of decrease ($i \rightarrow i-1$)	g_i	$g_i^{LC} = g_{i-1}$

The model addresses only the steady-state situation in which a long-stay patient is colonized and accounts only for length of stay, not the severity of illness

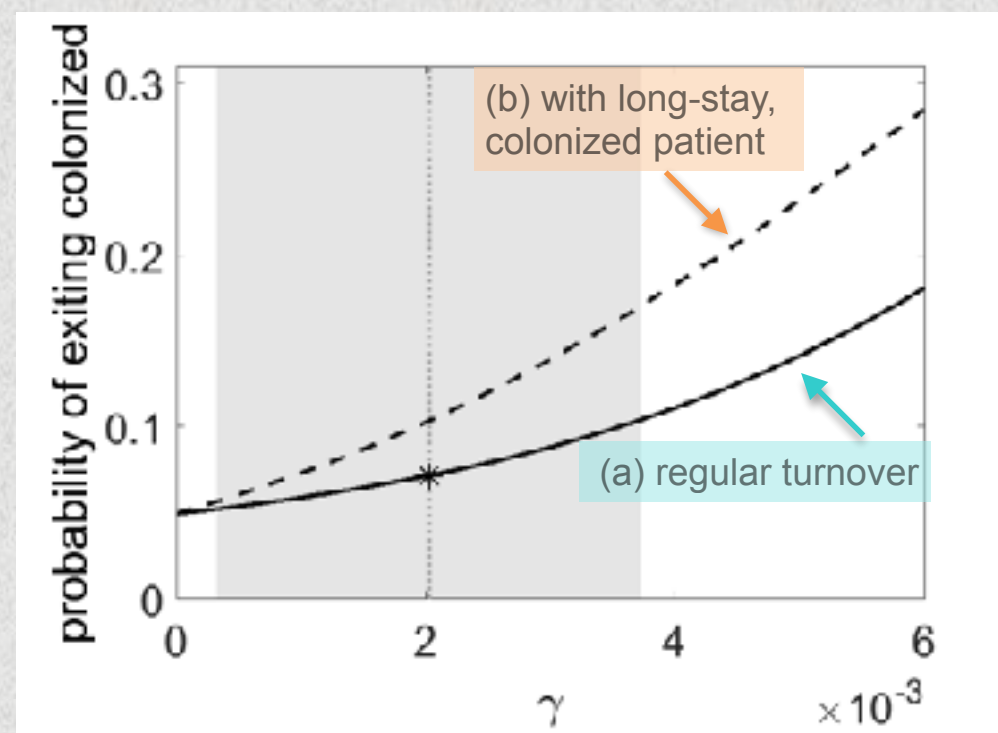
Best-Fit Parameters*

name	definition	units	value	
n	number of beds	number of beds in the hospital unit	beds	13
β	turnover rate (1/average length of stay)	probability per unit time per patient that the patient exits and a new patient enters	1/d	0.071
ϕ	pre-existing prevalence	probability that an entering patient is colonized	none	0.05
γ	patient-patient transmission rate	probability of transmission from colonized to uncolonized patient per colonized-uncolonized patient pair per unit time	1/d	0.002 +/- 0.0017
ψ	prior-to-new colonization probability	probability of transfer of colonization from a bed's prior colonized occupant to the bed's uncolonized incoming patient	none	0.0009

Best-fit parameters inferred from surveillance data of a 13-bed NYC hospital unit (Ong et al, PLOS One, in press)

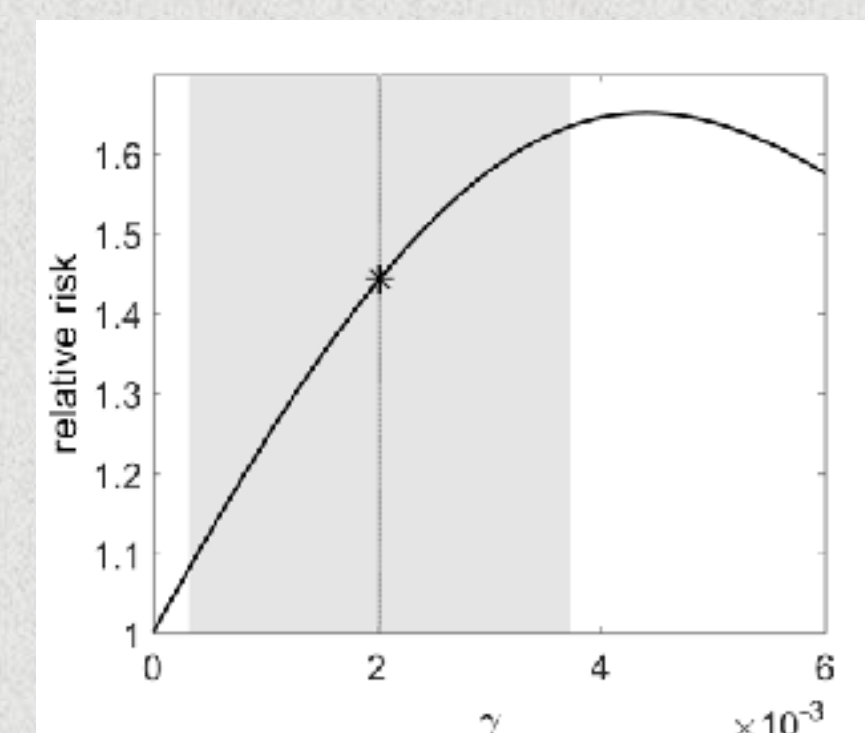
Comparison of Results

Probability of Exiting Colonized from a Unit with a Long-Stay Colonized Patient



regular turnover
 long-stay, initially colonized patient.
 $\gamma = 0.002$
 uncertainty for γ +/- SD (0.000329, 0.003729)
 * probability at best-fit parameters (ϕ, γ, ψ)

Relative Risk of Exiting Colonized from a Unit with a Long-Stay Colonized Patient



Plot of the relative risk of exiting colonized for a patient in a unit containing a single colonized long-stay patient versus one without at different rates of patient-patient transmission (γ +/- SD, shaded area).

Results

	Regular Turnover	Hospital Unit with Long Stay Patient
Probability of Exiting Colonized	7.2% (5.7-10%)	10.4% (5.7-16%)
Relative Risk (+/- SD)	—	1.44 (1.08-1.63)

Conclusions

- The presence of a **single CRE-colonized long-stay patient increases the risk of colonization of other patients in the unit by about 44%** (range 8% to 63%)
- **Relative risk is highly sensitive to the patient-patient transmission rate**
- **One possible high-yield target** for screening and decolonization of CRE is the **long-stay patient**, who not only has longer exposure time for possible colonization, but who also poses a **disproportionate risk** to other patients within hospital units.
- Focusing efforts on **isolation or decolonization of long-stay patients** may be an effective intervention for reducing colonization pressure within a hospital unit, while avoiding some of the possible negative consequences and cost of universal decolonization.

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