

Modeling the Spread of Antimicrobial Resistance: Concepts, Data and Predictions

Heinrich zu Dohna

Rockefeller University
Laboratory of Populations

Outline

- Why model?
- Basic components of transmission models
- Adding complexity: biological processes
- Adding complexity: transmission structure
- Results
- Future directions

Why model dynamics of antimicrobial resistance?

- Antimicrobial resistance occurs in many commensals
- Complete eradication of commensals is unfeasible
- How to use existing antibiotics is as important as finding new ones
- Requires understanding of dynamics of transmission and evolution of resistance

Modeling questions

- Is endogenous colonization or transmission more important for the spread of antimicrobial resistance?
- How to best combine different antibiotics?
- What is the most efficient way to minimize spread?

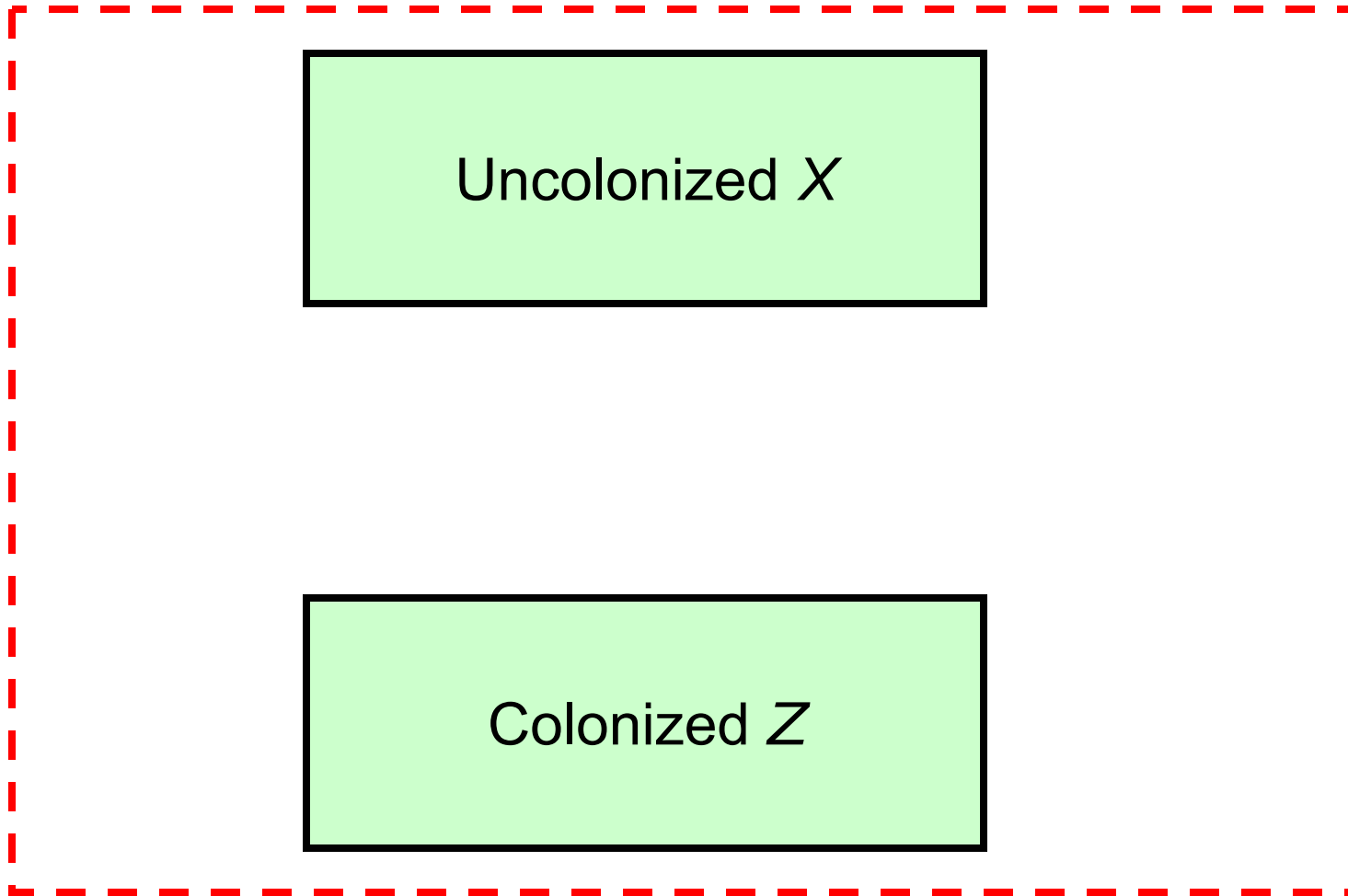
Basic transmission model

Population boundary (e.g. ward, hospital)

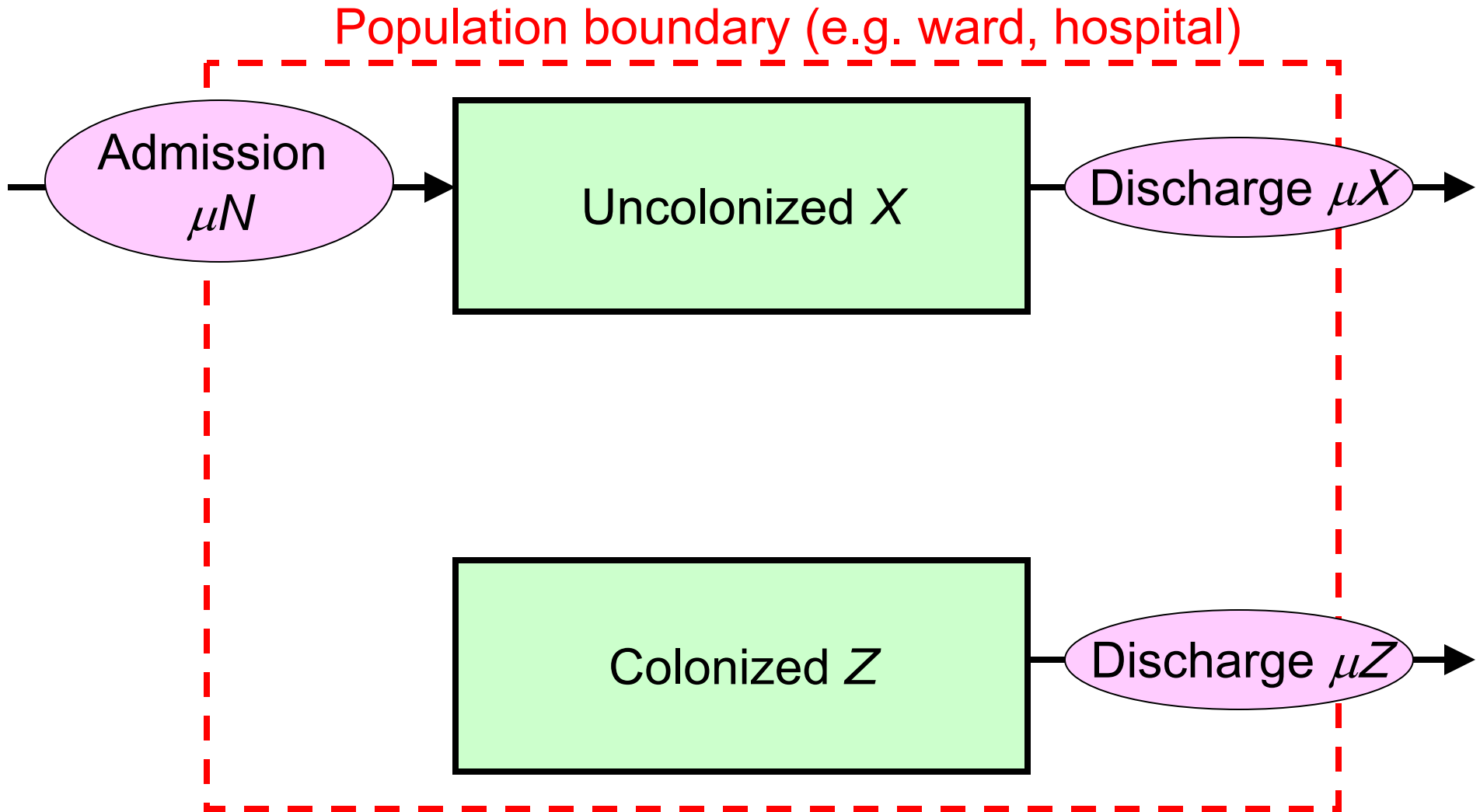


Basic transmission model

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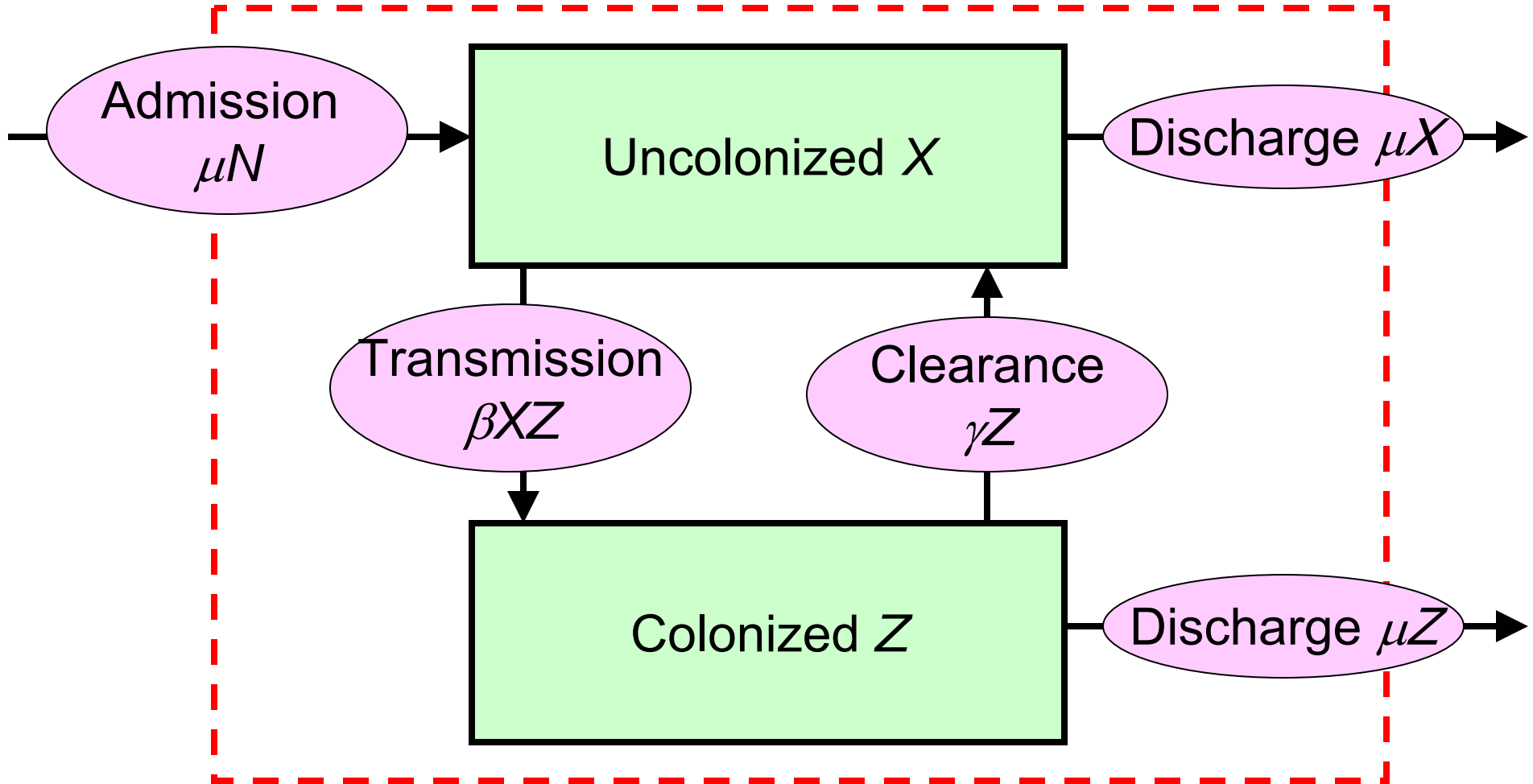


Basic transmission model



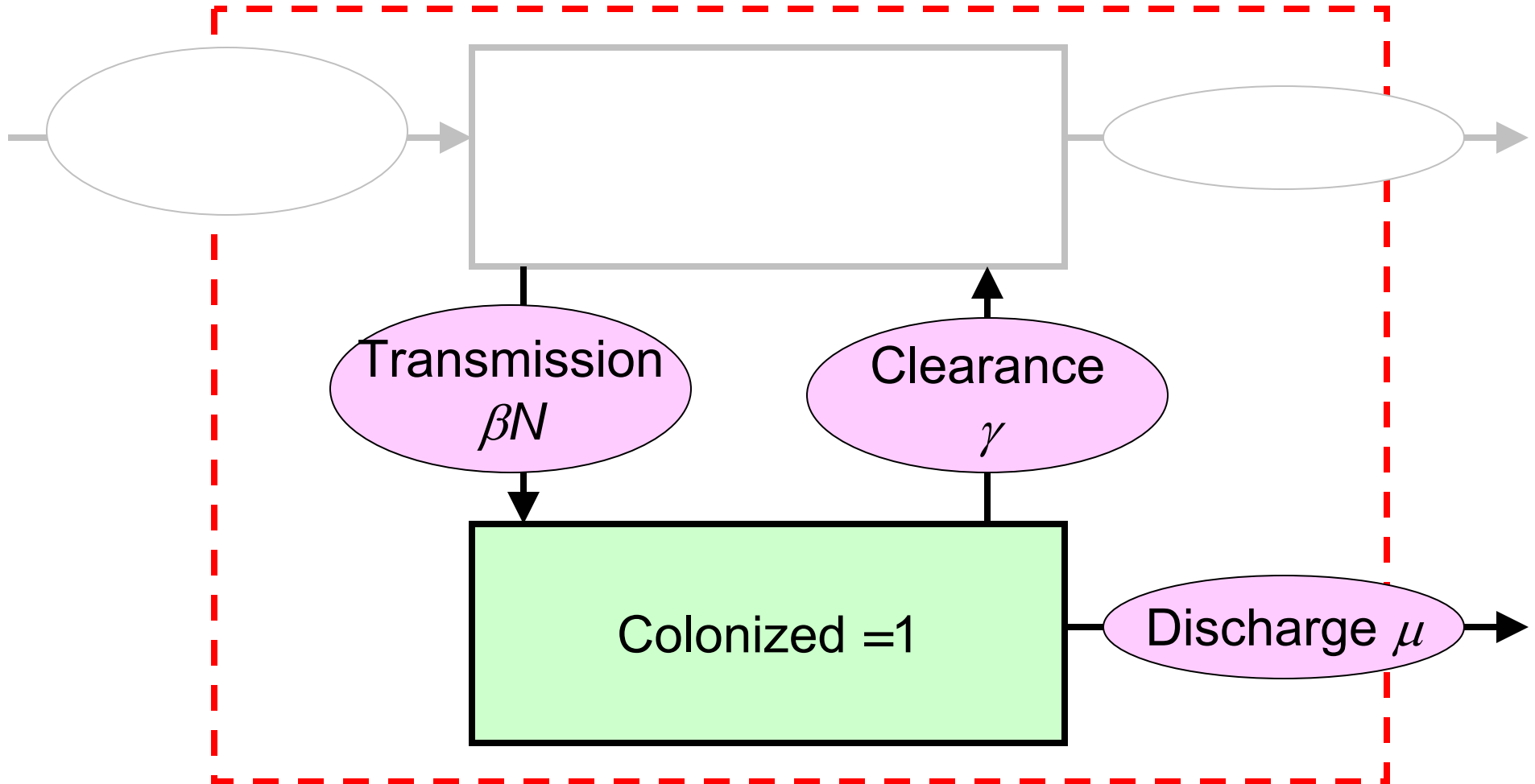
Basic transmission model

Population boundary (e.g. ward, hospital)



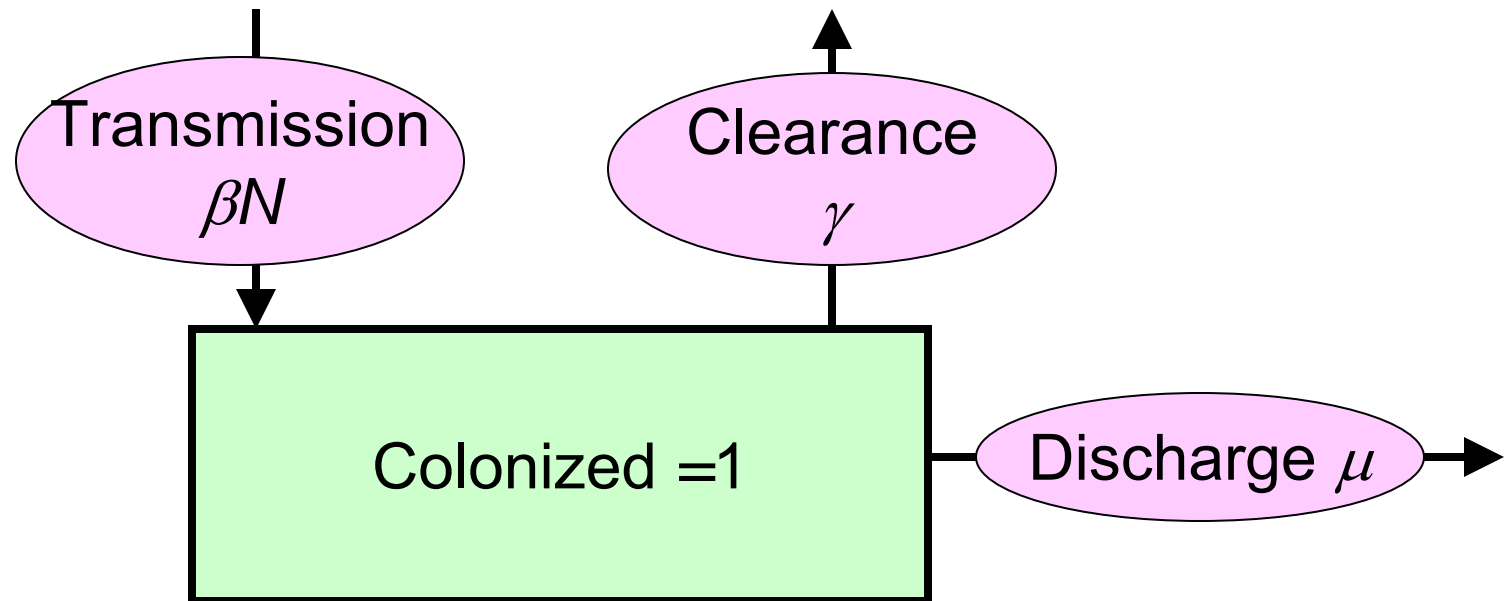
The concept of R_0

Population boundary (e.g. ward, hospital)



The concept of R_0

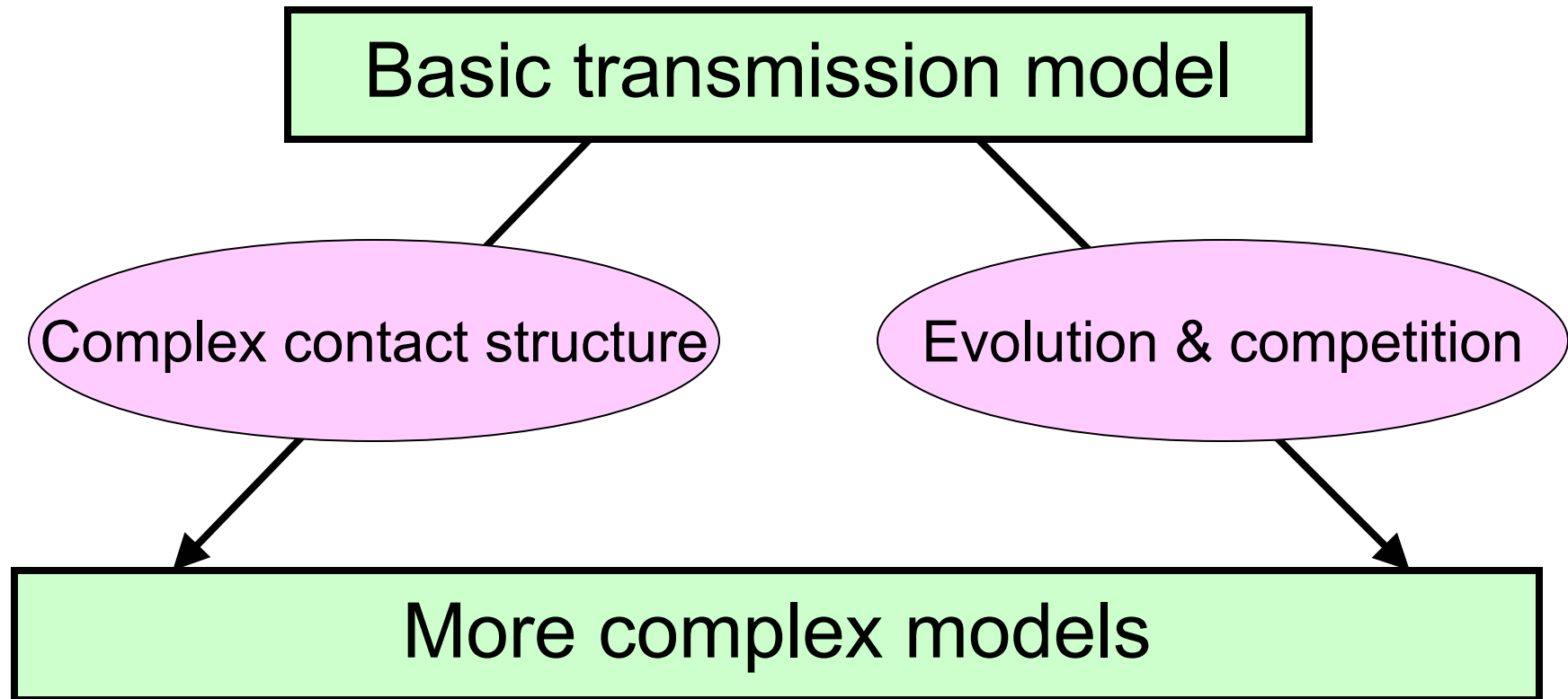
$$\frac{\beta \cdot N}{\mu + \gamma} \geq 1 \quad \rightarrow \quad \text{Colonization can spread}$$



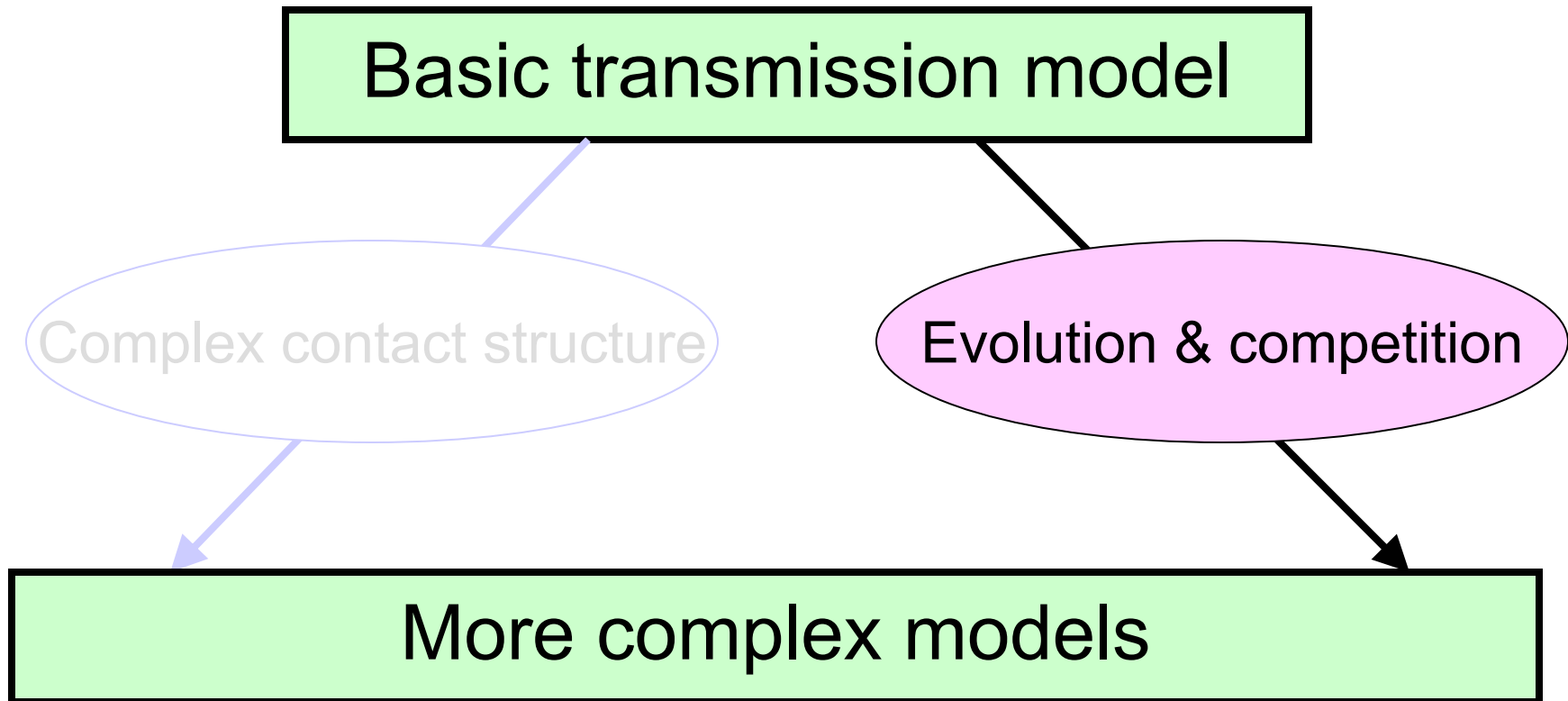
Results of transmission models

- Dynamics
- Equilibria
- R_0

Extensions of basic model



Extensions of basic model



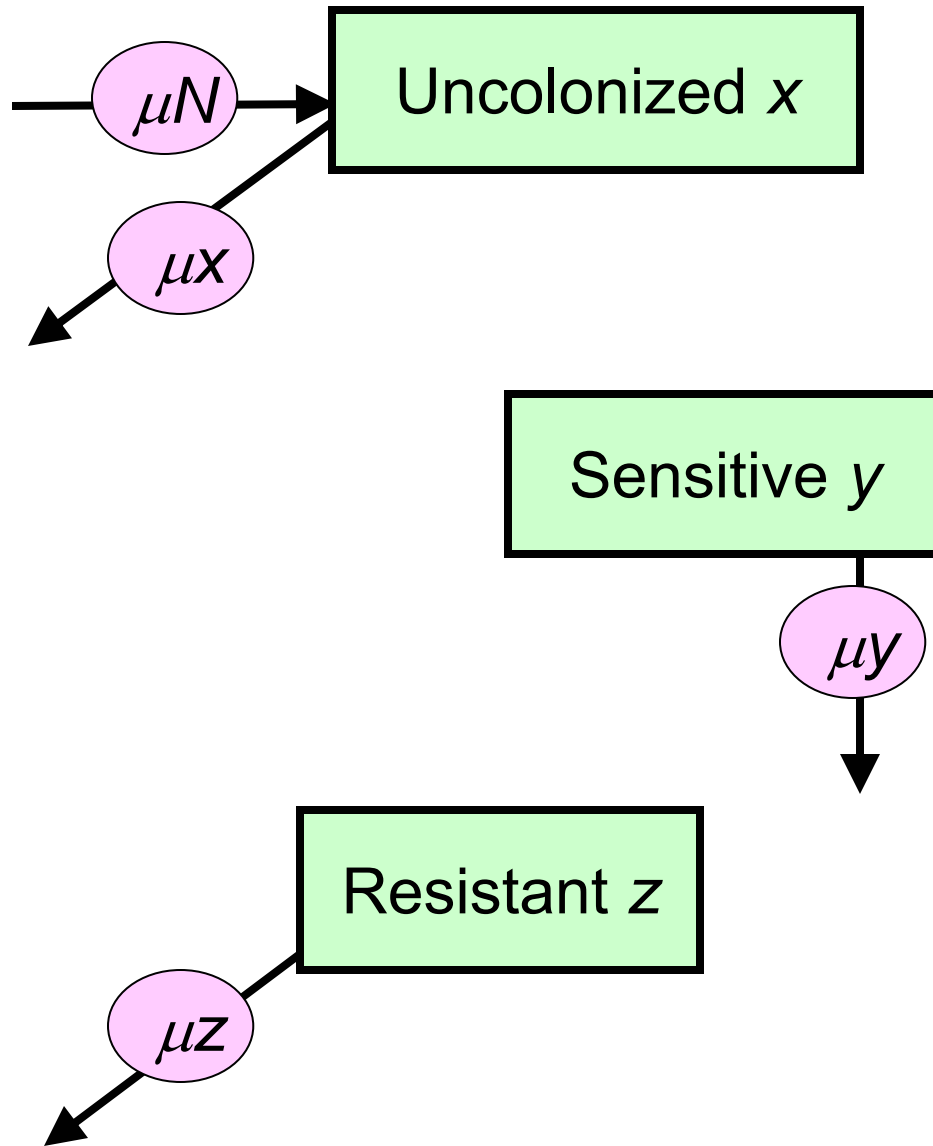
Competition & Evolution

Uncolonized x

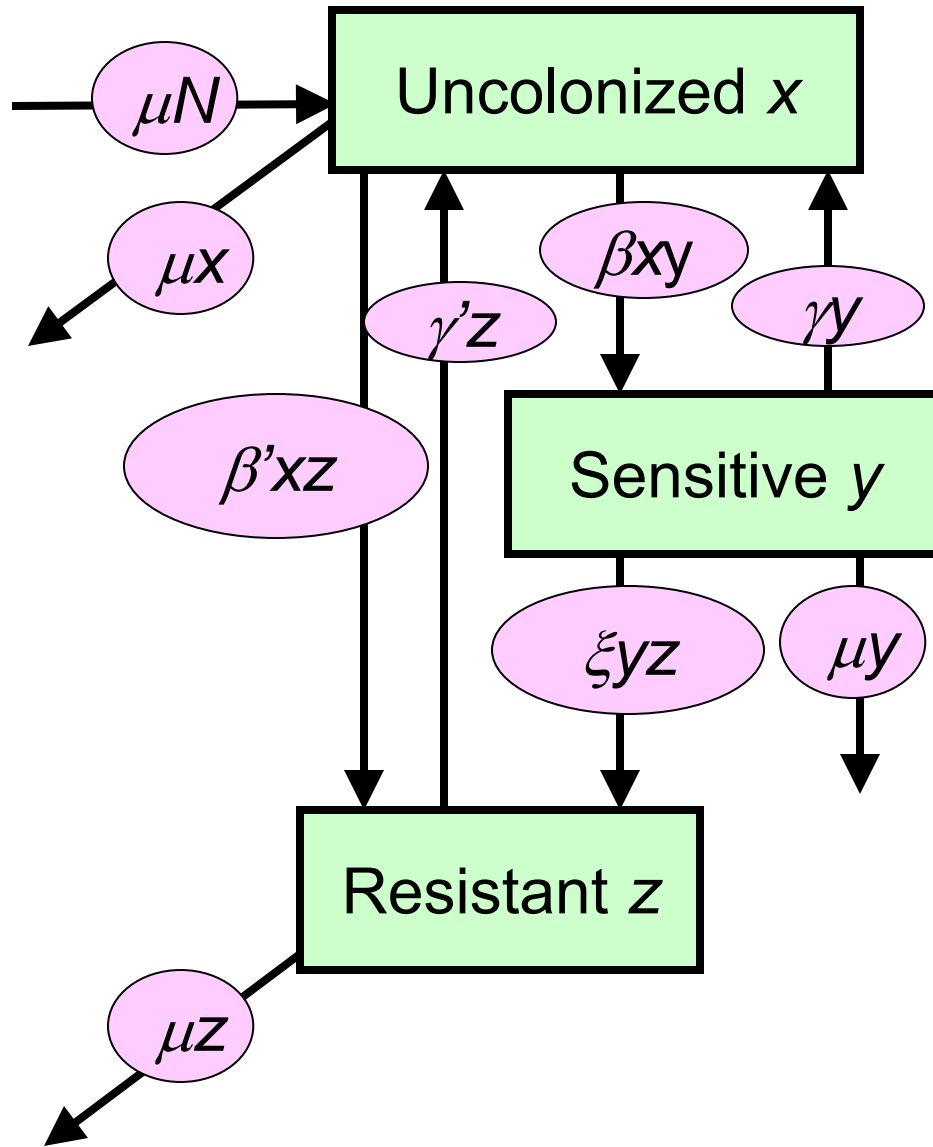
Sensitive y

Resistant z

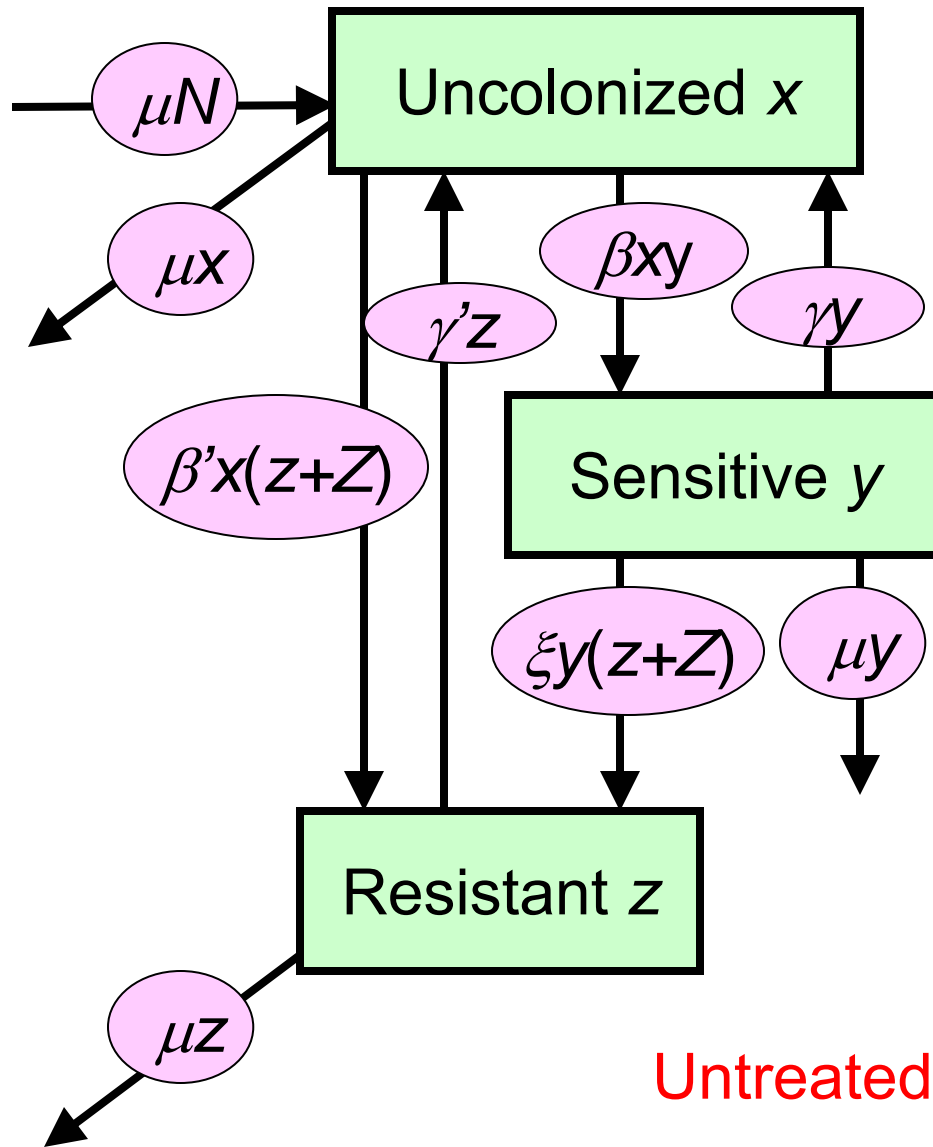
Competition & Evolution



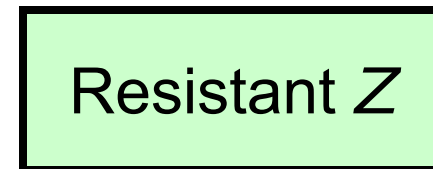
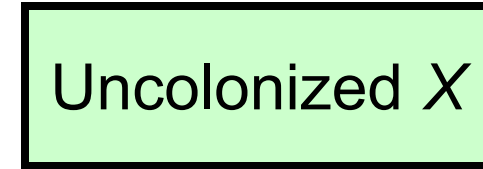
Competition & Evolution



Competition & Evolution



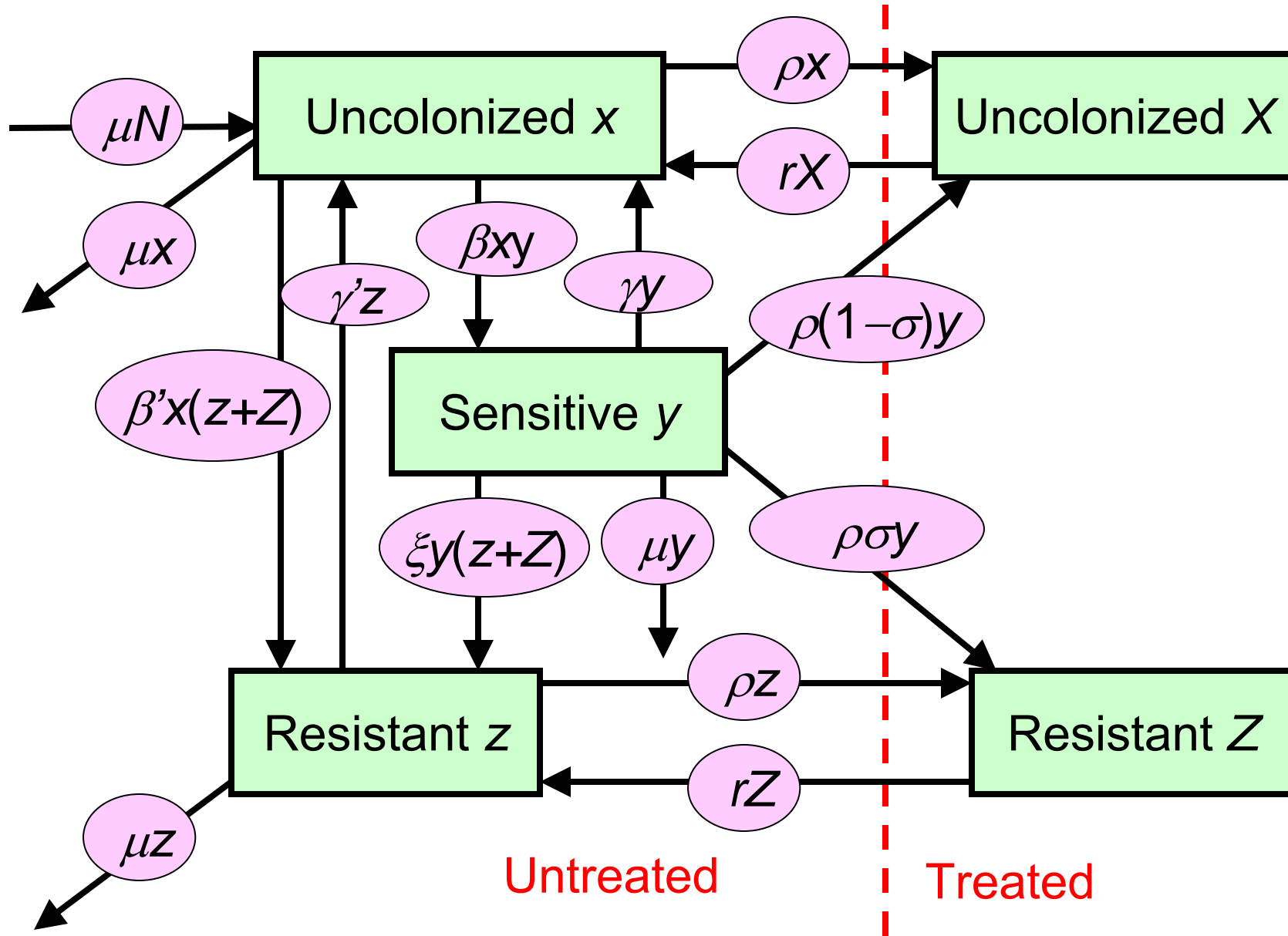
Untreated



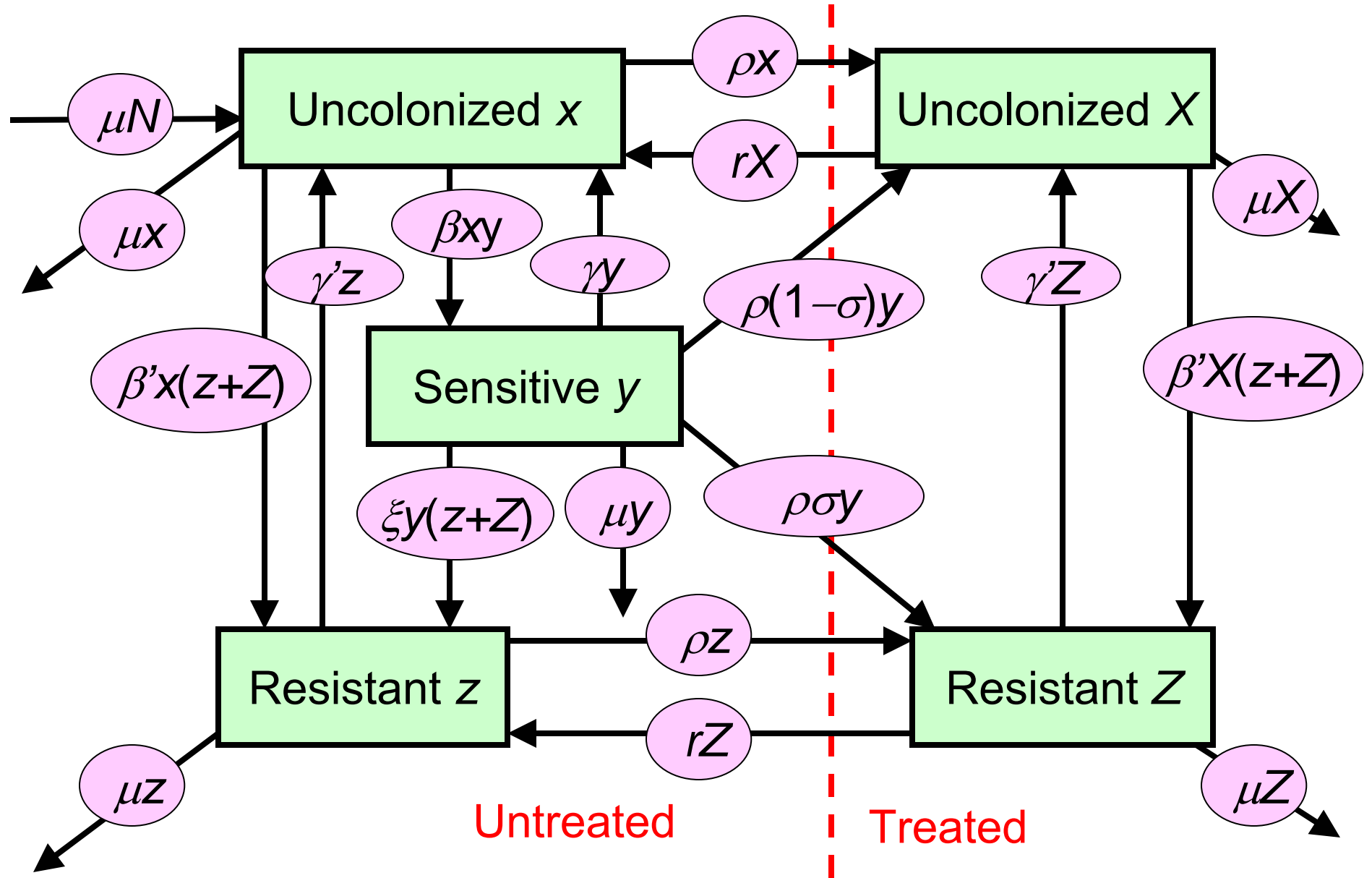
Treated

Austin et al. 1997

Competition & Evolution



Competition & Evolution



Austin et al. 1997

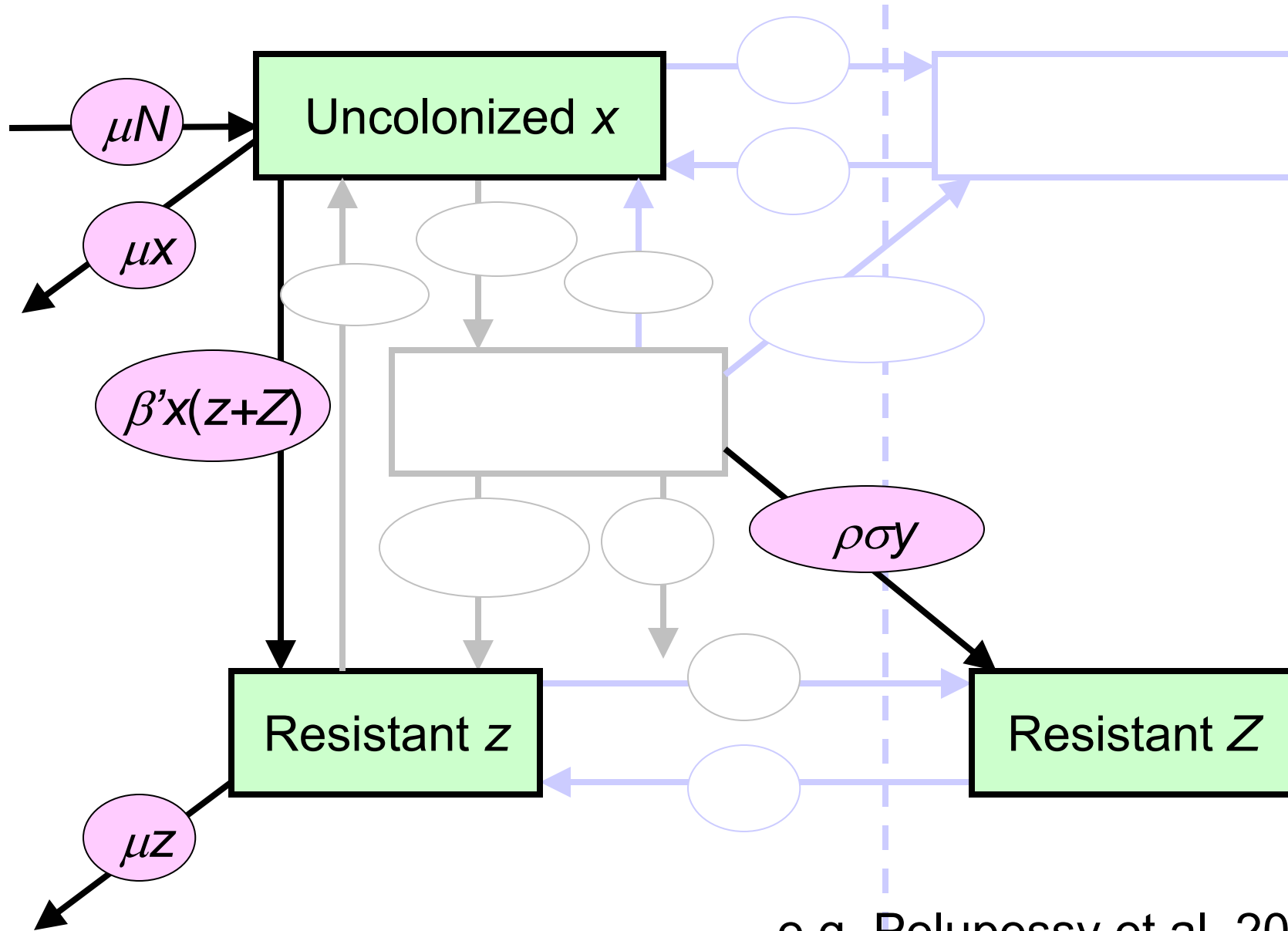
Qualitative predictions

- Conditions for threshold treatment rate ρ below which resistant strains die out
- Simultaneous use of different antibiotics better than sequential use
- Odds ratio not indicative of the population level effect of antibiotics
- Reducing transmission reduces resistant but not sensitive colonization

Quantitative predictions

- Require quantitative parameter estimates
→ Simplified model

Simplified model

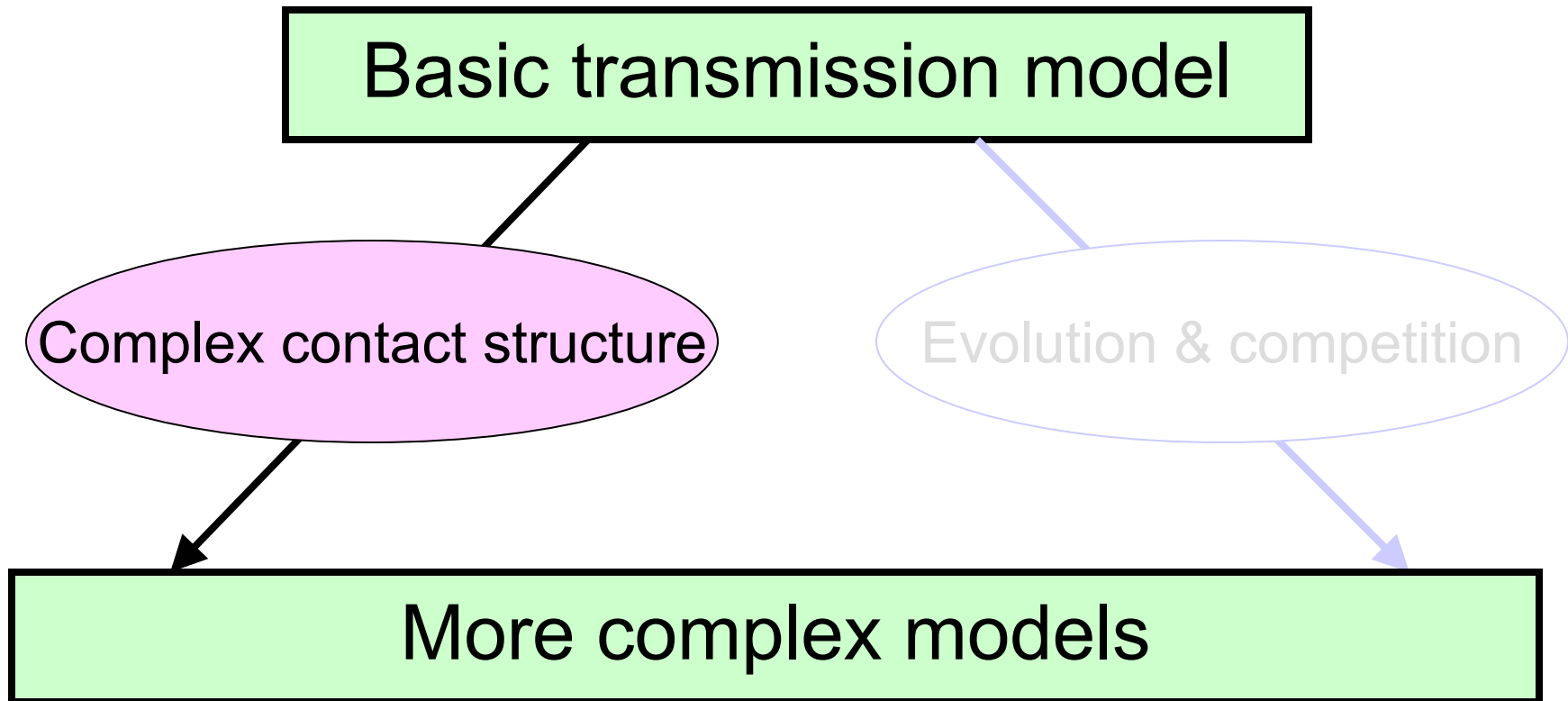


e.g. Pelupessy et al. 2002

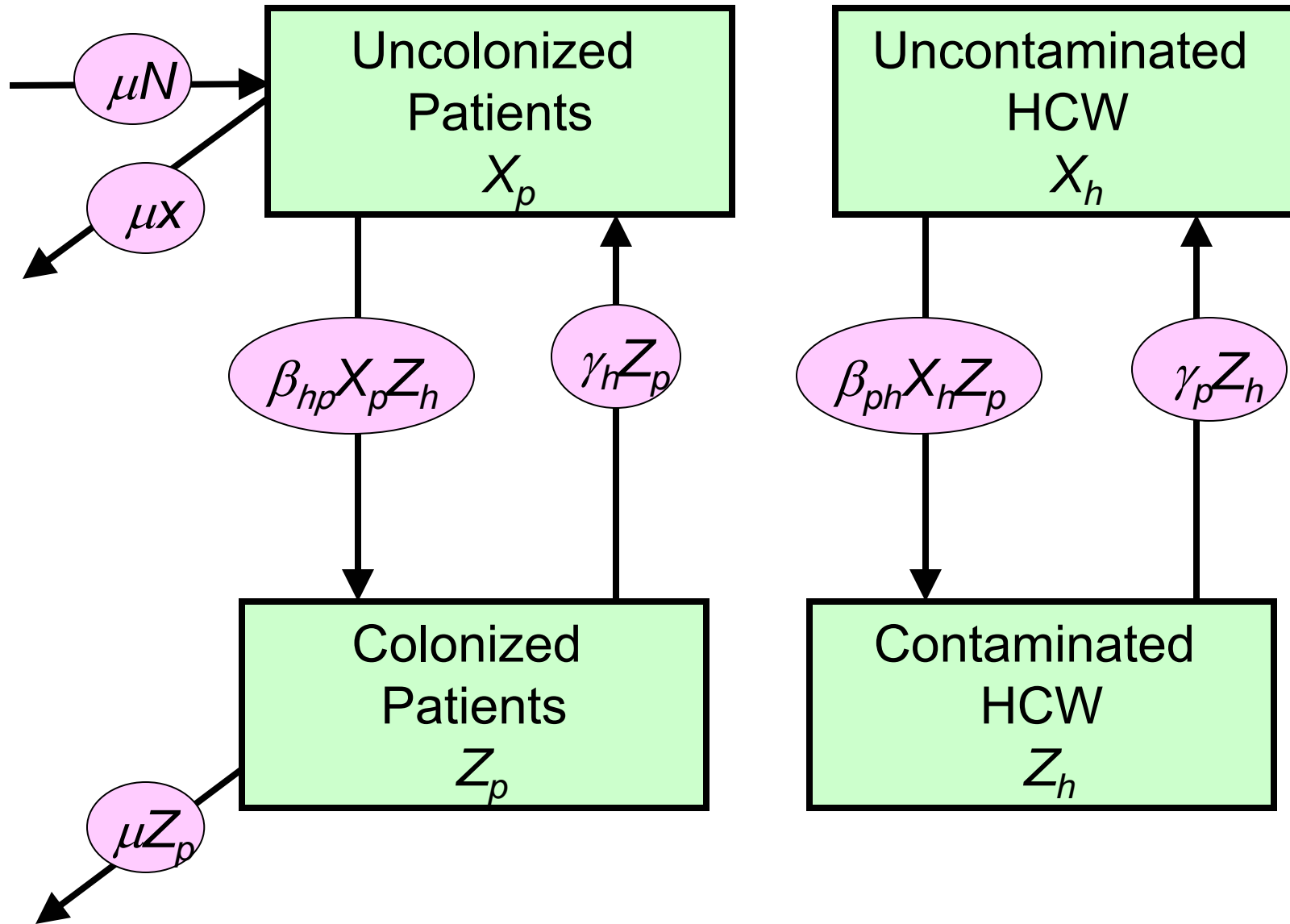
Estimates of β

Pathogen	Method	Data	Value	Citation
MRSA	β chosen to achieve specified R_0	none	-	Cooper et al. 2004
MRSA	Endemic curve	Prevalence in USA, UK	-	Bootsma et al. 2006
MRSA VRE	Hidden Markov model	Infection incidence ICU, USA	.33/day .26/day	Cooper & Lipsitch 2004
VRE <i>P. aeruginosa</i>	Markov model	Screening in ICU (Netherlands?)	.09/day .065/day	Pelupessy et al. 2002
VRE	Mean prevalence	ICU Chicago	0.08/day 0.55/day	Austin et al. 1999

Extensions of basic model



More realistic contact structure I

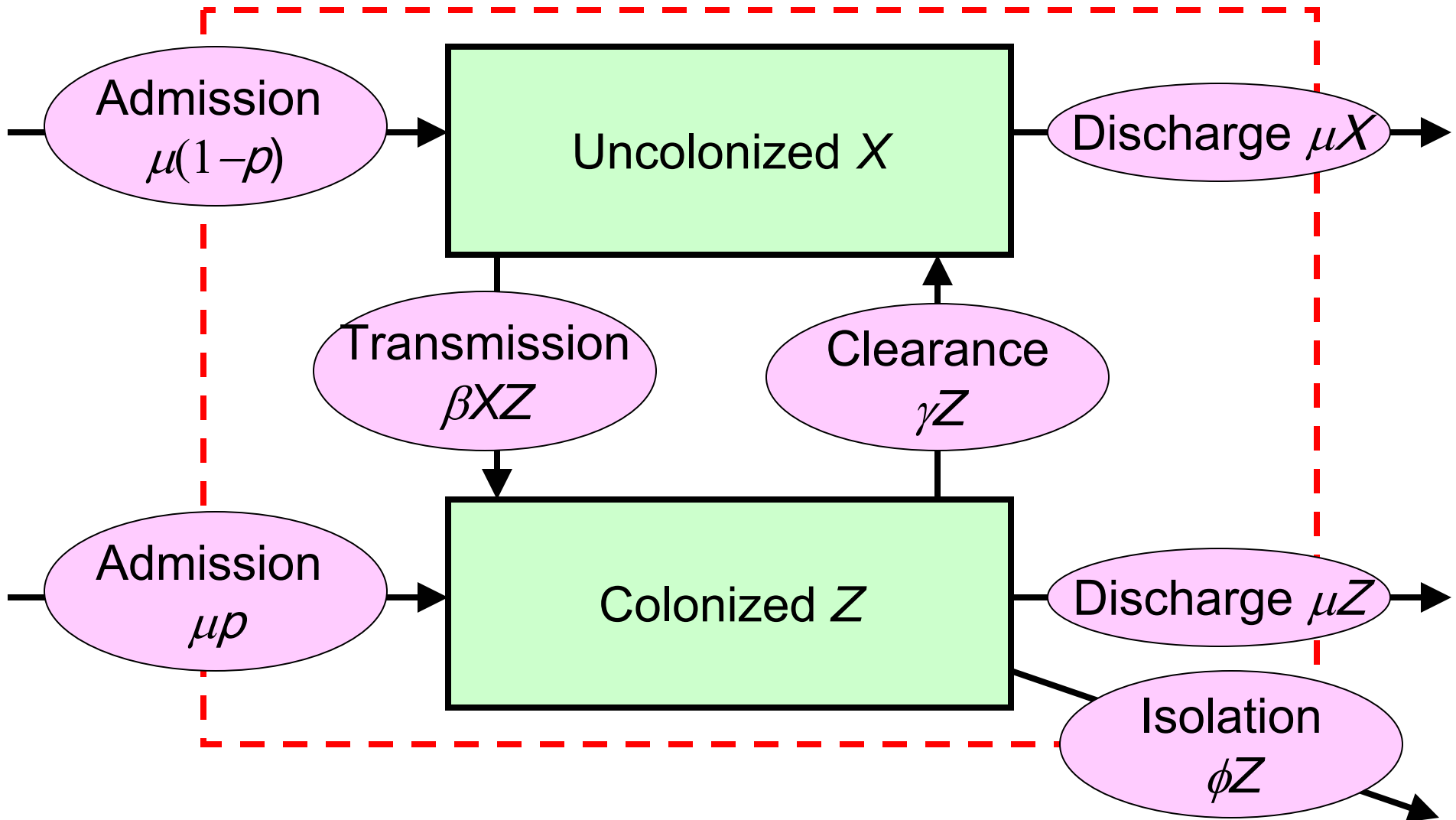


More realistic contact structure II

- Within and between ward transmission
- R_0 for entire population (re-admissions)
- Variation among individuals in transmission

Core transmission model

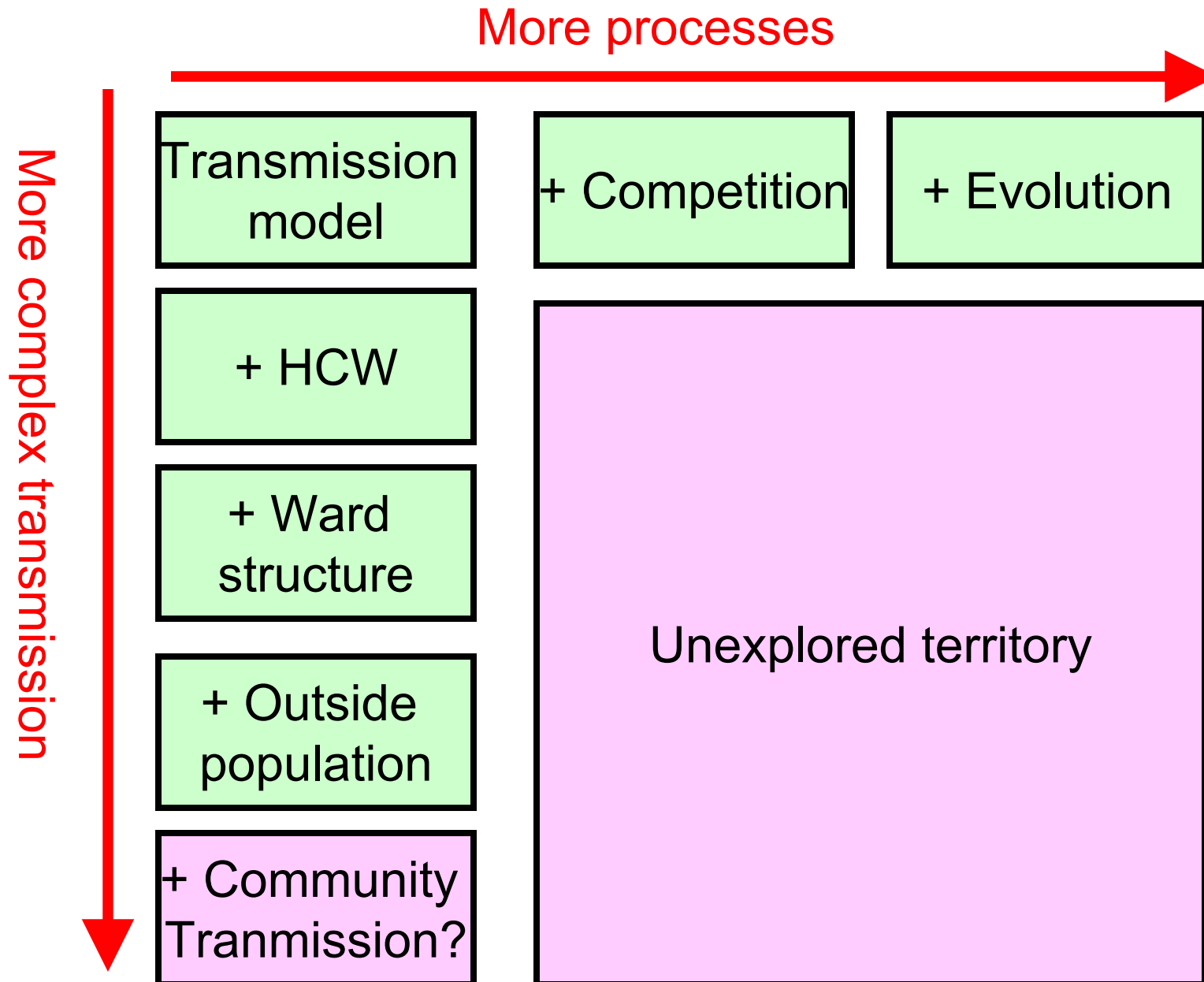
Ward



Results

- Effect of HCW depends on model structure
- Detection of colonization crucial for isolation rate
- Hospital $R_0 \leq$ global R_0
- Efficient detection and removal can lead to global $R_0 < 1$
- Coordination among hospitals crucial

Overview of different models



Future directions

- Parameter estimates for competition & evolution
- Transmission beyond βXZ
- Community transmission