Transboundary problems in infectious diseases

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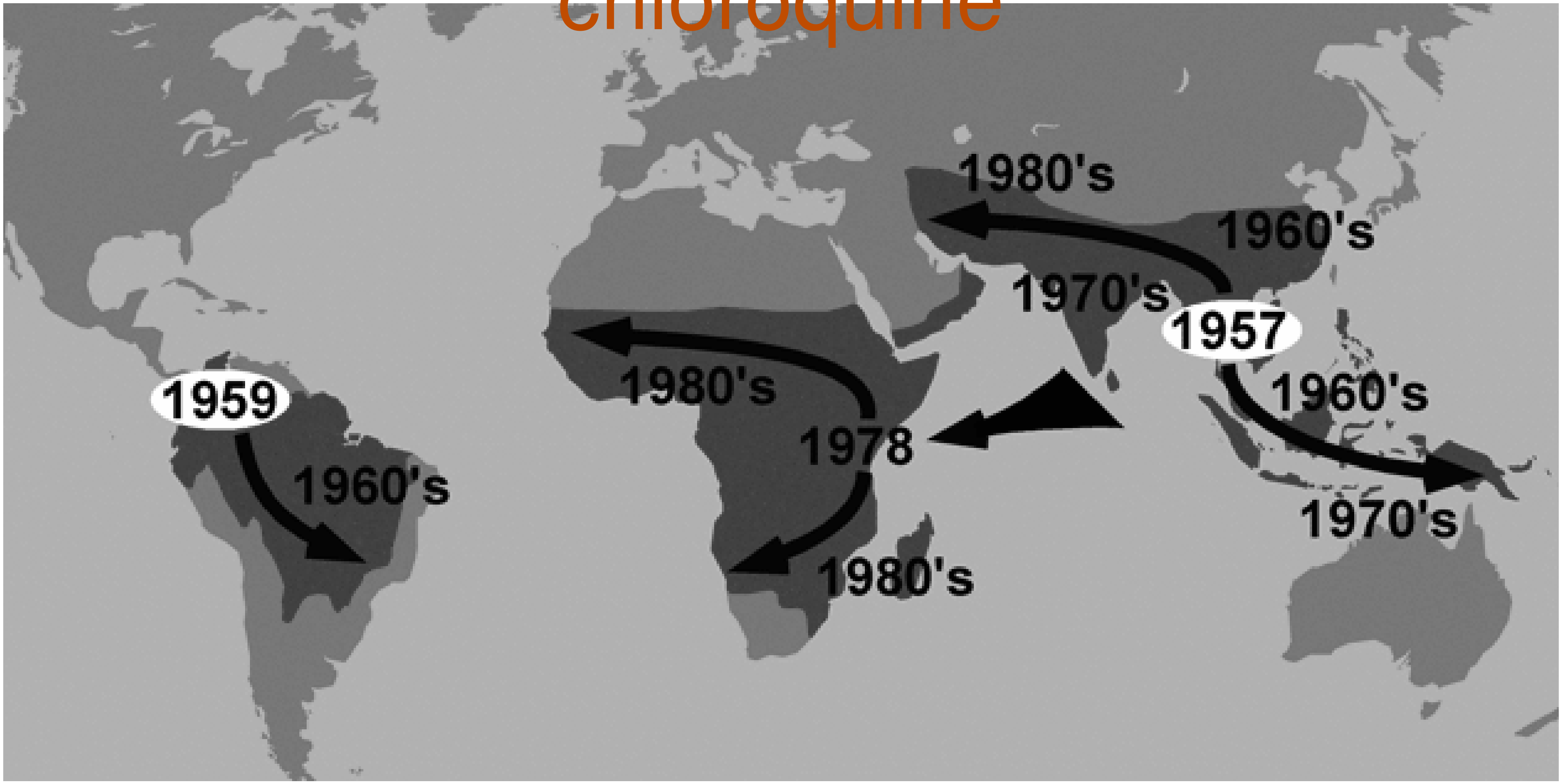
Infection control is a global public good

- Non-excludable and non-rival in consumption
- Examples include
  - Efforts to control infections in hospitals
  - Information on infectious disease outbreaks
  - Control of drug resistant pathogens globally

Spread of *Pfcrt* mutations conferring resistance to chloroquine



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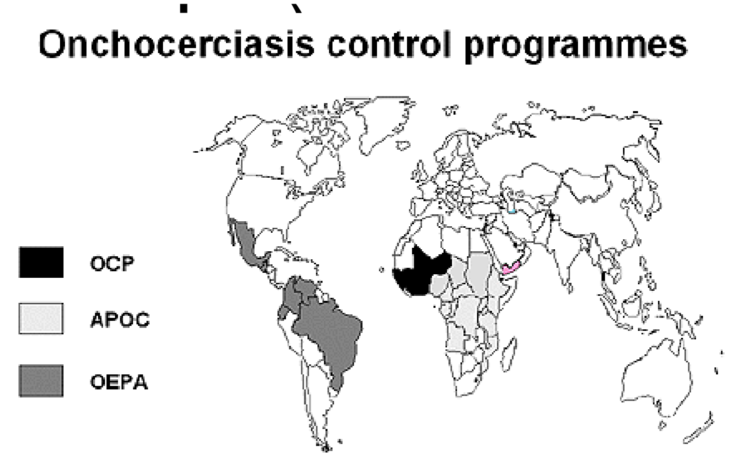
Other cross-country approaches

- Of the 25 countries that eliminated malaria, all were islands, or contiguous with countries that had eliminated malaria (at least in the bordering
- West African Oncho Control Program (OCP)



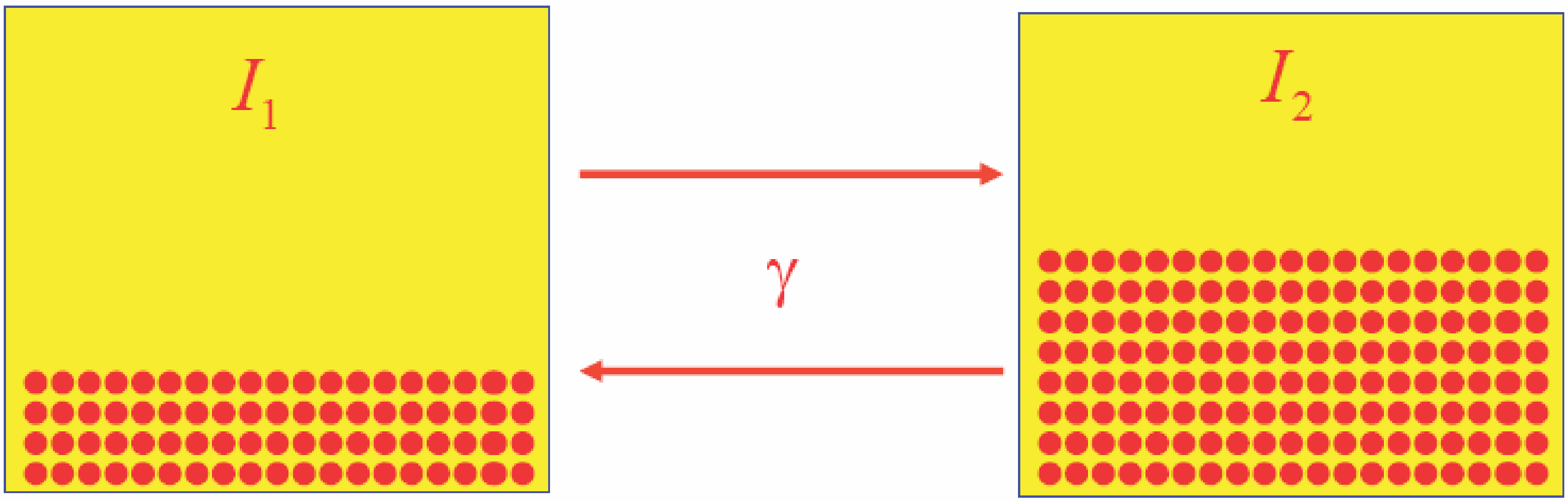
Spillovers

- Epidemiological
- Economic
  - Countries respond to increased control in neighbors by either stepping up their own control or by cutting back (free-riding)
  - A country's optimal investment in vaccination depends on own returns as well as rate of incoming measles cases

Typologies of two-patch transboundary problems

- Single policy maker with full control over infection control in two patches
- Decentralized policymakers with control only over their own patches
- Single policymaker with subsidy tool to incentivize decentralized decisionmakers

Optimising control strategies



Region 1

Region 2

$$\frac{dI_1}{dt} = (\beta I_1 + \gamma I_2)(N - I_1) - \mu I_1$$

$$\frac{dI_2}{dt} = (\beta I_2 + \gamma I_1)(N - I_2) - \mu I_2$$

Rowthorn, Laxminarayan, Gilligan *J Roy Soc Int*

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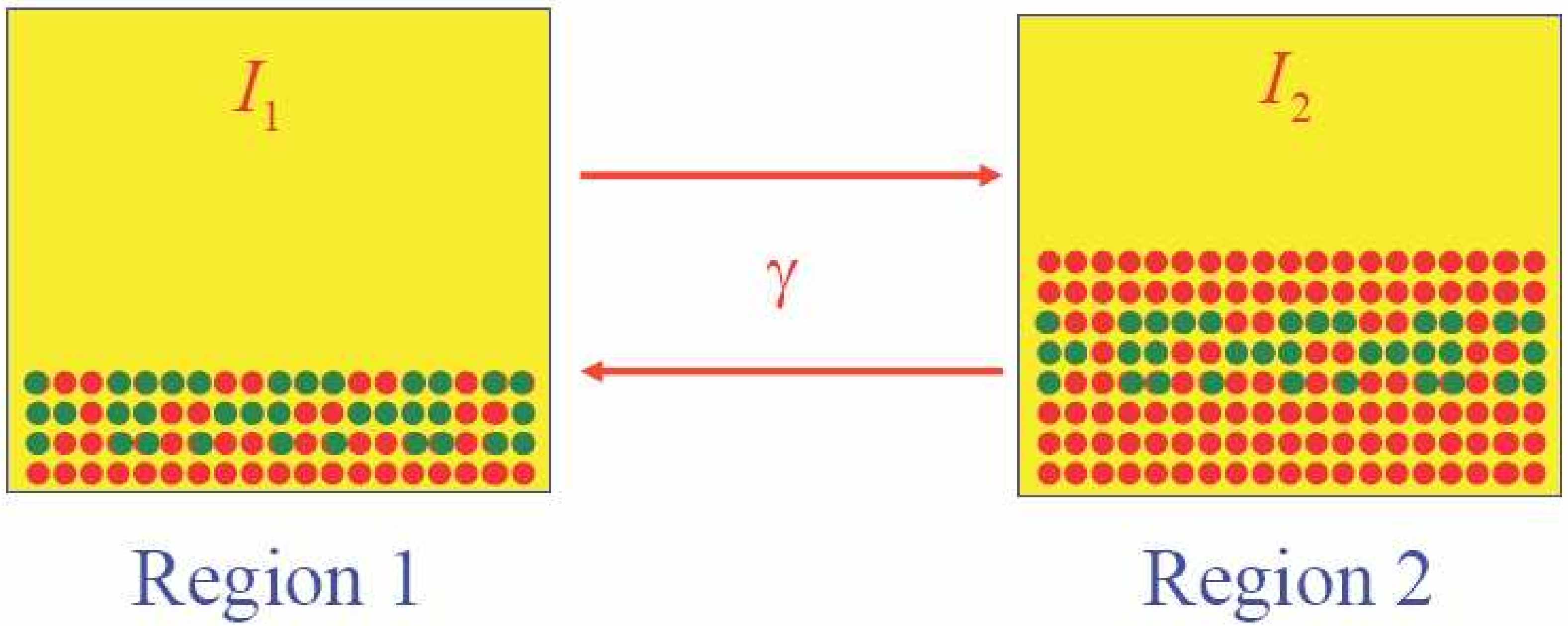
Optimising control strategies

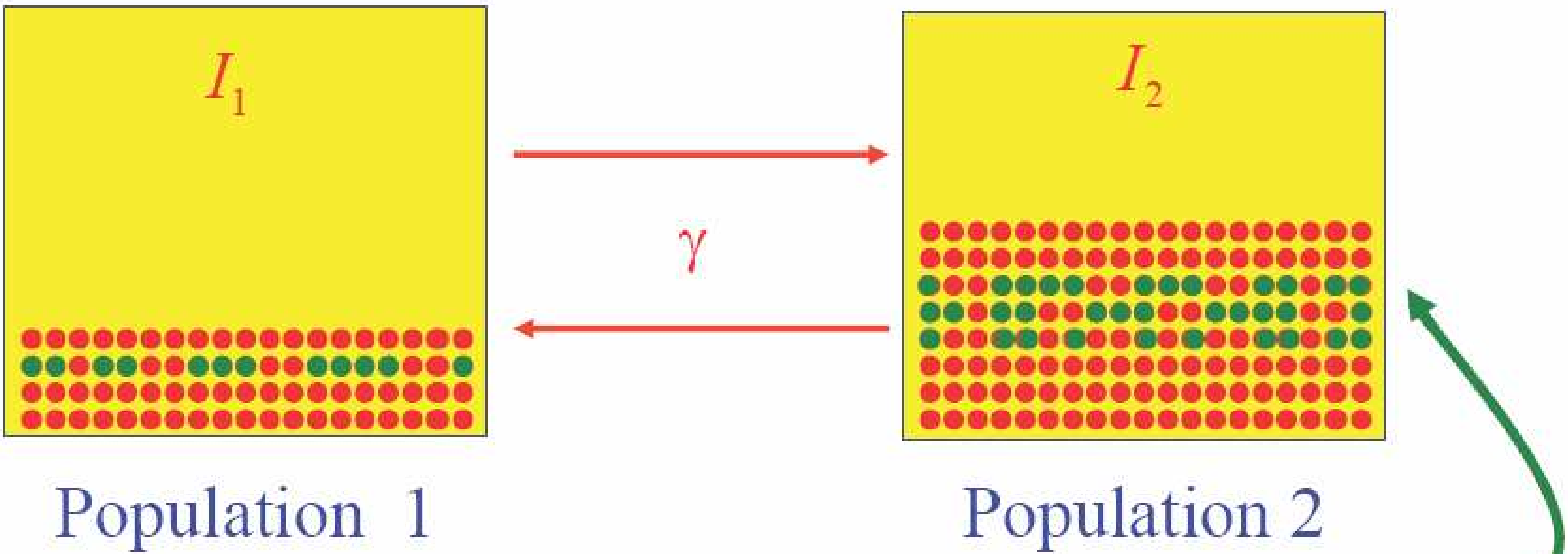


$$\frac{dI_1}{dt} = (\beta I_1 + \gamma I_2)(N - I_1) - \mu I_1 - \alpha F_1$$

$$\frac{dI_2}{dt} = (\beta I_2 + \gamma I_1)(N - I_2) - \mu I_2 - \alpha F_2$$

Rowthorn, Laxminarayan, Gilligan *J Roy Soc Int*

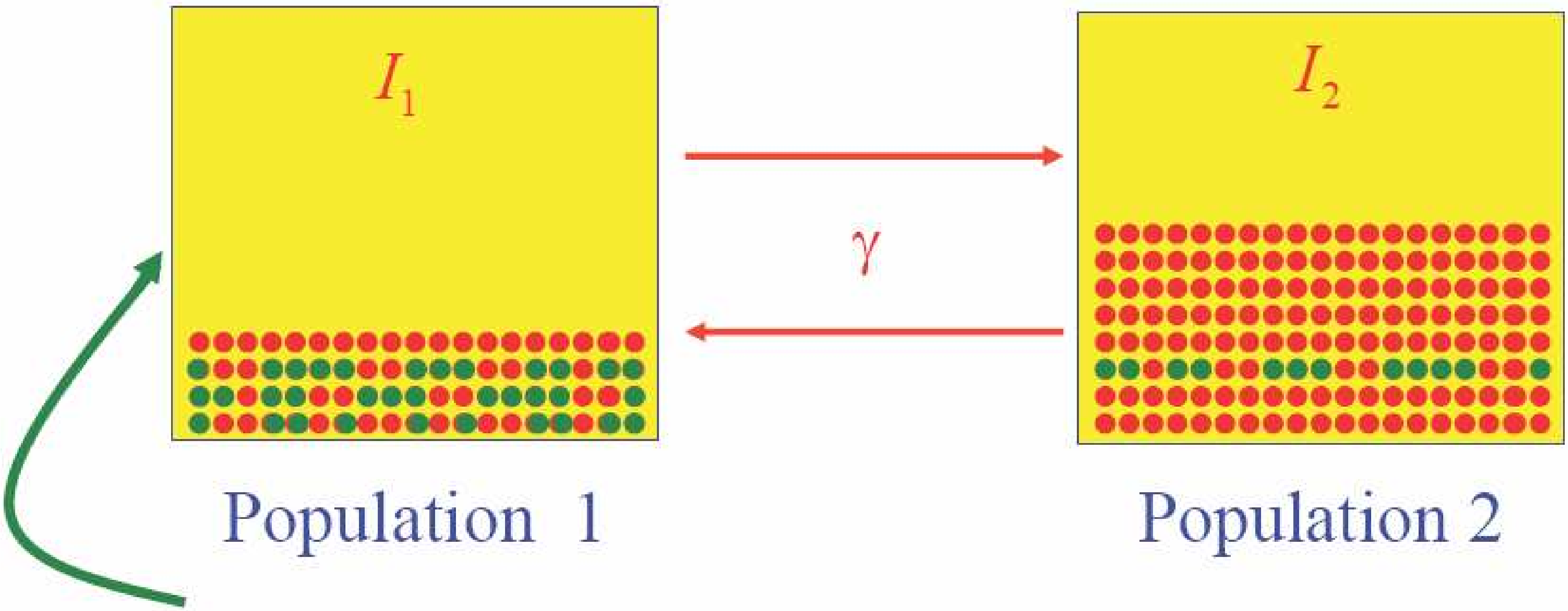
Optimising control strategies



Strategy 1 **Give preference to <u>more</u> infected region (Pop 2) to equalise levels of infection**

Rowthorn, Laxminarayan, Gilligan *J Roy Soc Int*

Optimising control strategies



Strategy 2 Give preference to less infected region (Pop 1)

Rowthorn, Laxminarayan, Gilligan *J Roy Soc Int*

Allocating resources

Expenditure on drugs is subject to the budget constraint $c\,(F_1 + F_2) \le M$

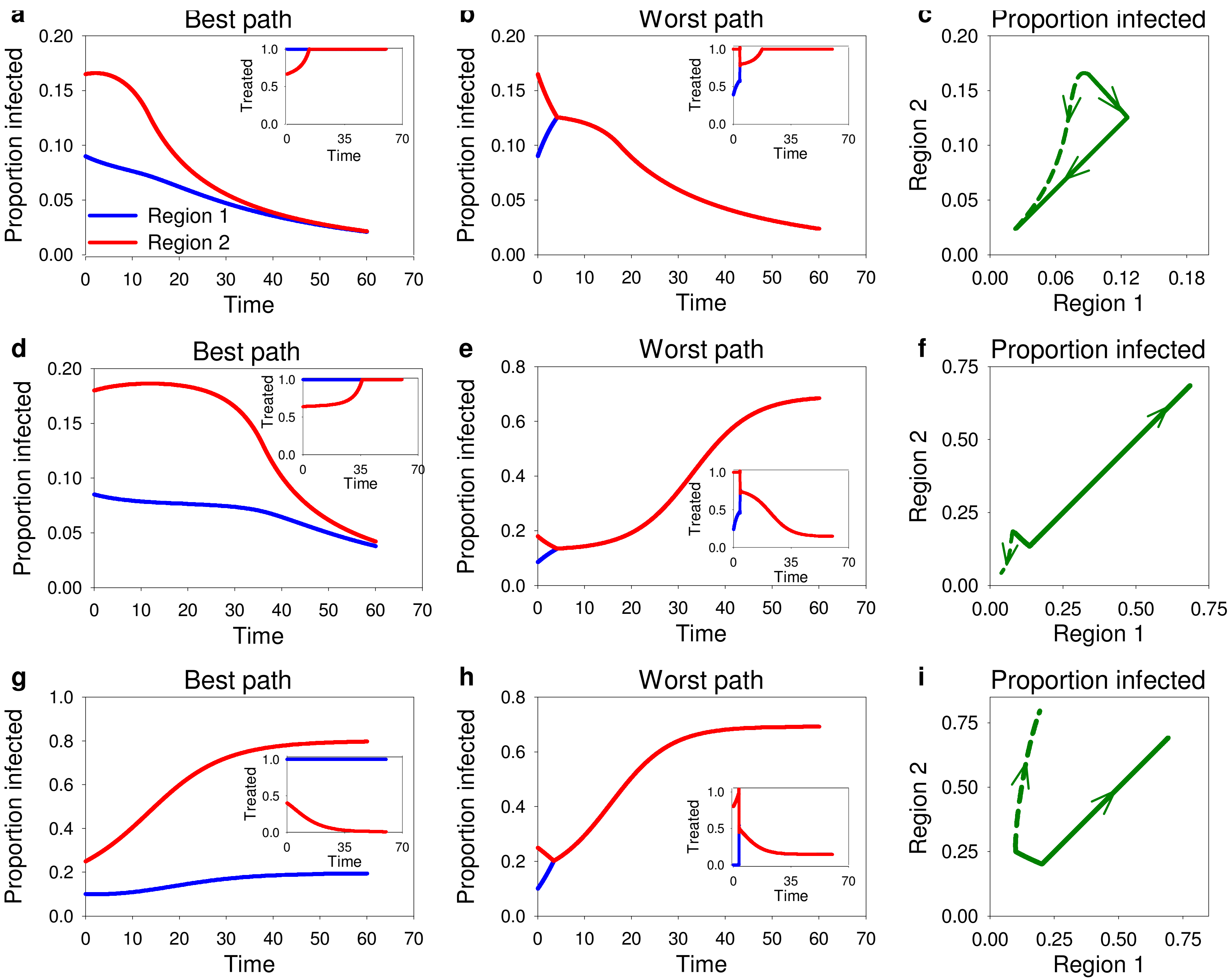
Finance is not transferable through time.

Problem is to choose F_1 and F_2 so as to minimise the following integral

$$V = \int_0^K e^{-rt}\,(I_1 + I_2)\,dt$$

Optimal allocation

- At low levels of infection in both populations
  - Preferentially treat population with higher transmission coefficient because of greater economic value associated with greater potential to prevent secondary infections
- At high levels of infection
  - Preferentially treat population with lower levels of infection since the higher probability of re-infection in high infection populations reduces the economic value of treatment



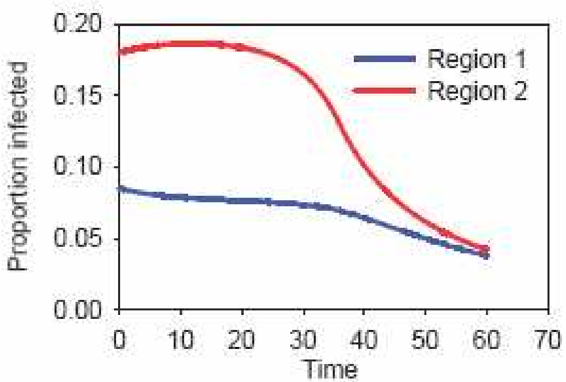
Rowthorn, Laxminarayan, Gilligan *Submitted*

Linking epidemiology and economic modelling

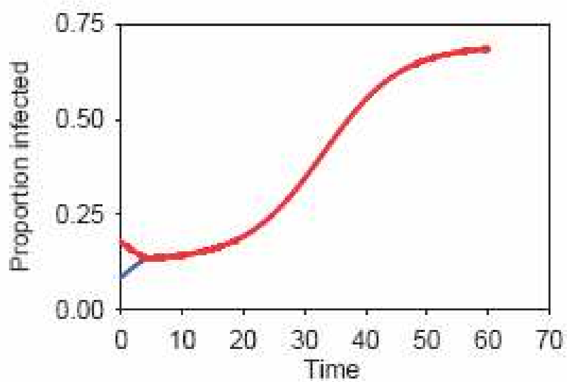
Current analysis: ***intuitive strategies may be seriously in error***

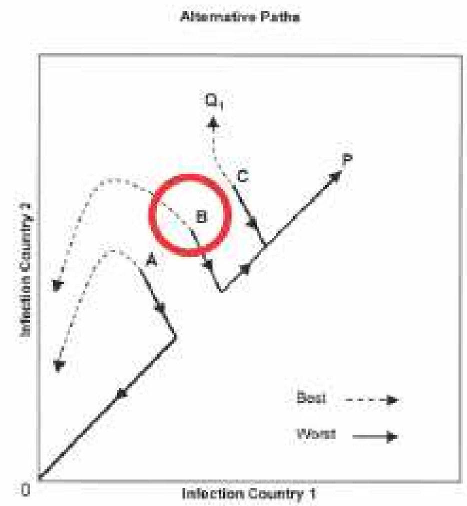
Proportion Infected (*I*)

Best (Strategy 2)



Worst (Strategy 1)





(Time)

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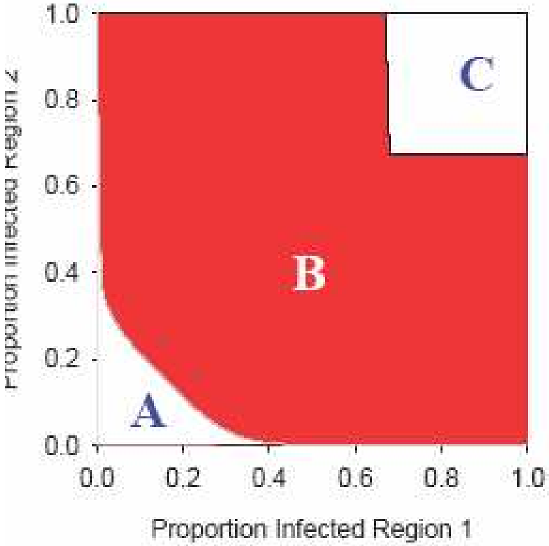
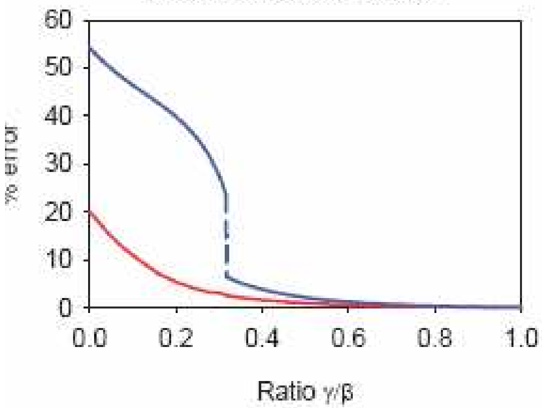
Effect of changing γ on instability zone (B)

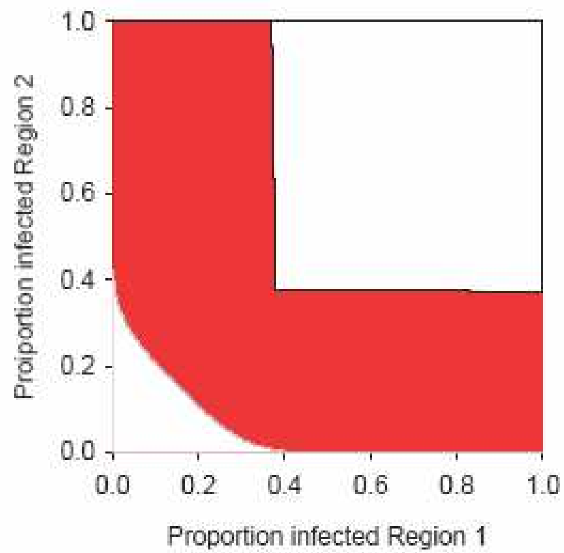
Instability zone for γ / β = 0

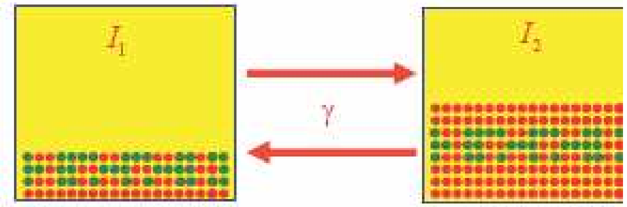


Error caused by worst policy compared with best policy



Instability zone for γ / β = 0.008

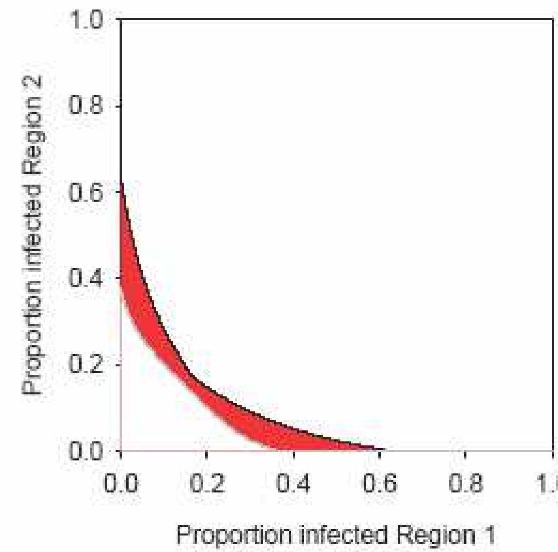




Region 1 **Region 2**

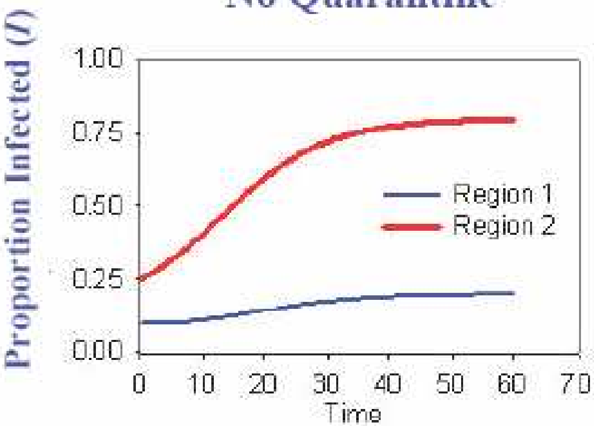
$$\frac{dI_1}{dt} = (\beta I_1 + \gamma I_2)(N - I_1) - \mu I_1 - \alpha F$$

Instability zone for γ / β = 0.02

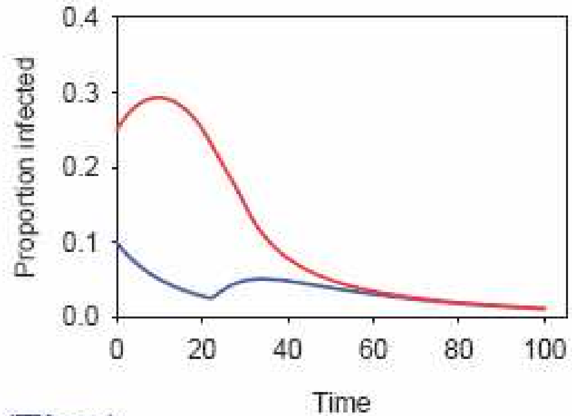


Optimising Quarantine in Zone C

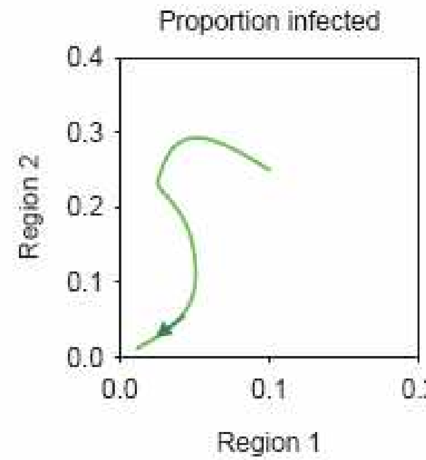
No Quarantine

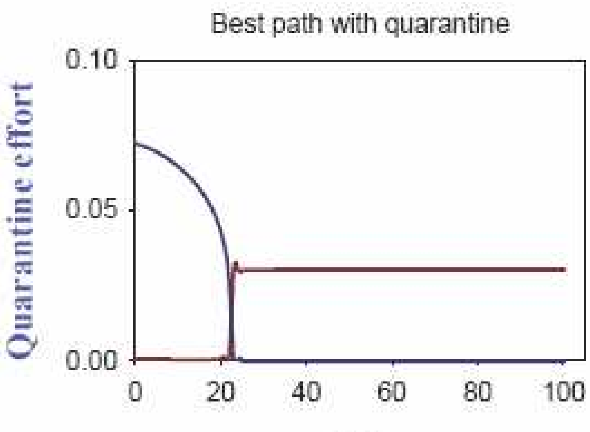


Quarantine



(Time)

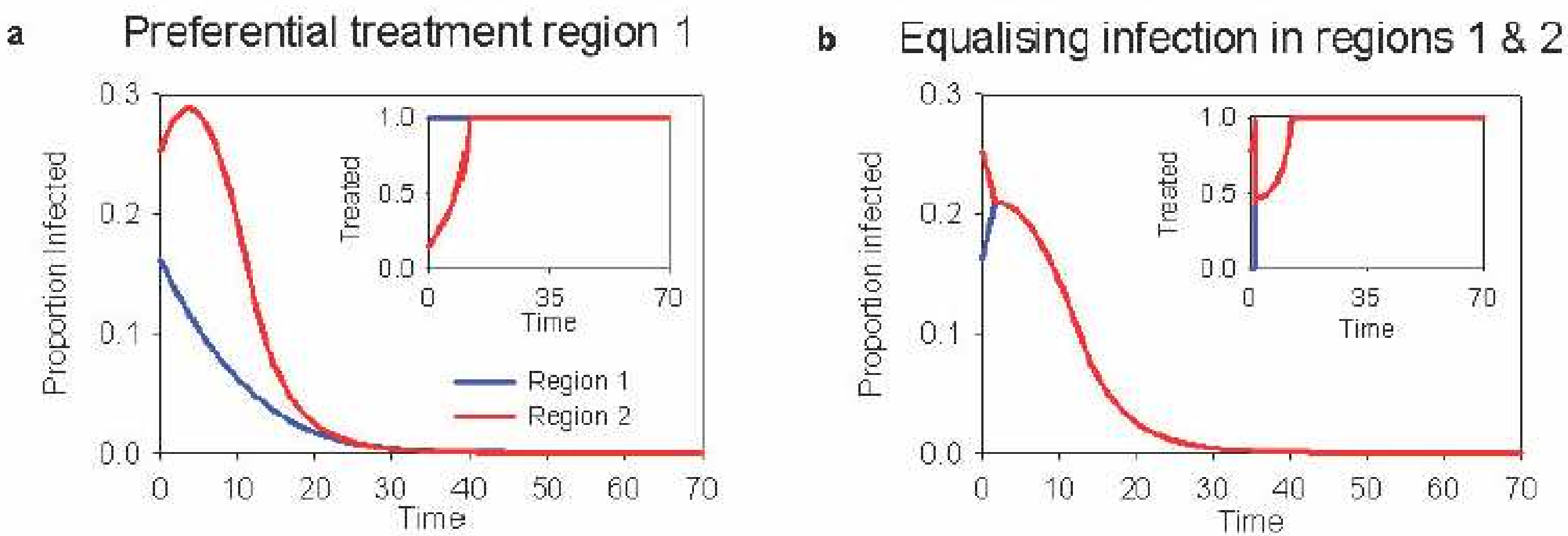




Conclusion

Combination of quarantine with preferential treatment of the less infected region can bring explosive disease under control

Optimising Control strategies: SIR



Conclusion

Preliminary analysis: SIR

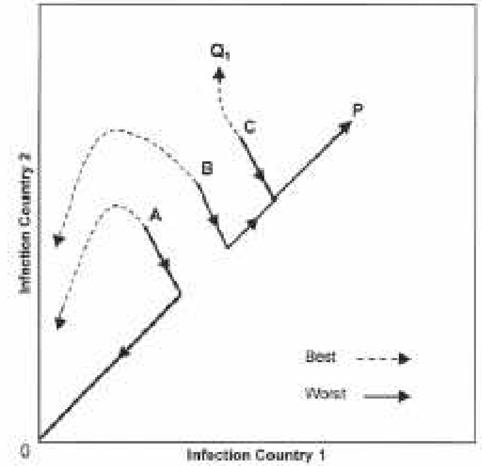
Preferential treatment of region with lowers *I* (& higher *S*) minimises discounted infection

Optimising control strategies

Summary

- Equalising infection in the two regions is the <u>worst</u> possible strategy
- For the <u>best</u> possible strategy: give preference to the less infected region
- A combination of quarantine and preferential treatment of the less infected region can bring explosive disease under control
- The strategy is proved for SIS: appears to hold for SIR

Alternative Paths



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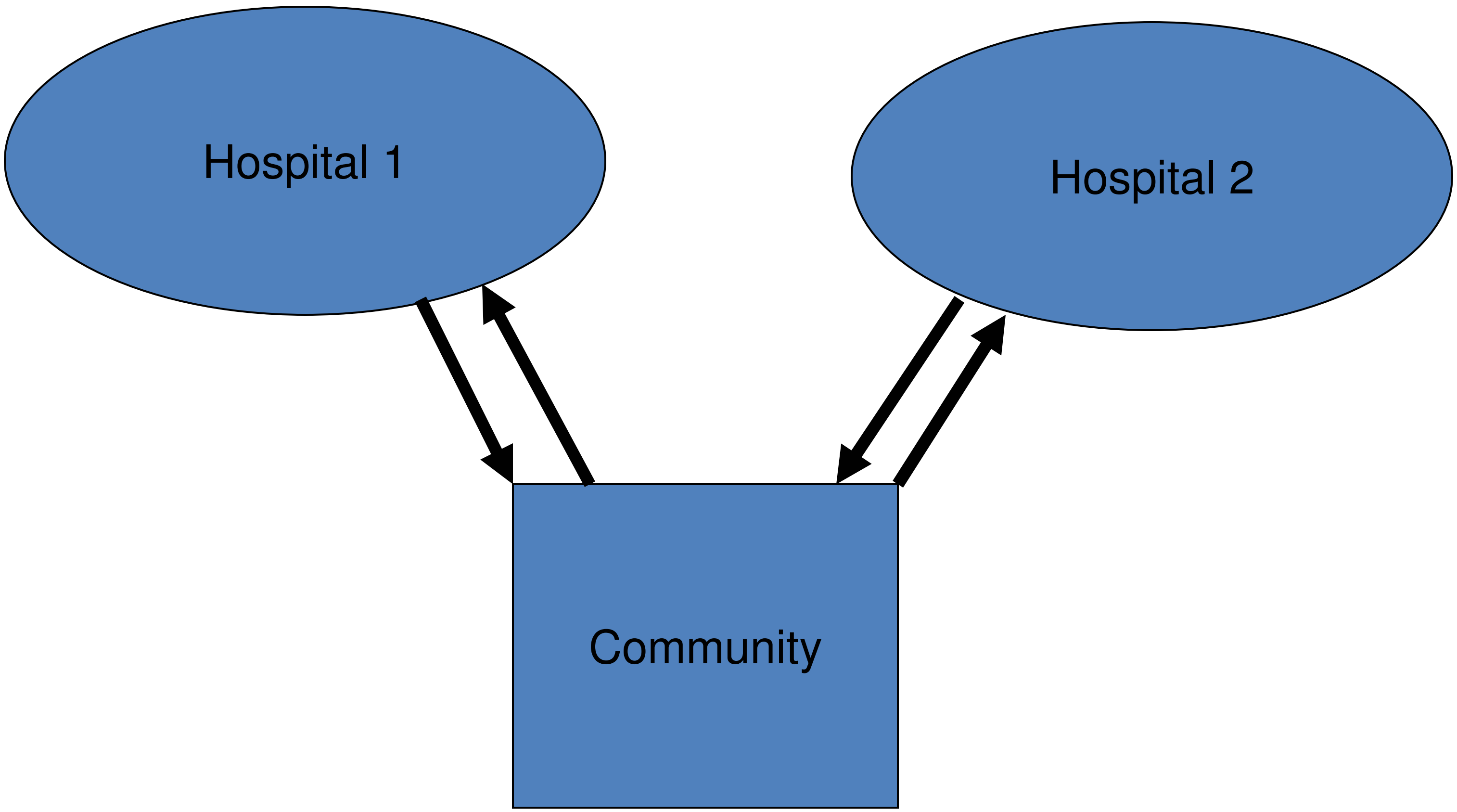
Hospital Infections

- 1.7 million hositalizations associated with an infections
- 99,000 deaths each year associated with these infections
- Burden borne by Medicare/Medicaid and private insurers

Is the scale of the problem the hospital?

- Hospitals are “sources” for colonization with resistant pathogens
- Health facilities often “share” patients (humans are the vector)
- Positive external benefits of active surveillance and infection control


Hospital 1
Hospital 2
Community

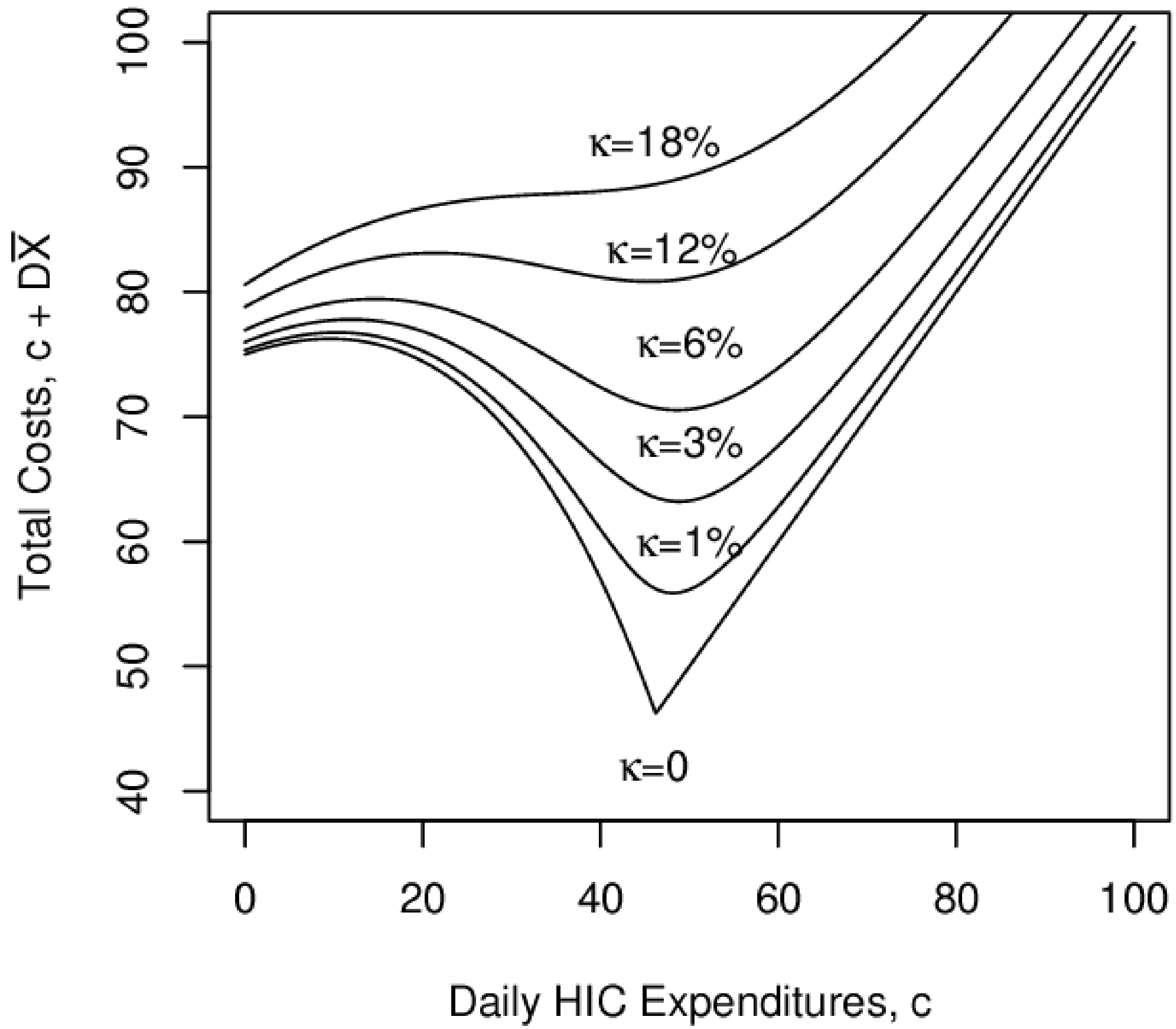
The dynamics are given by

$$\dot{X} = \beta(c)X(1 - X) - \sigma(X - \kappa), \quad [1]$$

where the superdot denotes the derivative with respect to time. Let $S(c) = \beta(c)/\sigma$ denote the single-stay reproductive number, the number of cases, per case per visit, as a function of expenditures when resistance is absent. $S(c)$ is effectively the basic reproductive, R_0, in this model but not in structured population models (see below and ref. 11). The equilibrium prevalence is given by

$$\bar{X}(c) = \frac{S(c) - 1 + \sqrt{[S(c) - 1]^2 + 4\kappa S(c)}}{2S(c)}. \quad [2]$$

Smith, Levin, Laxminarayan PNAS, 2005



Smith, Levin, Laxminarayan, 2005 *PNAS*

Multi-institution epidemics

$$\dot{X} = \beta(c)X(1 - X) - \lambda X - \sigma(X - Z)$$
$$\dot{Y} = \beta(\tilde{c})Y(1 - Y) - \lambda Y - \sigma(Y - Z)$$
$$\dot{Z} = r(X/n + (n - 1)Y/n - Z) - \lambda Z.$$

Smith, Levin, Laxminarayan, 2005 *PNAS*

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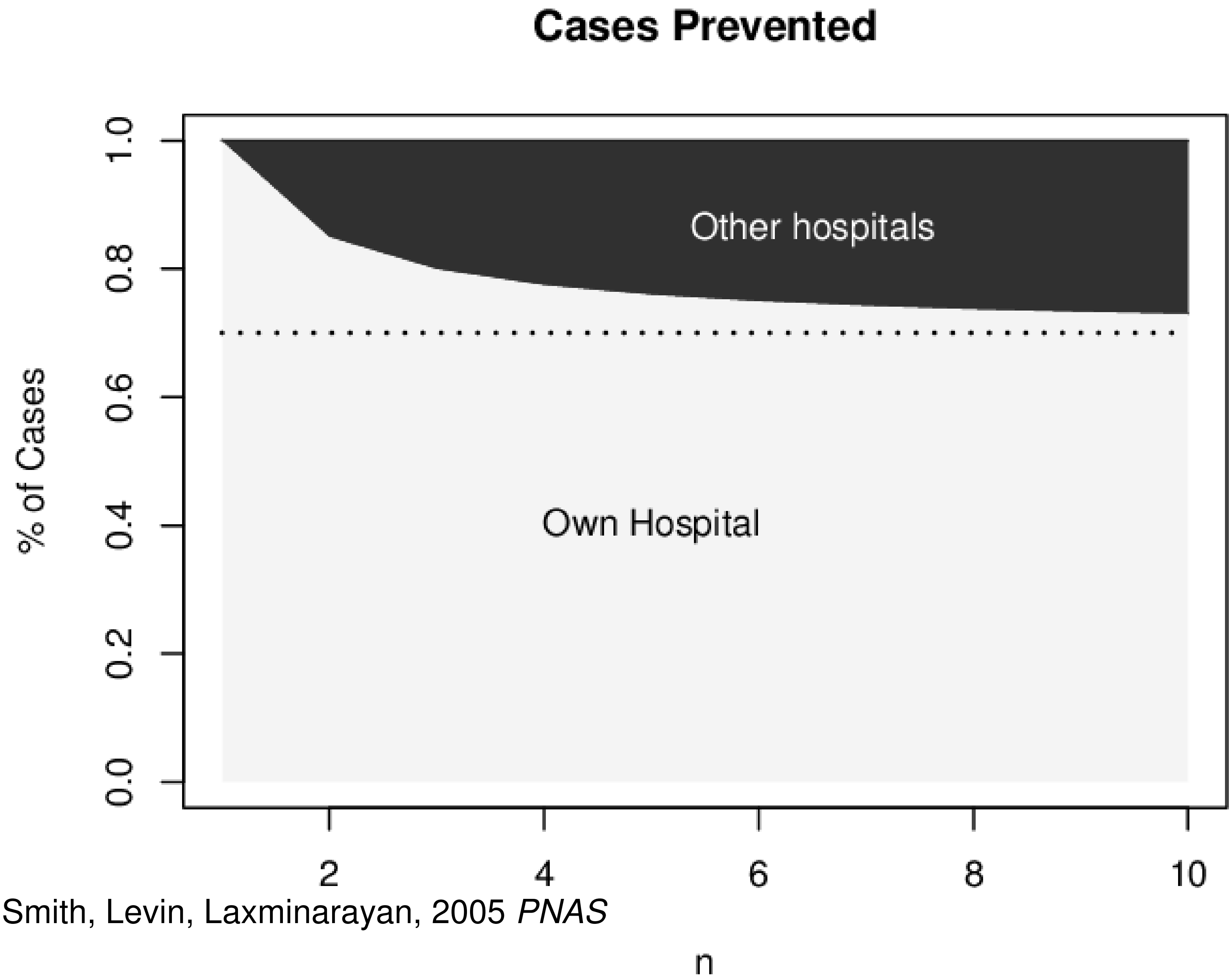

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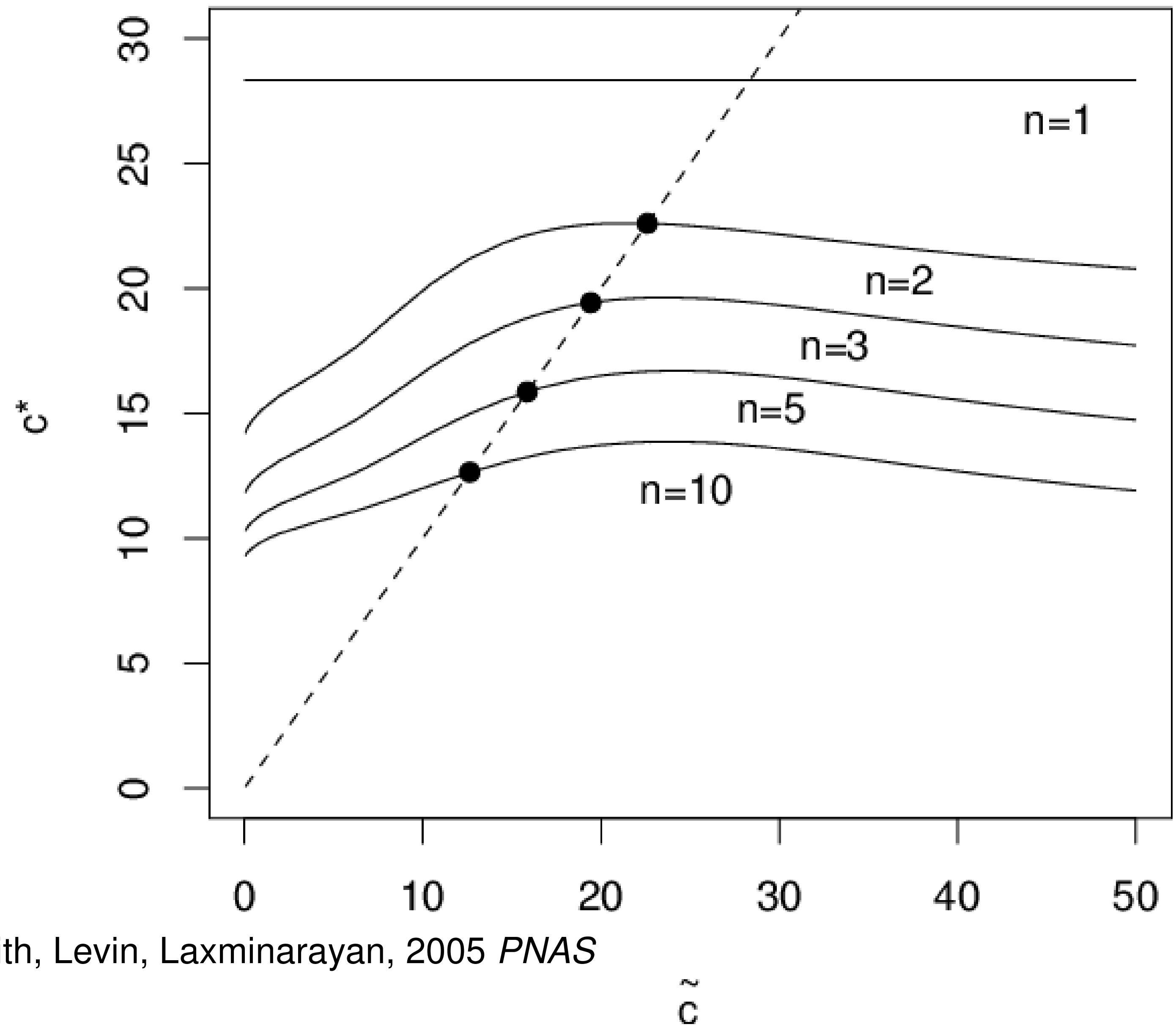

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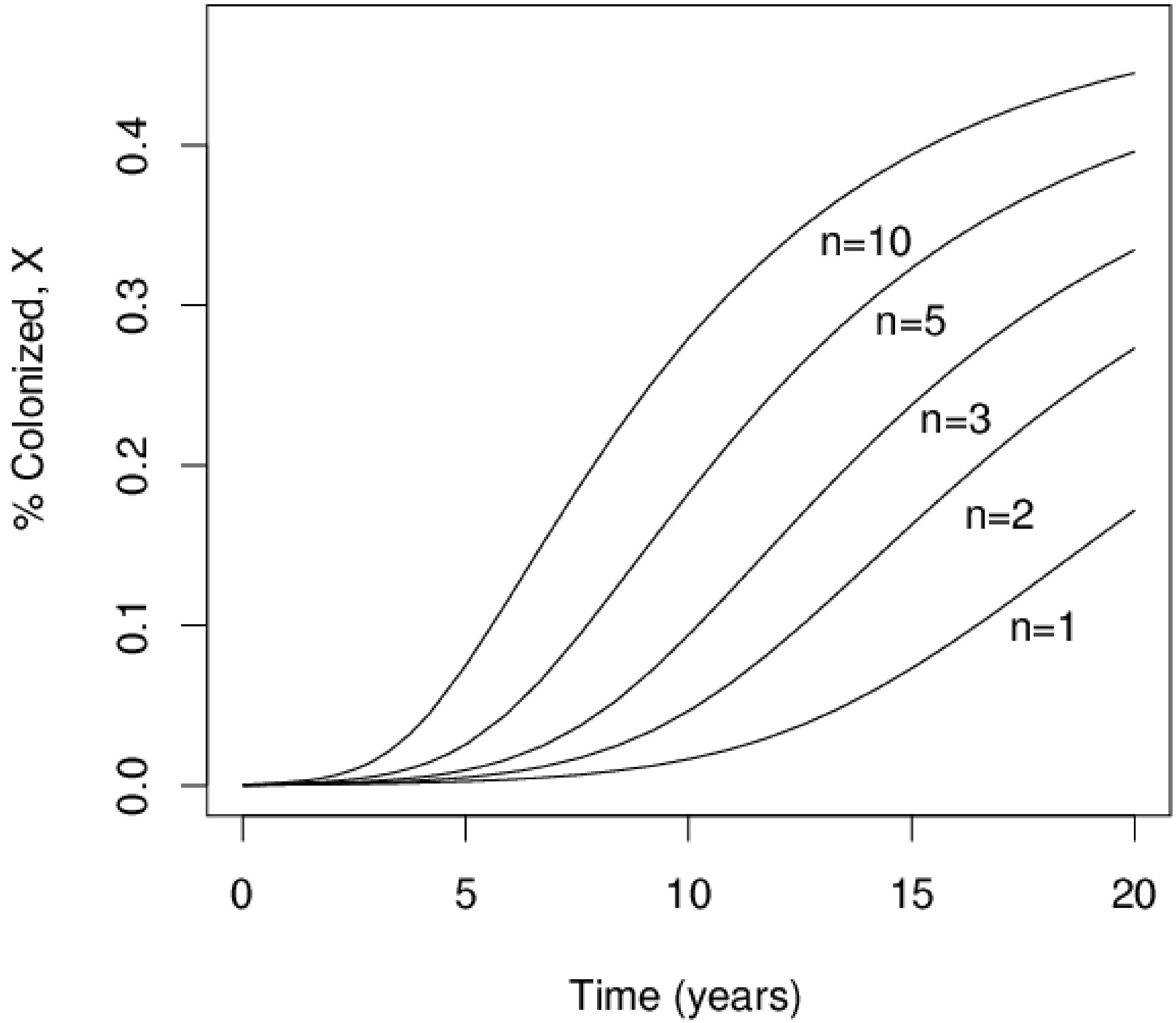
% Colonized, X
0.0
0.1
0.2
0.3
0.4
n=10
n=5
n=3
n=2
n=1
0
5
10
15
20
Time (years)

Regional coordination

- Dutch experience: frequency of MRSA infections is < 0.5% after an intensive ''search-and-destroy'' campaign, compared with 50% in some areas
- In Siouxland (Iowa, Nebraska, S. Dakota), an epidemic of VRE was reversed
- Would this work in the United States with many hospitals all with different ownership?
- Could we pay hospitals to do better?

Disease control and elimination efforts across countries

- With asymmetric countries, it may pay some to eliminate and some not to eliminate (even if all others have), and yet global eradication may be efficient
- The game then becomes one of the richer countries financing elimination in poorer countries

Question

- When is control a strategic substitute across countries and when is it a complement?
  - Both possible depend on disease prevention cost function and epidemiological characteristics

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30

Country incentives for measles control

- Benefits of discontinuing or lowering level of vaccination;
- Cost of achieving elimination;
- Cost and system capacity to maintain surveillance and effective outbreak control;
- Connectivity to other endemic areas and the risk of importation of cases

Post-elimination issues for measles

- Need to maintain a stock of immunity – that is costly to replace in the short run
- Investment in immunity requires continued vaccination
- Risk of bioterrorism related or other introductions will determine optimal investment in maintaining immunity

SIR model with immigration of infecteds

$$\dot{S} = \mu(1-p) - \mu S - \beta SI - \eta S$$

$$\dot{I} = \beta SI + \eta S - (\mu + \nu)I$$

$$\dot{R} = \nu I + p\mu - \mu R$$

Klepac, Laxminarayan, Grenfell, In Progress

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Total cost of vaccination and infection

$$Cost = \begin{cases} c(p) + c_I \bar{I}, & p < p_c \\ c(p), & p \geq p_c \end{cases}$$

$$c(p) = ae^{xp}$$

Klepac, Laxminarayan, Grenfell, In Progress

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Cost minimizing level of coverage

$$p^* = \frac{1}{x} \ln\left(\frac{c_I \mu}{ax(\mu + \nu)} \right)$$

Klepac, Laxminarayan, Grenfell, In Progress

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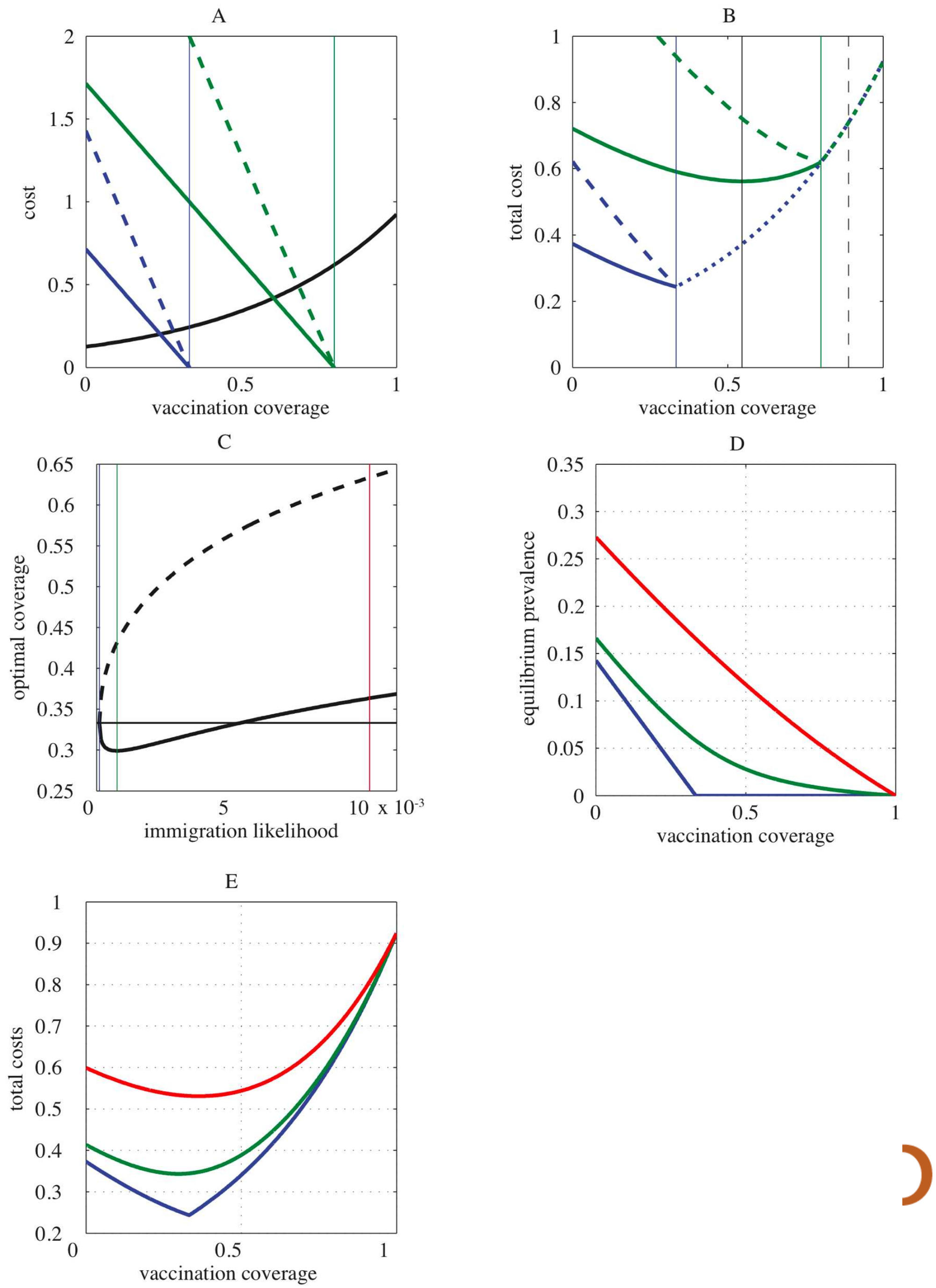

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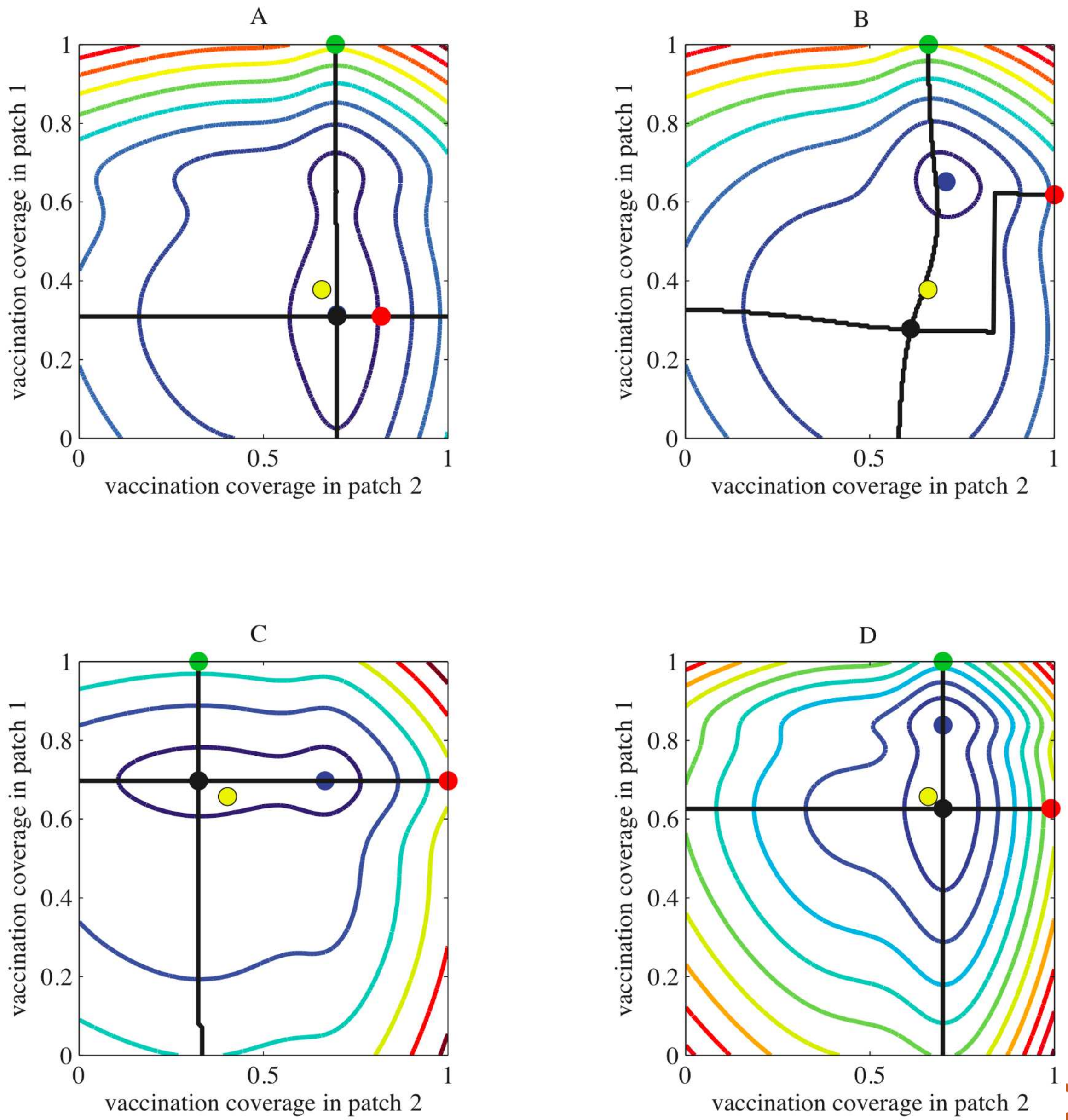
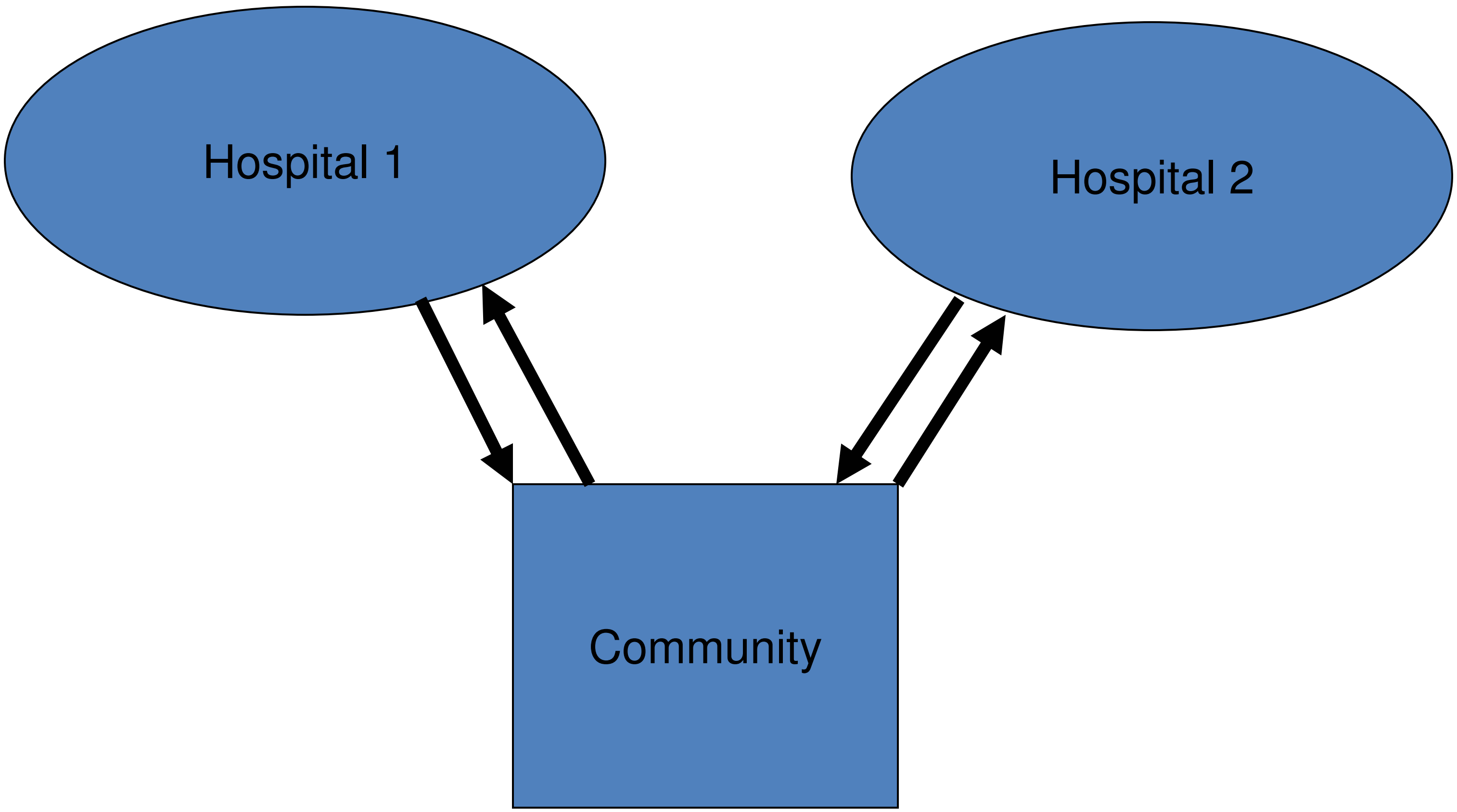

A
B
C
D
vaccination coverage in patch 1
vaccination coverage in patch 2
0
0.2
0.4
0.6
0.8
1
0.5

Bottom line

- With SIR models, no cessation of vaccination after elimination, the criteria for optimal coverage are purely economic
- With any level of immigration of infecteds, elimination becomes impossible
- Response of optimal coverage to immigration depends on infection costs
- With weak coupling, the Nash equilibrium is close to the global optimum. Opposite is true for strong coupling

Competitive outcome

- Depends on whether disease control is a strategic substitute or complement across countries
- Both possible depend on disease prevention cost function and epidemiological characteristics


Hospital 1
Hospital 2
Community

Subsidies for infection control results in…

- Greater infection control in the subsidized hospital
- Indirect network effect on unsubsidized hospital
- Which hospital to subsidize depends on economic returns to infection control within that hospital

How do hospitals respond to an infection control subsidy?

Cooperators

Spend *more* than they would have without subsidy

Free riders

Spend *less* than they would have without subsidy (but overall infection control increases to small extent)

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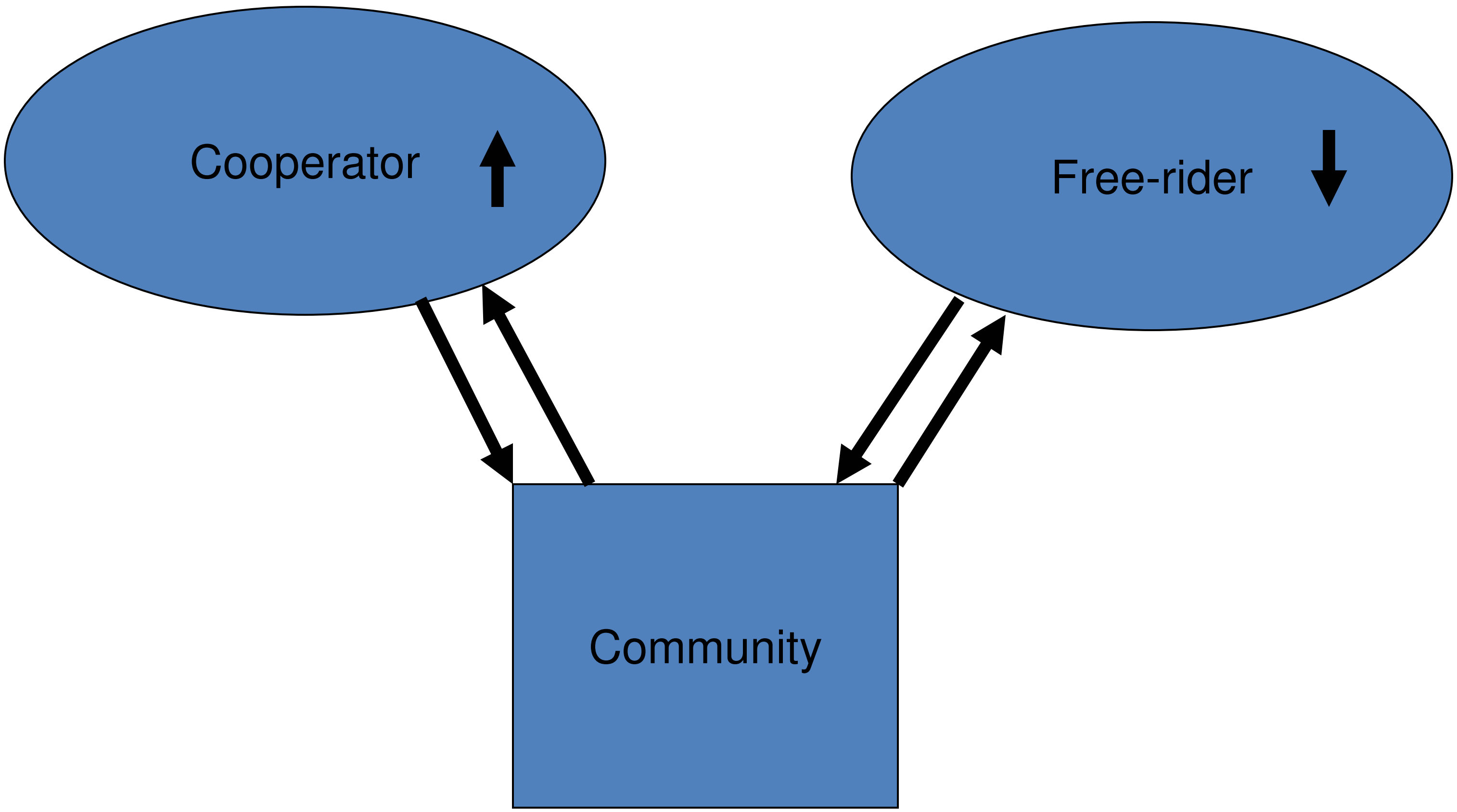
How do hospitals respond to greater infection control in other hospitals?

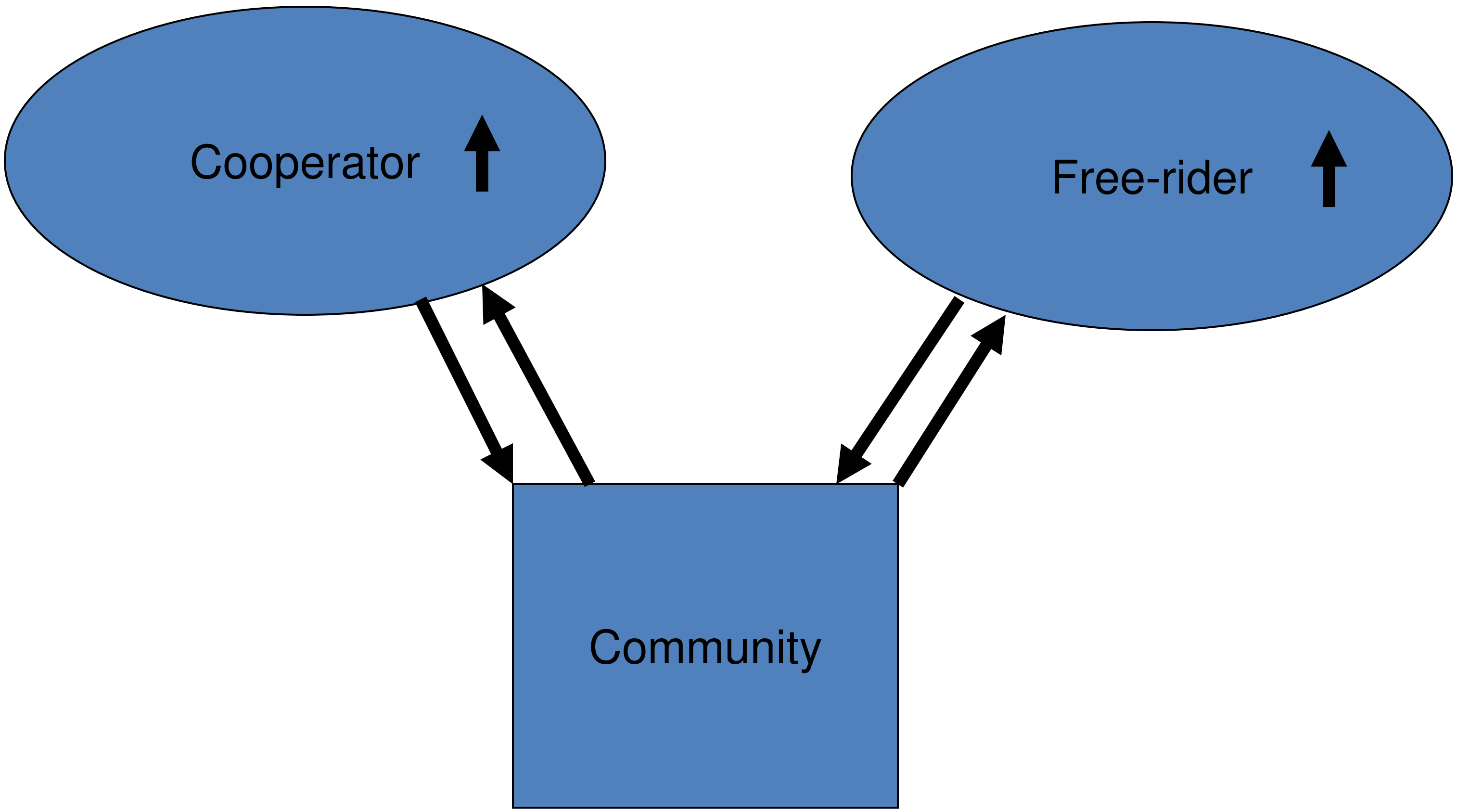
Cooperators

Increase infection control

Free riders

Lower infection control


Cooperator
Free-rider
Community


Cooperator
Free-rider
Community

Result

A. Subsidizing cooperators increases their infection control but decreases infection control in free-riders

B. Subsidizing free-riders makes a small difference to their infection level but increases infection control in cooperators

Final thoughts

- Control of infectious diseases involve challenges in the coordination in the supply and management of local, regional and global public goods
- Challenge is in incentivizing sub-populations to behave in ways that are consistent with local, regional or global interests
- Useful application of game theory to infectious disease models

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