Parameter Uncertainty

Sensitivity analysis:
deterministic epidemic models

- So far, have dealt with reasonably simple models

- Few state variables and, critically, few parameters
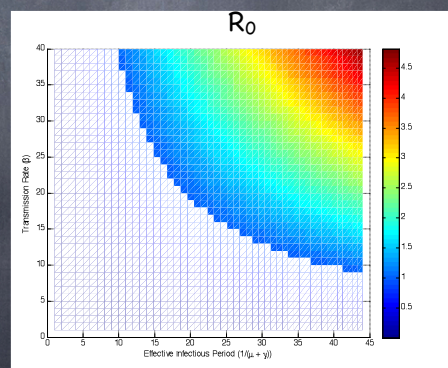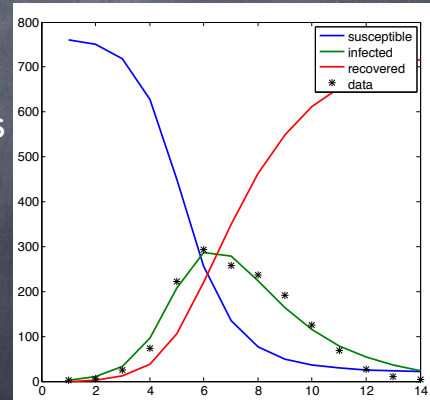
Sensitivity analysis: deterministic epidemic models

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- Complex models have many parameters about which we have little information

Motivation

- In 2000, ~30% of gay men in San Francisco were infected with HIV, 50% of whom were taking combination antiretroviral therapy (ART)

- ART effective at reducing AIDS death rate in San Francisco, but does not completely eliminate infectivity

  - unclear whether net effect of increased distribution of ART would be to increase or decrease incidence of HIV

- Blower et al. introduced following model (Blower, S.M., et al. 2000. A tale of two futres: HIV and antiretroviral therapy in San Francisco. Science 287:650-654.)

Blower et al. (2000) model
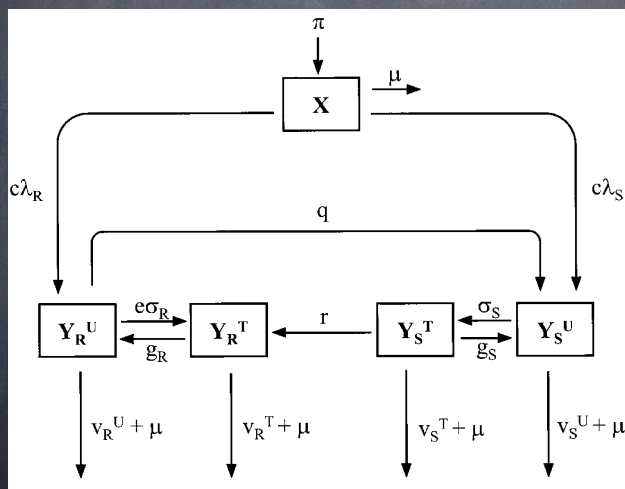
X -- susceptible
Y_R^U -- untreated, infected with drug-resistant strain etc

Lots of model parameters

- π -- rate at which gay men join sexually active community

- $1/\mu$ -- average time during which new partners are acquired

- c -- average number of new sex partners per year

- p -- probability of a drug-resistant case (relative to a drug-sensitive case) transmitting drug-sensitive viruses

- 1/q -- average time for an untreated drug-resistant infection to revert to a drug-sensitive infection

- σ -- per capita effective treatment rate

- e -- relative efficacy of ART in treating drug-resistant infections

- r -- rate of emergence of resistance due to acquired resistance

- g -- proportion of cases that give up ART per year

- ν -- average disease progression rate

Model predictions
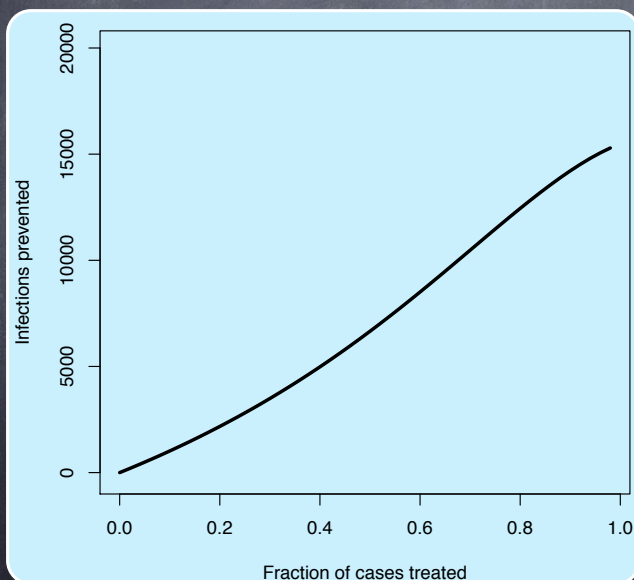
- ART could prevent ~15,000 cases of 20 years

- How reliable is this?
- Model has 20 parameters
- Few (if any) known exactly

Sensitivity analysis: deterministic epidemic models

- To know <u>robustness</u> of model predictions, require a way of exploring output of a family of parameterized models

- If number of unknown parameters is bigger than, say, 2 then systematic grid search would be computationally intractable

- Qualitatively investigate variability in model output that is generated from uncertainty in parameter inputs

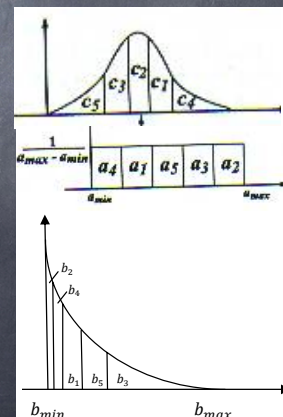- Perform multiple model evaluations using randomly chosen values for parameters

Monte Carlo analysis

- Assume parameters described by specific distribution and split parameter space into equal width intervals

- Then choose one from each interval
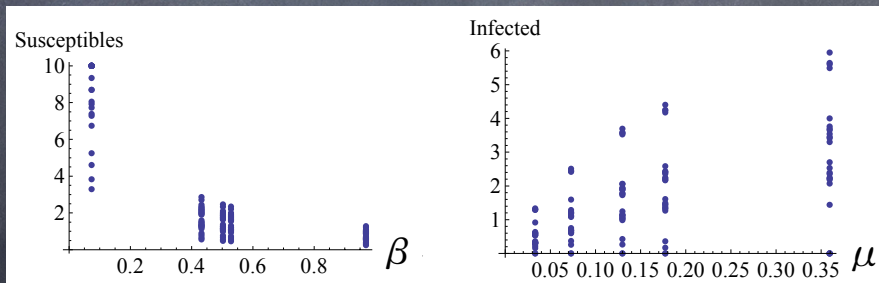
$0 < \beta < 10$ Normal distribution

$1/7 < \gamma < 1$ Uniform distribution
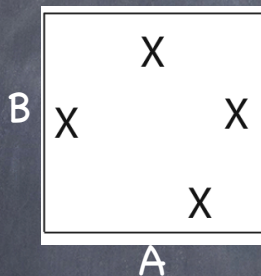
$0 < \mu < 1/2$ Beta distribution

Monte Carlo analysis

- Using parameter combinations determined by Monte Carlo simulation, examine scatter plots of output against each parameter

Susceptibles

Infected

β

μ

- Problem: for SIR model, if we choose 5 random values for each parameter, need to perform 5^3 computations

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Assume 2 unknown parameters

B

A

B

A
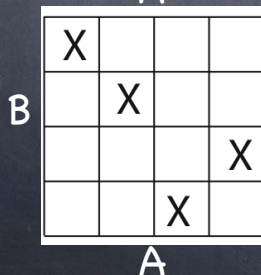
In **random sampling**, new sample points are generated without taking into account previously generated sample points

    eg, for i=1:10

        A(i) = rand*(Amax – Amin) + Amin;
        B(i) = rand*(Bmax – Bmin) + Bmin;
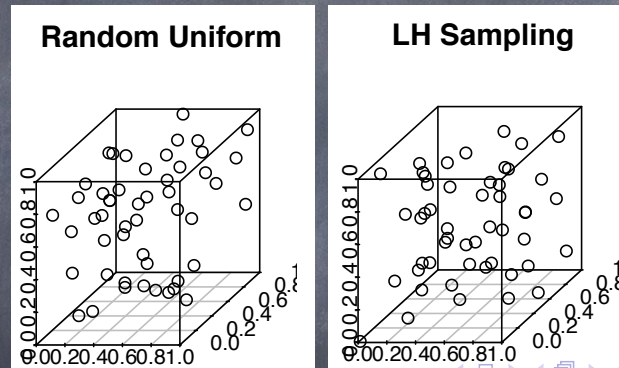   end

In **Latin Hypercube sampling** one must first decide how many sample points to use and for each sample point remember in which row and column sample point was taken
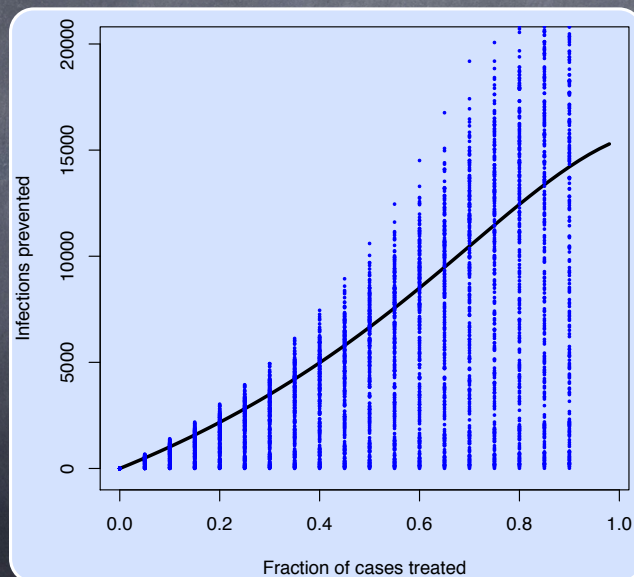
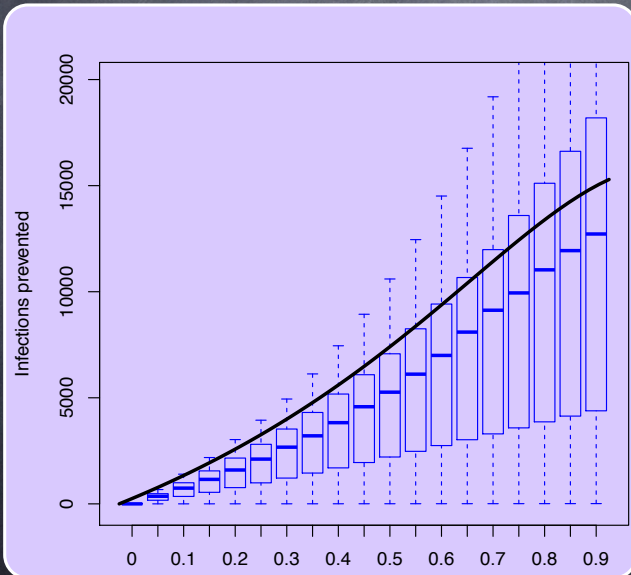Programs available for use in R & Matlab

LHS

Random Uniform

LH Sampling

Typically, LHS random numbers in unit interval (0,1)
Need to 'stretch': A = LHS_rand*(Amax–Amin)+Amin

Results of LHS
Specified ranges of 18 parameters
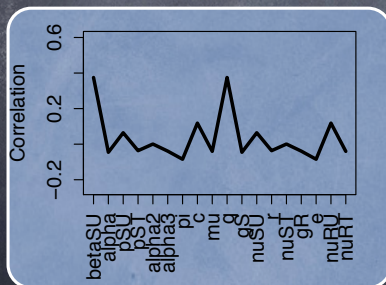
Box-Whisker plot

Evidently, our best guesses at parameter values are somewhat optimistic

At least ART is not found to be counter-productive in this respect → an open question at time of this study
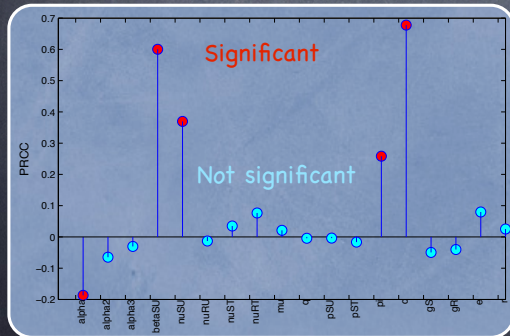
Which parameters important?

- Can explore correlation between vectors of parameters studied and outcome of interest (in this case, # cases prevented)

Can further use partial rank correlation to establish sensitivity of conclusions to specific parameters

Which parameters important?

- BUT, linear correlation ignores fact that model output for each value of a parameter simultaneously includes changes in other parameters

Can use partial rank correlation to establish sensitivity of conclusions to specific parameters

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Summary

- Important to distinguish between two sources of error in model predictions

  I. Variability: arises from stochasticity in process and measurement

  - solution is to explore many model realizations

  II. Uncertainty: results from absence of information on parameters/processes

  - solution is (efficient) sensitivity analysis