# Parameter Uncertainty

# Sensitivity analysis: deterministic epidemic models

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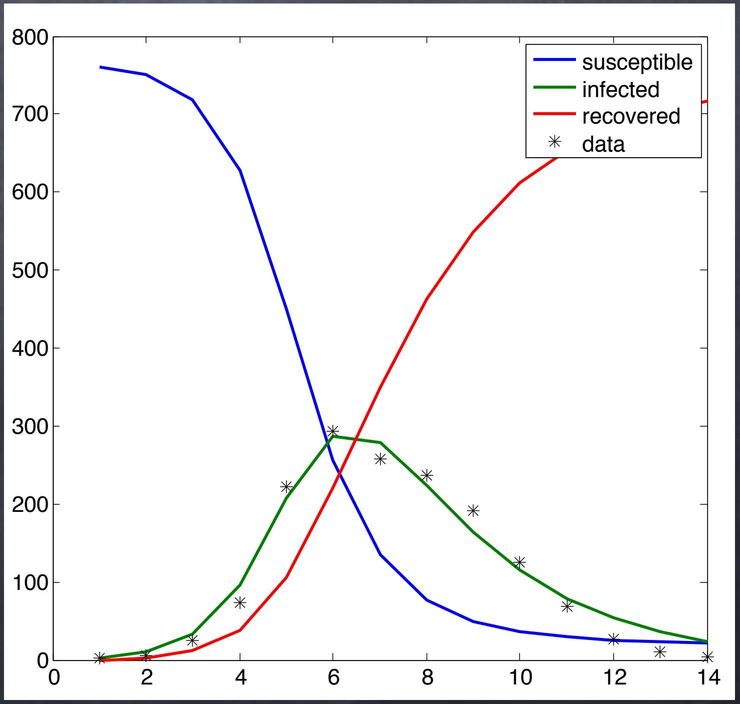


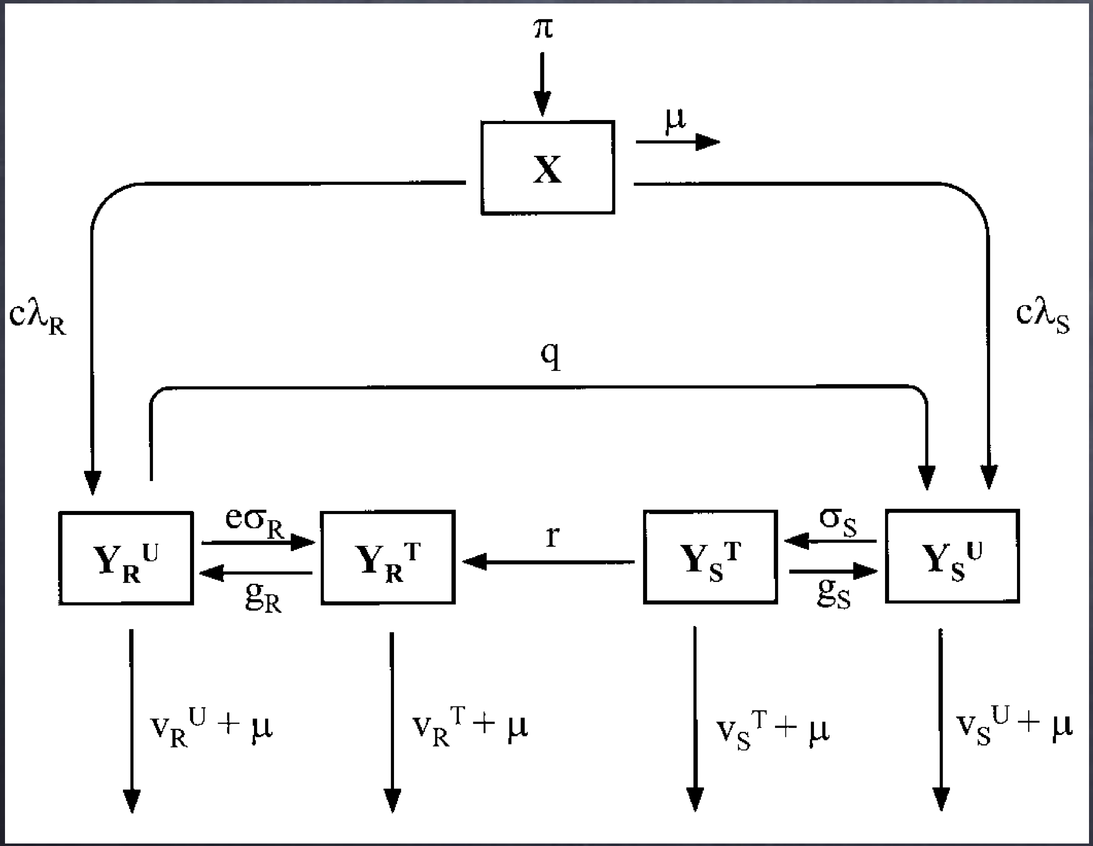
# Sensitivity analysis: deterministic epidemic models

- So far, have dealt with reasonably simple models
- Few state variables and, critically, few parameters
- Resorted to simple(ish) methods for inferring key quantities of interest
- 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



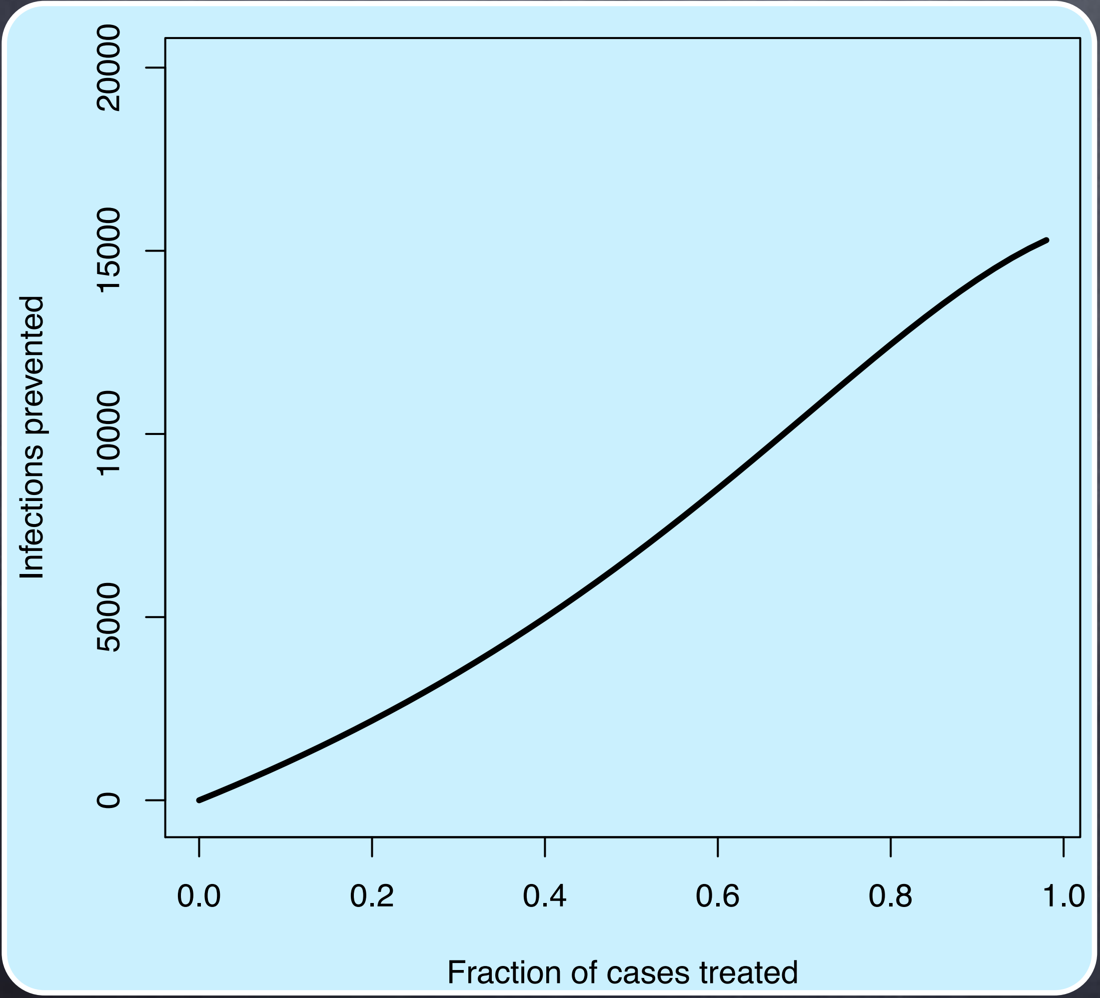

X -- susceptible

$Y_R^U$ -- untreated, infected with drug-resistant strain etc

# Lots of model parameters

- $\pi$ -- 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
- $\sigma$ -- 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
- $\nu$ -- 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 robustness 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

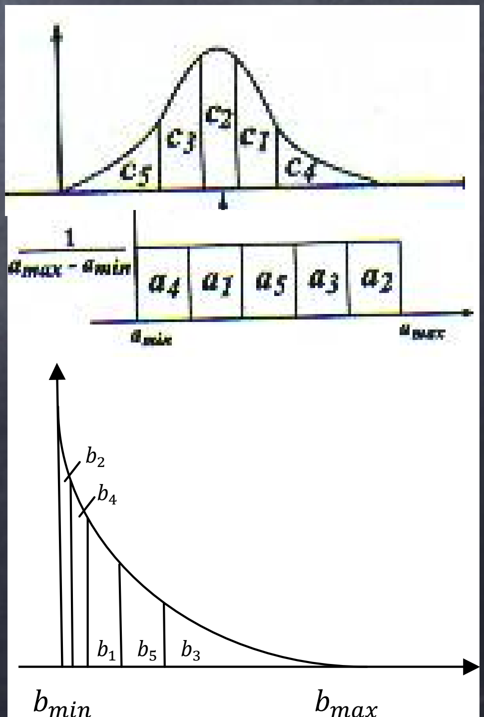
# Monte Carlo analysis

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

$0 < \beta < 10$ Normal distribution

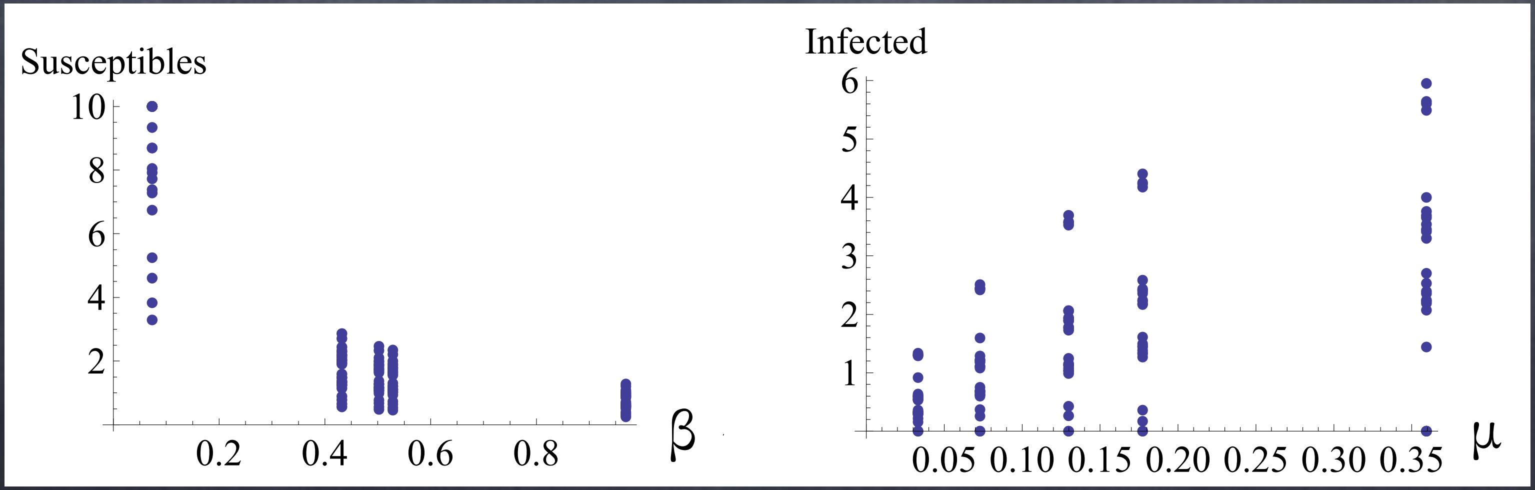
$1/7 < \gamma < 1$ Uniform distribution

$0 < \mu < 1/2$ Beta distribution



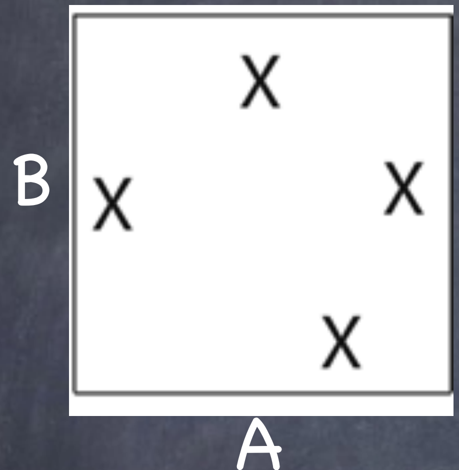
# Monte Carlo analysis

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




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

# Assume 2 unknown parameters



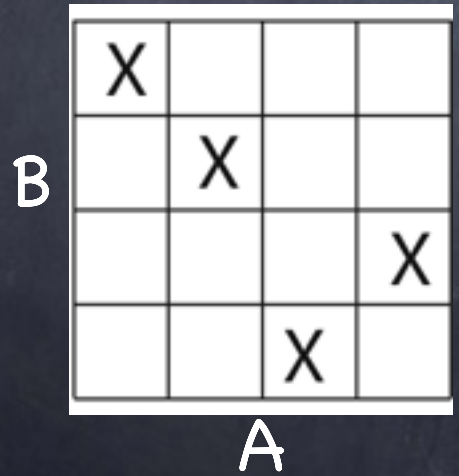

In **random sampling**, new sample points are generated without taking into account previously generated sample points

eg, for i=1:10

$A(i) = rand*(A_{max} - A_{min}) + A_{min};$

$B(i) = rand*(B_{max} - B_{min}) + B_{min};$

end



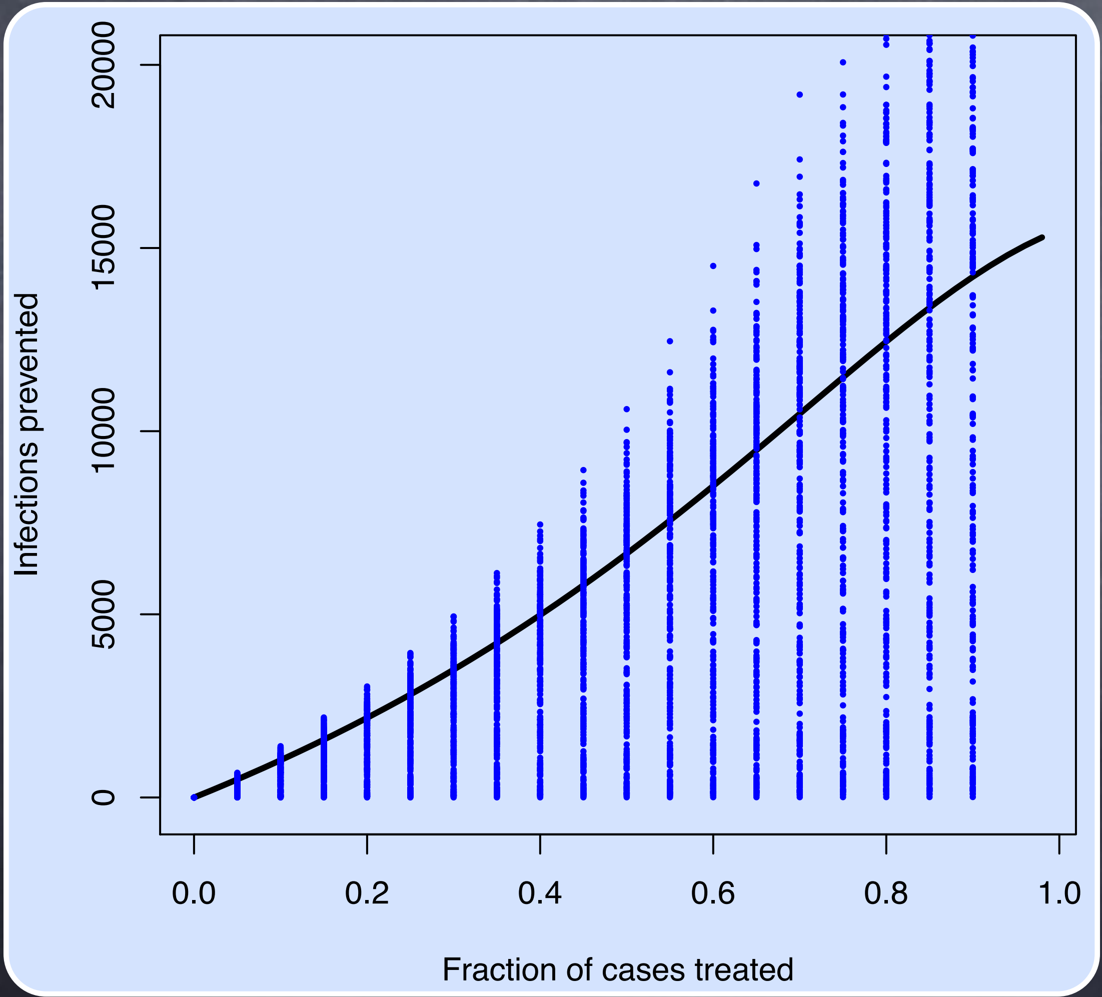

In **Latin Hypercube sampling** one must first decide how many sample points to use and for each sample point remember in which row and column sample point was taken

Programs available for use in R & Matlab

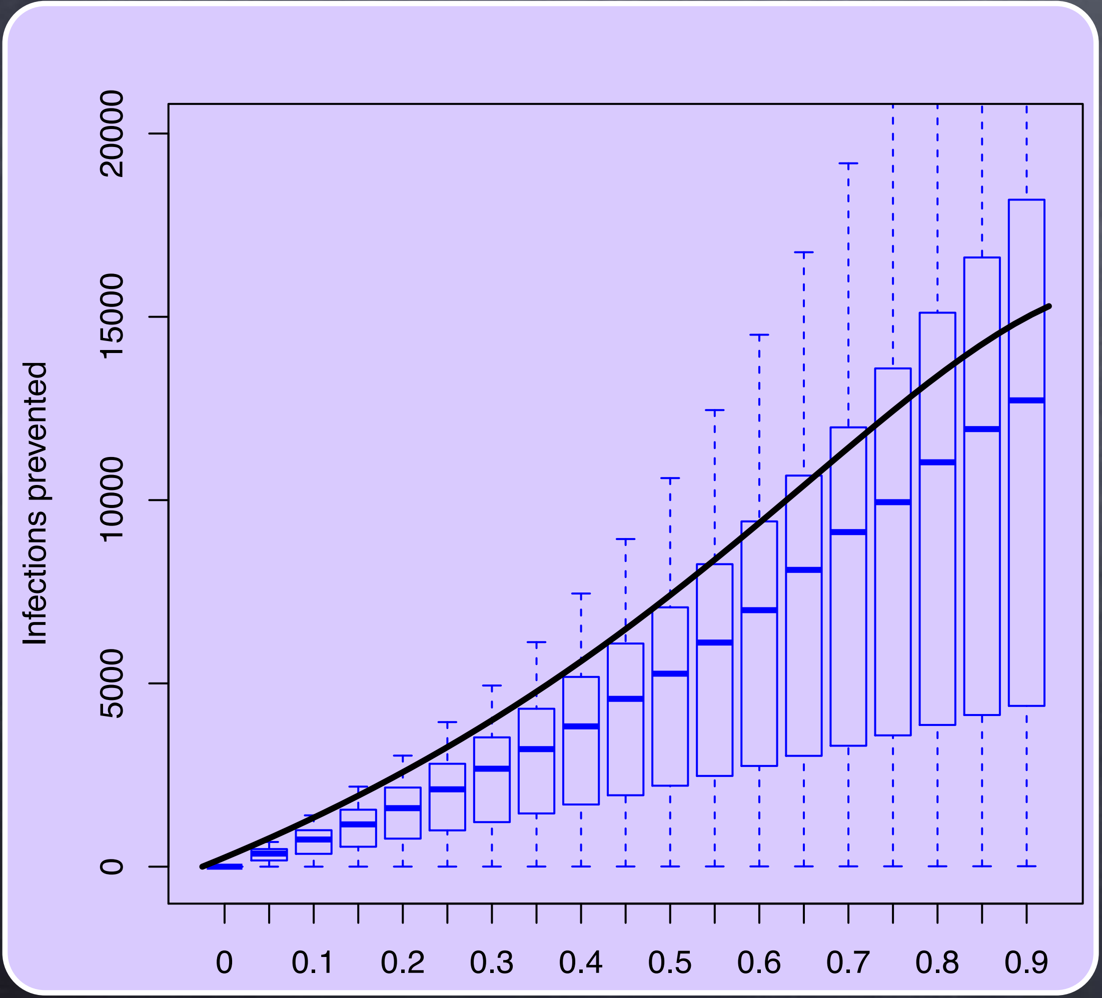
Typically, LHS random numbers in unit interval (0,1)

Need to 'stretch': $A = LHS\_rand*(A_{max}-A_{min})+A_{min}$

# Results of LHS
# Specified ranges of 18 parameters



# Box-Whisker plot

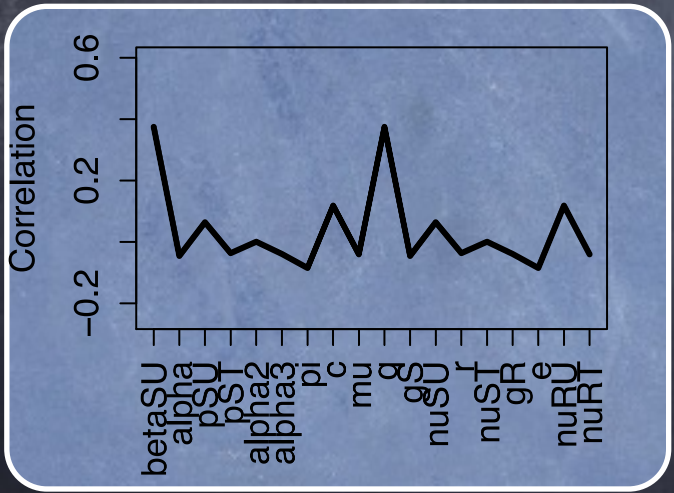



Evidently, our best guesses at parameter values are somewhat optimistic

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

# Which parameters important?

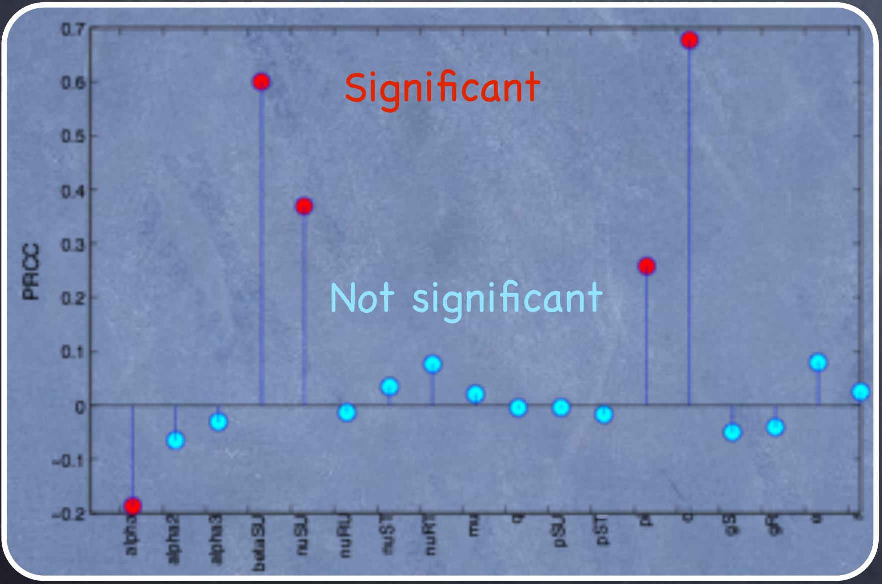
- Can explore correlation between vectors of parameters studied and outcome of interest (in this case, # cases prevented)




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




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

# 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