# Investigating Discrepancy in Computer Model Predictions

Jeremy Oakley[1] and Mark Strong[2]

[1]School of Mathematics and Statistics, and [2]School of Health and Related Research, University of Sheffield

# Application: health economic modelling in medical decision making

- A health-care provider wishes to spend budget efficiently
- Considers both treatment costs and clinical effectiveness
- In UK, National Institute for Health and Clinical Excellence (NICE) decides whether some treatments are available on NHS, based on cost-effectiveness
- Treatment efficacy and costs combined into measure of cost-effectiveness (net-benefit), used for decision-making
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**Model discrepancy**

Model is not perfect. How close is the model prediction to reality?

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- (Almost) required by NICE, referred to as “probabilistic sensitivity analysis” (PSA)

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- We define the model discrepancy as $\delta = Z - f(X)$
- In health economic modelling, do not have data to learn about $\delta$
- What can we say about $\delta$?

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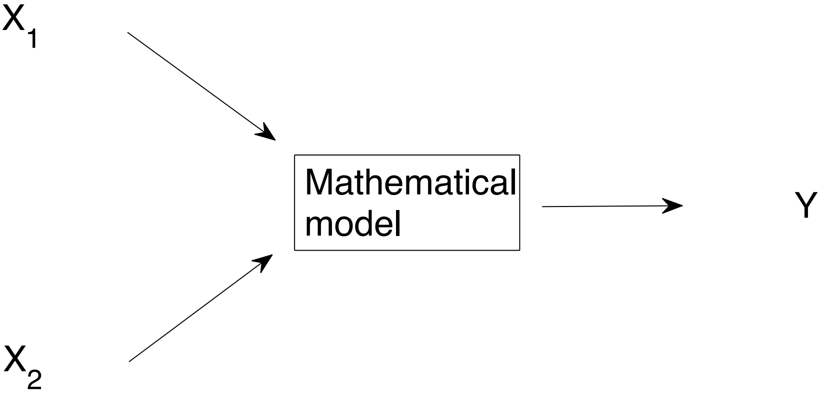
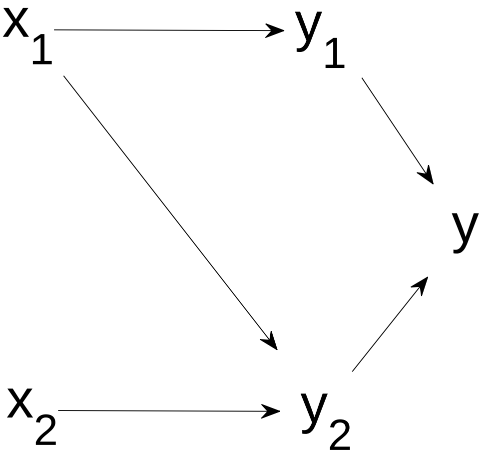
**Our approach**

'Open the black box' and incorporate discrepancy within the model

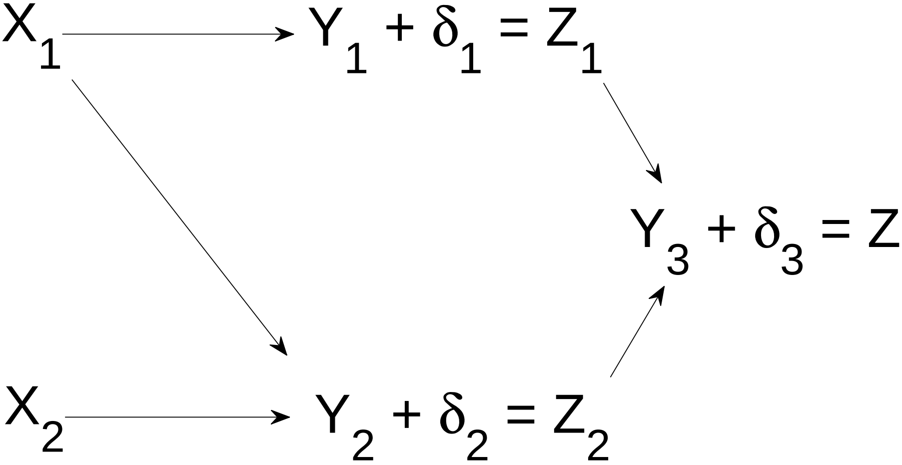
# The model



# Opening the black box



# Linking the model to reality



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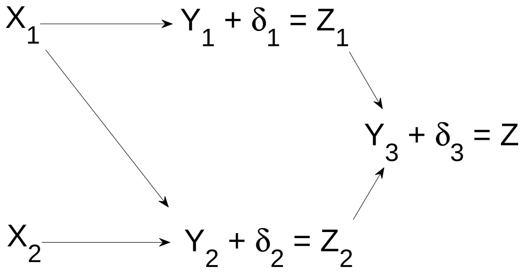

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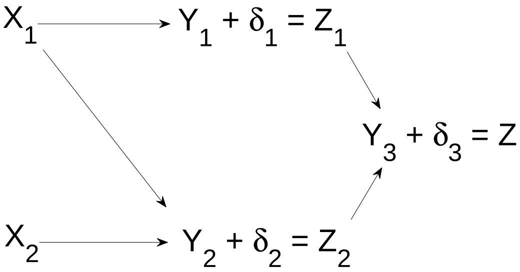


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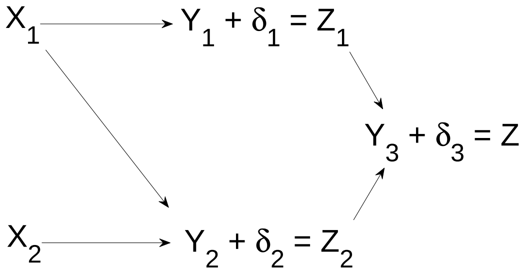


- Specify joint distribution for $X_1, X_2, \delta_1, \delta_2, \delta_3$
- Use variance-based sensitivity analysis to investigate how learning $\delta_i$ would reduce variance of $Z$

$$\frac{Var_{\delta_i}\{E(Z|\delta_i)\}}{Var(Z)}$$

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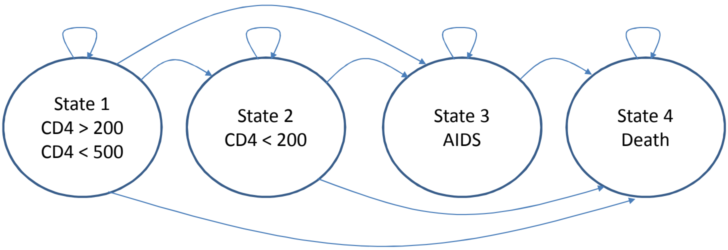
- Same framework of introducing discrepancy parameters within a model
- Now use standard decision theory (expected value of perfect information) for quantifying value of learning discrepancy parameters

# Case study: a Markov model




- Model described in Chancellor et al. (1997)
- Predicts costs and health outcomes for zidovudine monotherapy versus zidovudine plus lamivudine combination therapy in HIV patients
- Patients move between states once per year, for 20 years.

- Uncertain transition matrices for monotherapy

$$M_1 = \begin{pmatrix} p_{111} & p_{112} & p_{113} & p_{114} \\ 0 & p_{122} & p_{123} & p_{124} \\ 0 & 0 & p_{133} & p_{134} \\ 0 & 0 & 0 & 1 \end{pmatrix},$$

and for combination therapy: $M_2 =$

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- But constant $M_1$ and $M_2$ for all times steps is a source of model discrepancy

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- Need to elicit distribution for $\{\Delta_{d,t}\}_{d=1,2;t=1,\ldots,20}$

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$$
\begin{aligned}
h_{d,t} &= (M'_d + \Delta_{d,t})h_{d,t-1}, \\
\Delta_{dt} &= \begin{pmatrix} -(\delta_{d1t} + \delta_{d2t} + \delta_{d3t}) & \delta_{d1t} & \delta_{d2t} & \delta_{d3t} \\ 0 & -(\delta_{d4t} + \delta_{d5t}) & \delta_{d4t} & \delta_{d5t} \\ 0 & 0 & -\delta_{d6t} & \delta_{d6t} \\ 0 & 0 & 0 & 0 \end{pmatrix}.
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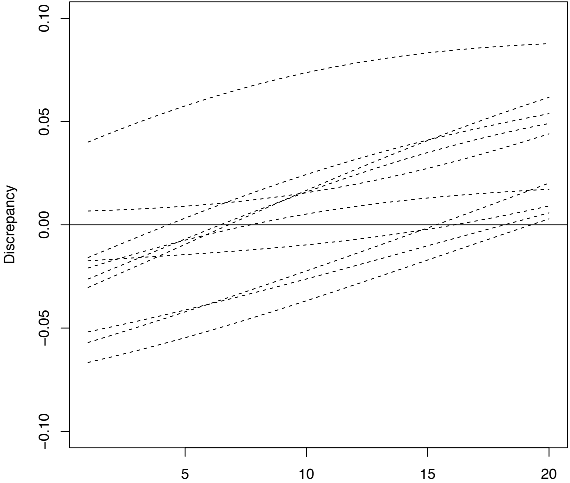
We consider three scenarios. In each case, multivariate normal distribution assumed for $\delta_{d1t}, \delta_{d2t}, \ldots$
For example

$$
\begin{aligned}
E(\delta_{dit}) &= \beta_{0,di} + \beta_{1,di}t \\
Cov(\delta_{dit}, \delta_{d'i't'}) &= \sigma_{di}\sigma_{d'i'}\psi_{d',d'}\phi_{i,i'} \exp\left\{-\left(\frac{t-t'}{\omega}\right)^2\right\}.
\end{aligned}
$$

# Scenario 1: probability of death increases over time

Discrepancy $\delta_{dit}$ for a single transition probability over time



# Scenario 2: efficacy of treatment decreases over time

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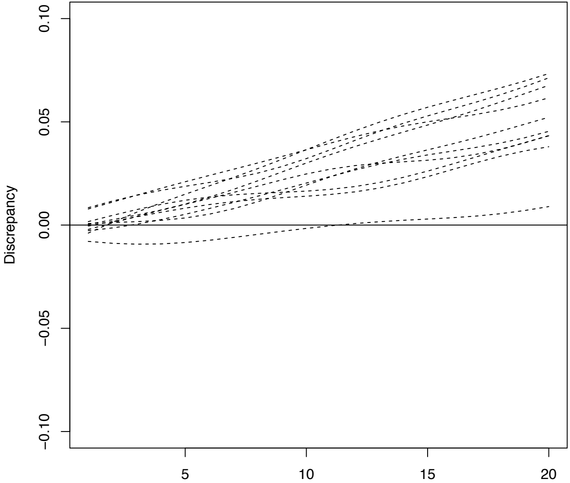

# Scenario 3: ???

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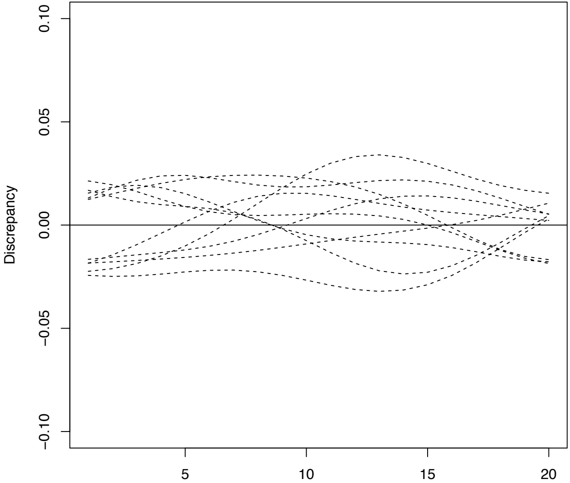

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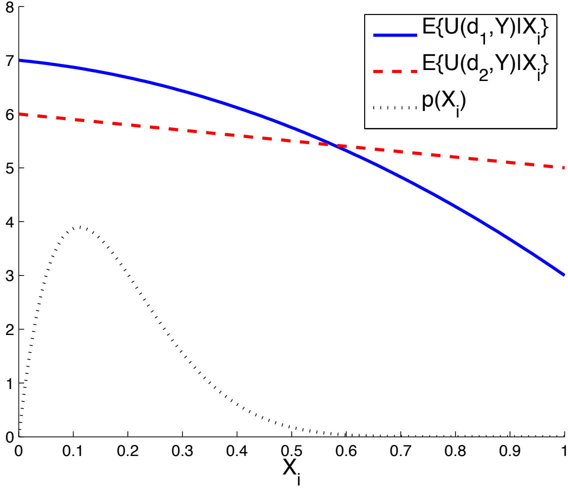
- Expected value of learning $X_i$ before making decision is

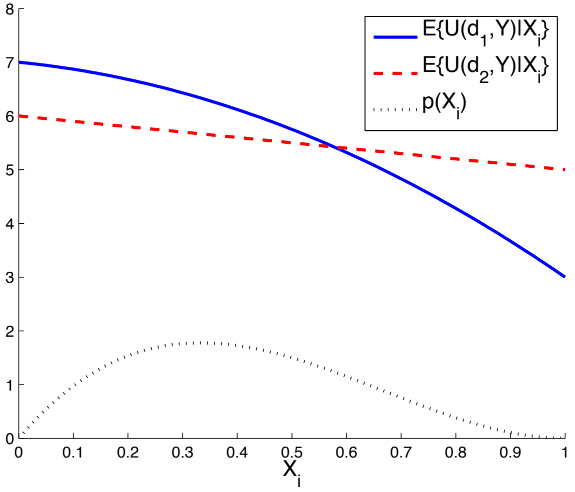
$$E_{X_i}\left[\max_d E\{U(d, Y)|X_i\}\right] - \max_d E_Y\{U(d, Y)\},$$

the **partial EVPI** of $X_i$ (**Expected Value of Perfect Information**)

# partial EVPI example 1



# partial EVPI example 2



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- EVPIs estimated using Monte Carlo sampling (for expensive models can use emulators to get EVPIs, Oakley, 2009)

# Results

- Partial EVPI: expected value in £ per patient of learning parameters, before choosing treatment option for patient population.
- Utility function is the net benefit
  £$\lambda \times$ mean years of life - mean cost per patient
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|---|---|---|---|---|
| | Base case | Scenario 1 | Scenario 2 | Scenario 3 |
| Transition probabilities | £0 | £0 | £0 | £1.17 |
| Relative risk | £169.91 | £193.09 | £64.63 | £164.55 |
| Costs | £194.41 | £201.72 | £65.17 | £167.53 |
| Discrepancy terms | - | £7.86 | £110.21 | £699.06 |
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For larger $\lambda$ (20,000-30,000), all partial EVPIs negligible.

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## And finally...a quick plug!

- Following on from UCM 2010...
- ...Uncertainty in Computer Models 2012
- Sheffield, July 2-4, 2012
- `www.mucm.ac.uk/UCM2012`