A novel approach to calculating confidence intervals for transition probabilities between health states in a cost-effectiveness model using the R package MSM

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R for HTA
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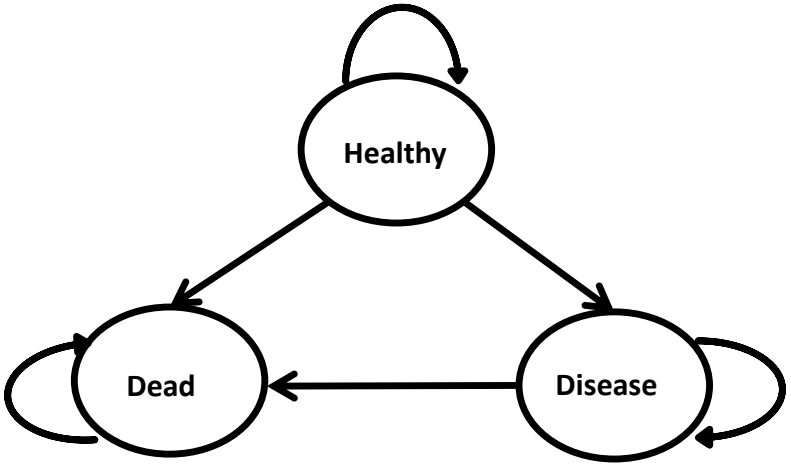
Background



- Cost-effectiveness models usually have a Markov component
- Movements in continuous time – discretise for CE model
- Some trials don't have a lot of data, some have 'full' follow-up
- R package 'msm' Chris Jackson
- More frequent in HTA submissions

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R package ‘msm’

$$q_{rs}(z(t)) = q_{rs}^{(0)} \exp(\beta_{rs}^{T} z(t))$$

- Proportional hazards
- Time varying characteristics z
- Q matrix – instantaneous risk of movements between health states
- P matrix – probabilities of moving between health states at time t
- P matrix is likely to change over time (with time dependent covariates)
  Time dependent covariates are assumed piecewise-constant

$$P(t) = \mathrm{Exp}(tQ)$$

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Jackson, C., 2007. Multi-state modelling with R: the msm package. *Cambridge, UK*, pp.1-53.

Are we making the right choice?

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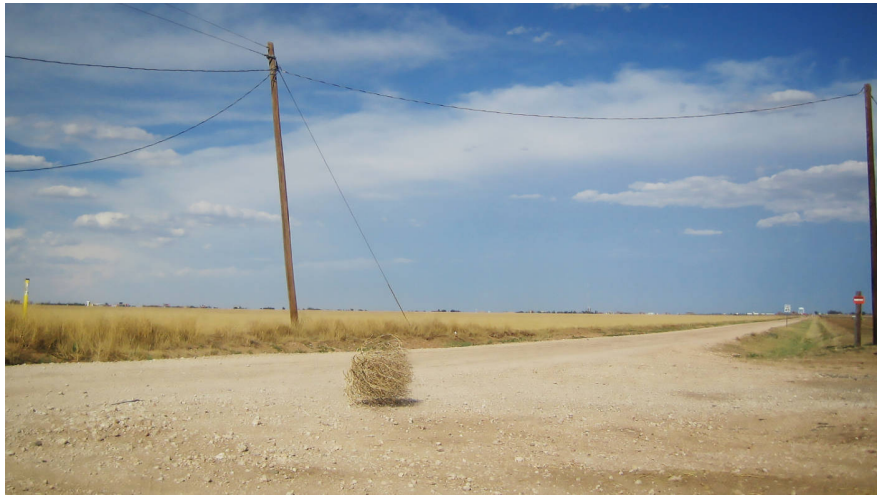
Uncertainty



- Impact of probabilities on cost-effectiveness
- Probabilistic sensitivity analysis
- Variance covariance matrix
- Bootstrapping

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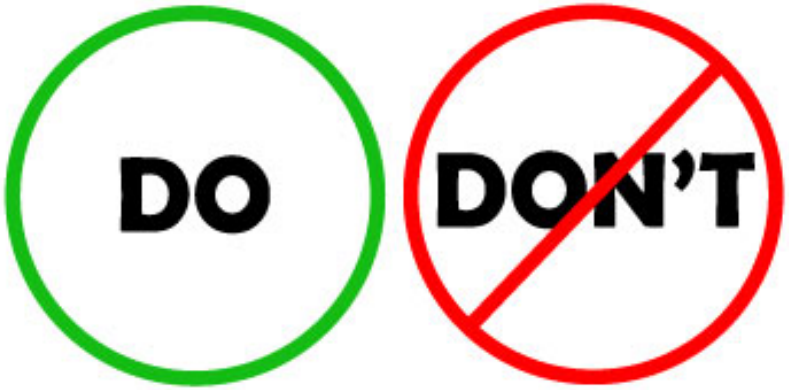
Uncertainty in *msm*



- Add covariates in model one at a time and use previous Q matrix
- Simulate random starting values for each msm model – take the best model
- Use Q matrix upper and lower estimates
- Use the individuals in the cohort

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Example – in *msm*

- Sharples et al. (2003) studied the progression of coronary allograft vasculopathy (CAV), a post heart transplant deterioration of the arterial walls
- 2816 state observations from 614 individuals

- State 1 - no CAV
- State 2 - mild/moderate CAV
- State 3 - severe CAV
- State 4 - death

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Let’s work through this!

- https://github.com/flossybap/R-for-HTA

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References

- Jackson, C., 2007. Multi-state modelling with R: the msm package. *Cambridge, UK*, pp.1-53.
- Jackson, C.H., 2011. Multi-state models for panel data: the msm package for R. *Journal of statistical software*, *38*(8), pp.1-29.
- Sharples LD, Jackson CH, Parameshwar J, Wallwork J, Large SR (2003). “Diagnostic Accu- racy of Coronary Angiography and Risk Factors for Post-Heart-Transplant Cardiac Allo- graft Vasculopathy.” Transplantation, 76(4), 679–682.

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