Developing relevant economic models with R for health technology assessment
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What is a relevant model?

> Based on available clinical evidence
> Quantifies decision uncertainty
> Transparent and reproducible
> Reusable and adaptable
Building an economic model for decision analysis

Example: a multi-state model in oncology

> 3 transitions where $h^{rs}(u)$ is the time-varying hazard for transitions from state $r$ to $s$ as a function of time $u$

1. Stable $\rightarrow$ Progression
2. Stable $\rightarrow$ Death
3. Progression $\rightarrow$ Death

> 3 health states
1. S1: Stable disease
2. P1: Progressed disease
3. D: Death
Parameterizing multi-state models

<table>
<thead>
<tr>
<th>Statistical method</th>
<th>R package</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Network meta-analysis</td>
<td>rjags/rbugs/rstan</td>
<td>Summary data from RCTs</td>
</tr>
<tr>
<td>Parametric &amp; spline models</td>
<td>flexsurv</td>
<td>Continuously observed processes</td>
</tr>
<tr>
<td>Non-parametric and semi-parametric models</td>
<td>mstate</td>
<td>Continuously observed processes</td>
</tr>
<tr>
<td>Exponential and piecewise exponential models</td>
<td>msm</td>
<td>Panel data</td>
</tr>
</tbody>
</table>

Fitting a multi-state Weibull model with flexsurv

```r
fit_weib <- flexsurv::flexsurvreg(Surv(years, status) ~ factor(strategy_id) * trans + shape(trans), data = mstate_data, dist = "weibull")
```

A “clock reset” model

hesim: a new R package for integrating statistical and economic models for decision analysis

Economic models are constructed by combining statistical models for disease progression, utility, and costs. Disease progression, QALYs, and costs are simulated, which are used for decision analysis.
Simulating an economic model

> Individual continuous time state transition models (iCTSTMs) can be used to simulate “clock-reset” multi-state models in hesim

> Disease progression, utilities and costs simulated as function of input data and parameters

**Input data for disease model**

**Parameters for disease model**

Simulated disease progression

R facilitates script based analyses

> Economic model combines disease model (i.e., transition model for iCTSTM), utility model, and cost models

\[
\text{econmod} \leftarrow \text{IndivCtstm}\$\text{new}(\text{trans_model} = \text{transmod}, \\
\text{utility_model} = \text{utilmod}, \\
\text{cost_models} = \text{costmods})
\]

> Which is used to simulate costs and quality-adjusted life-years (QALYs)

\[
\text{econmod}\$\text{sim_disease}() \\
\text{econmod}\$\text{sim_qalys}(\text{dr} = .03) \\
\text{ecpnmod}\$\text{sim_costs}(\text{dr} = .03)
\]

> And can be used for cost-effectiveness analysis

\[
\begin{align*}
\text{# with hesim} \\
& \text{ce} \leftarrow \text{econmod}\$\text{summarize()} \\
& \text{icea} \leftarrow \text{icea}(\text{ce}, \text{dr} = .03) \\
& \text{icea} \_\text{pw} \leftarrow \text{icea}\_\text{pw}(\text{ce}, \text{dr} = 0.03, \text{comparator} = 2)
\end{align*}
\]

\[
\begin{align*}
\text{# with BCEA} \\
& \text{qalys_mat} \leftarrow \text{matrix}(\text{ce}\$\text{qalys}\$\text{qalys}, \text{nrow} = \text{n_samples}, \text{byrow} = \text{TRUE}) \\
& \text{costs_mat} \leftarrow \text{matrix}(\text{ce}\$\text{costs}\$\text{costs}, \text{nrow} = \text{n_samples}, \text{byrow} = \text{TRUE}) \\
& \text{bcea} \leftarrow \text{BCEA}\_\text{bcea}(e = \text{qalys_mat}, c = \text{costs_mat}, \text{ref} = 2)
\end{align*}
\]
Making models reproducible with R Markdown

```r
# Constructing the model
We construct the economic model by combining the separate models for the health state transitions, utility, and costs.

```{r}
n_samples <- 100
```

```r
### Health state transition model
Health state transitions are simulated as a function of input data (which contains the covariates from the multi-state model describing differences in transition rates across treatments) and parameters (the coefficients from the multi-state NMA). These are automatically created as a function of the model structure, transition matrix, and patient population with `create_transmod.dotest()` and stored below in a data table named `transmod_data`. A fraction of patients are T790M mutation positive (and this fraction can vary across treatments). Coefficients from the multi-state NMA that are contained in `transmod_data` are extracted using `transmod_params()`.

Recall from the discussion above that an individual-level model is required to simulate a CTSTM that that is a mixture of clock-reset and clock-forward approaches. A model of health state transitions for an individual-level CTSTM (ICTSTM) can be constructed with the `IndivCstTrans` class in `Tenet`.

```{r}
# Input data
transmod_data <- create_transmod.data(struct, treat, pots)
# Print first 5 rows and 20 covariates from data
print(transmod_data[1:5, 1:10])
# Parameters
transmod_params <- create_transmod_params(n = n_samples, data = transmod_data)
# Print first 5 samples from the probability distribution and 4 covariates (which match those in 'transmod_data')
transmod_paramscoeffscale[1:5, 1:4]
```

### Increasing transparency with web apps

- Web apps can be built using R Shiny or by embedding R code into JavaScript
- Allows users to run custom analyses without any knowledge of R
Tailoring web apps to different audiences

> Web app for rheumatoid arthritis decision model aimed at general audience

So why R?

> A comprehensive ecosystem for fitting statistical models
> Computational efficiency
> Reproducible research
> Web apps
> Unit testing
Poll: Following our presentations, how much more likely are you to start using R for decision modelling?

Resources

> Gianluca’s R packages
  > [https://github.com/giabaio](https://github.com/giabaio)
  > [http://www.statistica.it/gianluca/page_software/](http://www.statistica.it/gianluca/page_software/)

> Toy decision tree model

> hesim
  > [https://innovationvalueinitiative.github.io/hesim/](https://innovationvalueinitiative.github.io/hesim/)

> IVI-RA Web apps
Location
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