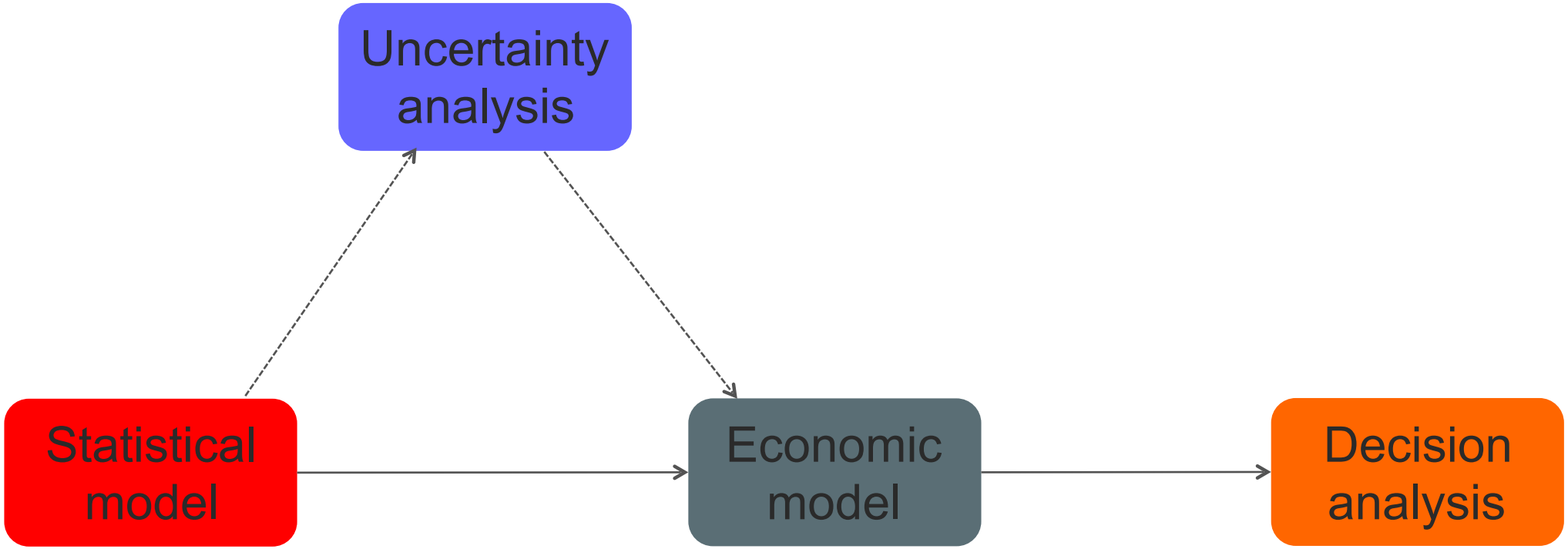
Developing relevant economic models with R for health technology assessment

Devin Incerti

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



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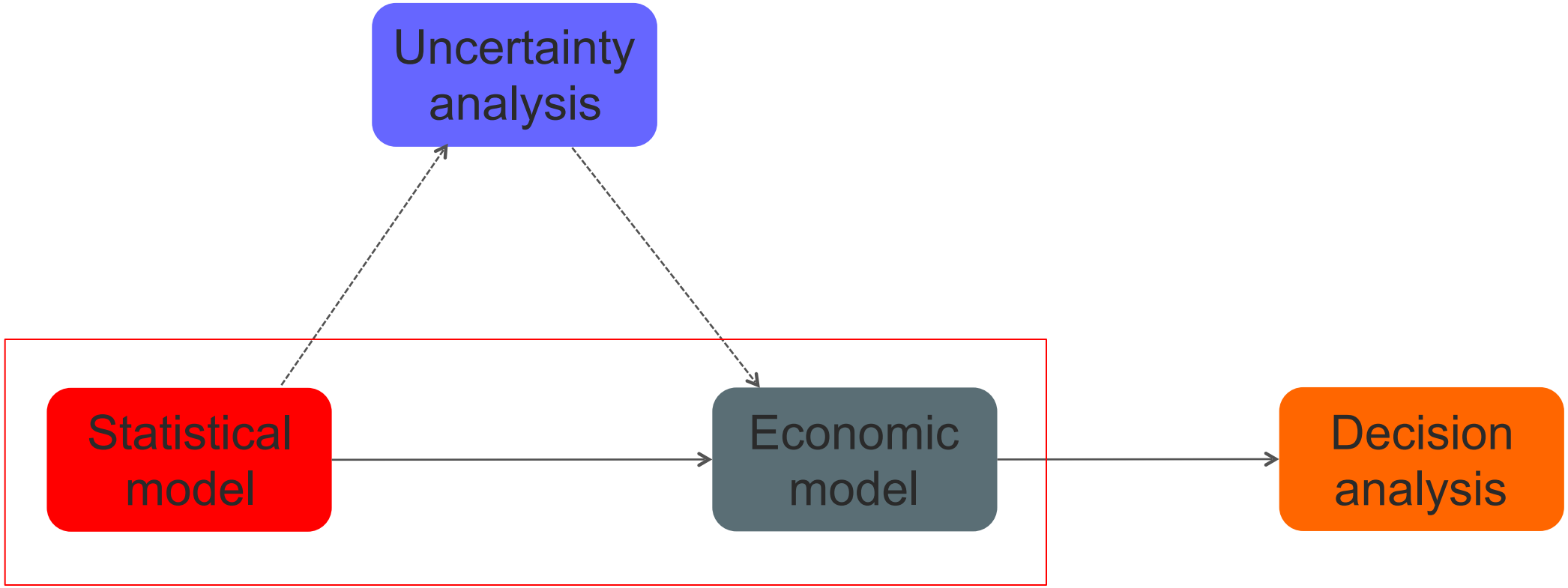
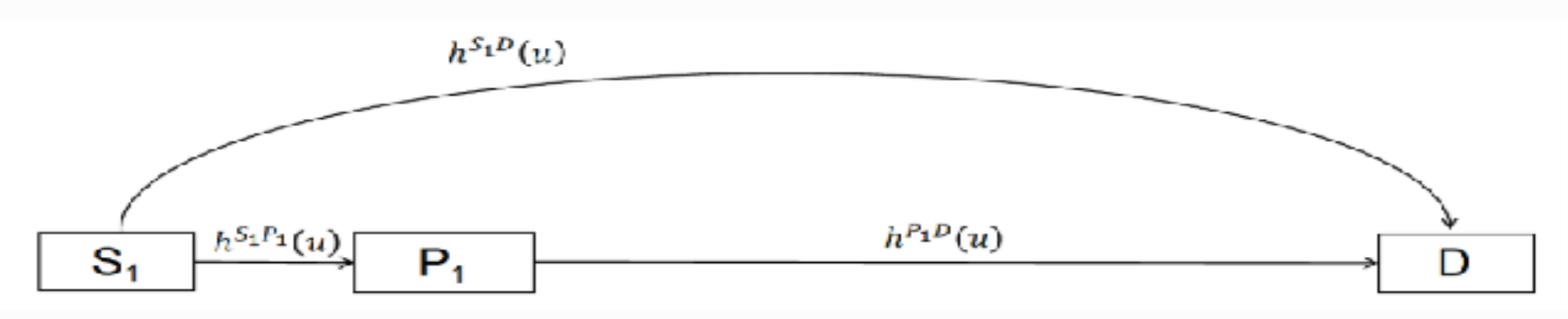


Example: a multi-state model in oncology



- 3 health states
  1. S1: Stable disease
  2. P1: Progressed disease
  3. D: Death

- 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 -> Progression
  2. Stable -> Death
  3. Progression -> Death

Parameterizing multi-state models

Statistical method	R package	Data
Network meta-analysis	`rjags/rbugs/rstan`	Summary data from RCTs
Parametric & spline models	`flexsurv`	Continuously observed processes
Non-parametric and semi-parametric models	`mstate`	Continuously observed processes
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Multi-state data with continuously observed processes

```
> head(mstate_data)
   patient_id strategy_id from to   Tstart    Tstop    years status trans
1:          1           1    1  2 0.020000 4.292950 4.292950      1     1
2:          1           1    1  3 0.020000 4.292950 4.292950      0     2
3:          1           1    2  3 4.292950 9.872690 5.579740      1     3
4:          2           1    1  2 0.020000 2.762491 2.762491      1     1
5:          2           1    1  3 0.020000 2.762491 2.762491      0     2
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Fitting a multi-state Weibull model with `flexsurv`

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fit_wei <- flexsurv::flexsurvreg(Surv(years, status) ~
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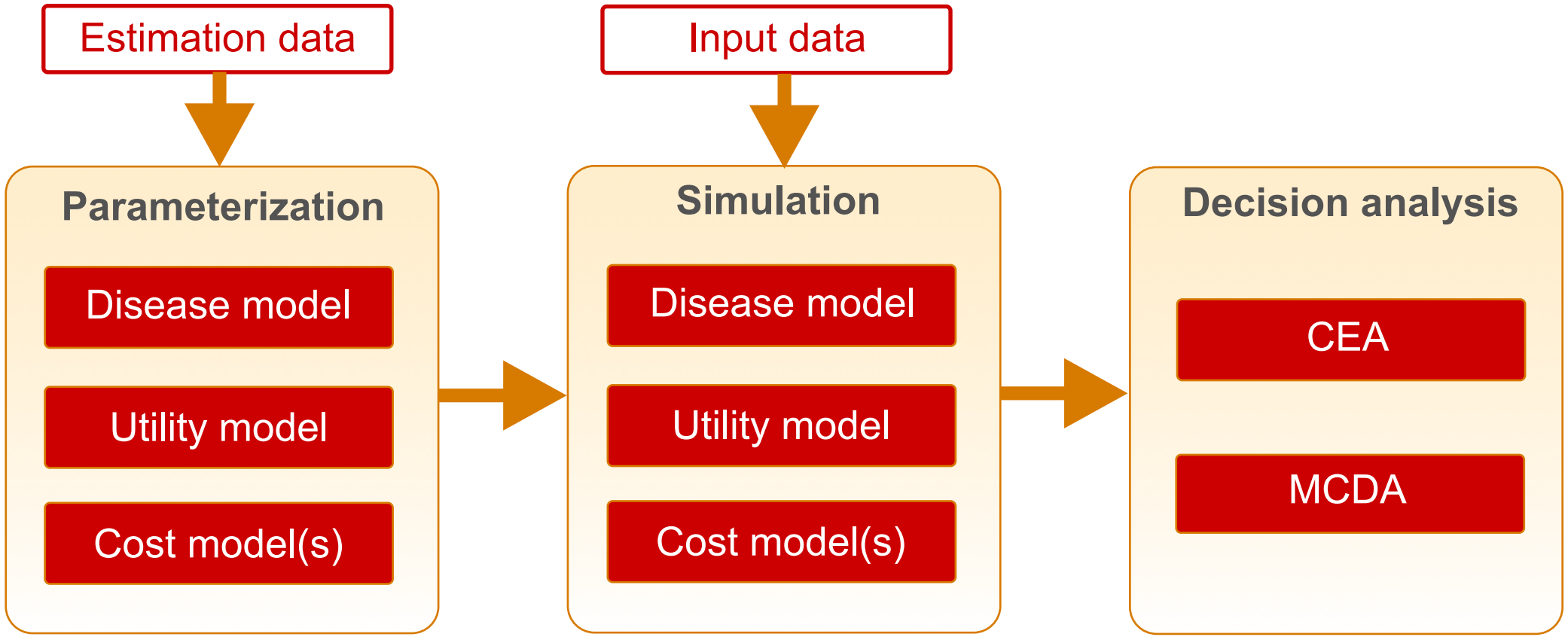
A "clock reset" model

`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*

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Parameters for disease model

Estimates:

	data mean	est	l95%	u95%	se	exp(est)	l95%	u95%
shape	NA	0.8274	0.7201	0.9779	0.0706	NA	NA	NA
scale	NA	5.2865	3.9219	7.1258	0.8053	NA	NA	NA
factor(strategy_id)2	0.4834	0.2084	-0.2959	0.6966	0.2532	1.2218	0.7438	2.0078
trans2	0.3992	0.9847	0.4685	1.5010	0.2634	2.6771	1.5976	4.4861
trans3	0.2016	-0.2770	-0.6554	0.1014	0.1931	0.7581	0.5192	1.1067
factor(strategy_id)2:trans2	0.2035	-0.9044	-1.5706	-0.2381	0.3399	0.4048	0.2079	0.7881
factor(strategy_id)2:trans3	0.0763	-0.4157	-1.0671	0.2357	0.3324	0.6599	0.3440	1.2658
shape(trans2)	0.3992	0.6986	0.3698	1.0275	0.1678	2.0110	1.4474	2.7939
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Simulated disease progression

	sample	strategy_id	patient_id	from	to	final	time_start	time_stop
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2:	1	1	1	2	3	1	0.6540819	1.6727070
3:	1	1	2	1	3	1	0.0000000	2.5778704
4:	1	1	3	1	2	0	0.0000000	0.6408648
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Uncertainty in parameters propagated to uncertainty in disease progression via PSA

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R code is a wrapper for underlying C++, which makes PSA with microsimulation fast

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

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```
# with hesim
ce <- econmod$summarize()
icea <- icea(ce, dr = .03)
icea_pw <- icea_pw(ce, dr = 0.03,
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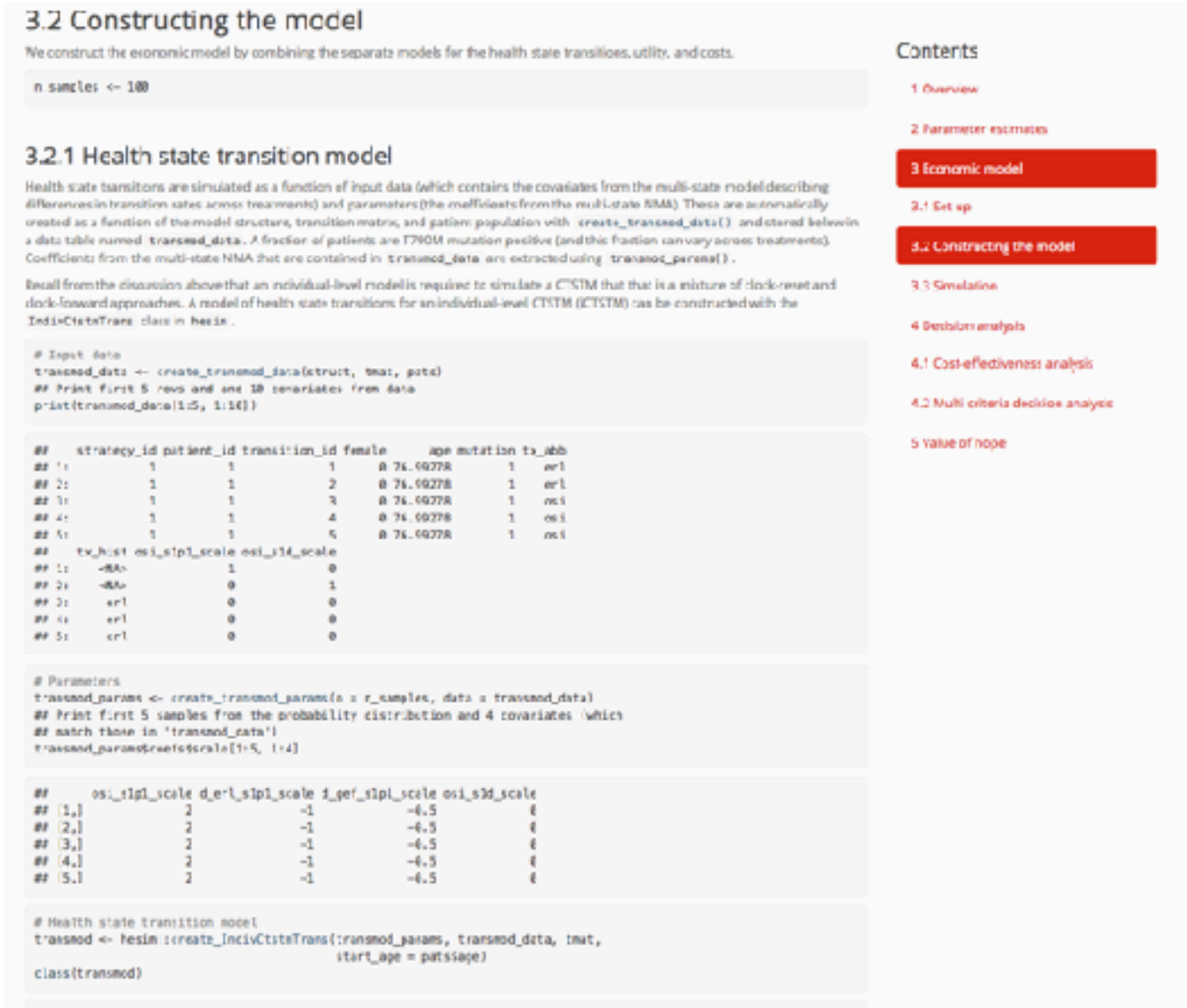
```
# with BCEA
qalys_mat <- matrix(ce$qalys$qalys, nrow = n_samples,
                    byrow = TRUE)
costs_mat <- matrix(ce$costs$costs, nrow = n_samples,
                    byrow = TRUE)
bcea <- BCEA::bcea(e = qalys_mat, c = costs_mat,
                   ref = 2)
```

Making models reproducible with R Markdown



3.2 Constructing the model

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

```
n_samples <- 100
```

3.2.1 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_data()` 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 `IndivCtstmTrans` class in `hesim`.

```
# Input data
transmod_data <- create_transmod_data(strucr, tmat, patc)
## Print first 5 rows and and 10 covariates from data
print(transmod_data[1:5, 1:16])
```

```
##    strategy_id patient_id transition_id female      age mutation tx_abb
## 1:           1          1             1      0 76.69278        1    erl
## 2:           1          1             2      0 76.69278        1    erl
## 3:           1          1             3      0 76.69278        1    osi
## 4:           1          1             4      0 76.69278        1    osi
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##    tx_hist osi_s1p1_scale osi_s1d_scale
## 1:    <NA>             1             0
## 2:    <NA>             0             1
## 3:     erl             0             0
## 4:     erl             0             0
## 5:     erl             0             0
```

```
# 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_params$rcoefs$scale[1:5, 1:4]
```

```
##      osi_s1p1_scale d_erl_s1p1_scale d_gef_s1p1_scale osi_s1d_scale
## [1,]              2               -1             -0.5             0
## [2,]              2               -1             -0.5             0
## [3,]              2               -1             -0.5             0
## [4,]              2               -1             -0.5             0
## [5,]              2               -1             -0.5             0
```

```
# Health state transition model
transmod <- hesim::create_IndivCtstmTrans(transmod_params, transmod_data, tmat,
                                          start_age = patsage)
class(transmod)
```

Contents

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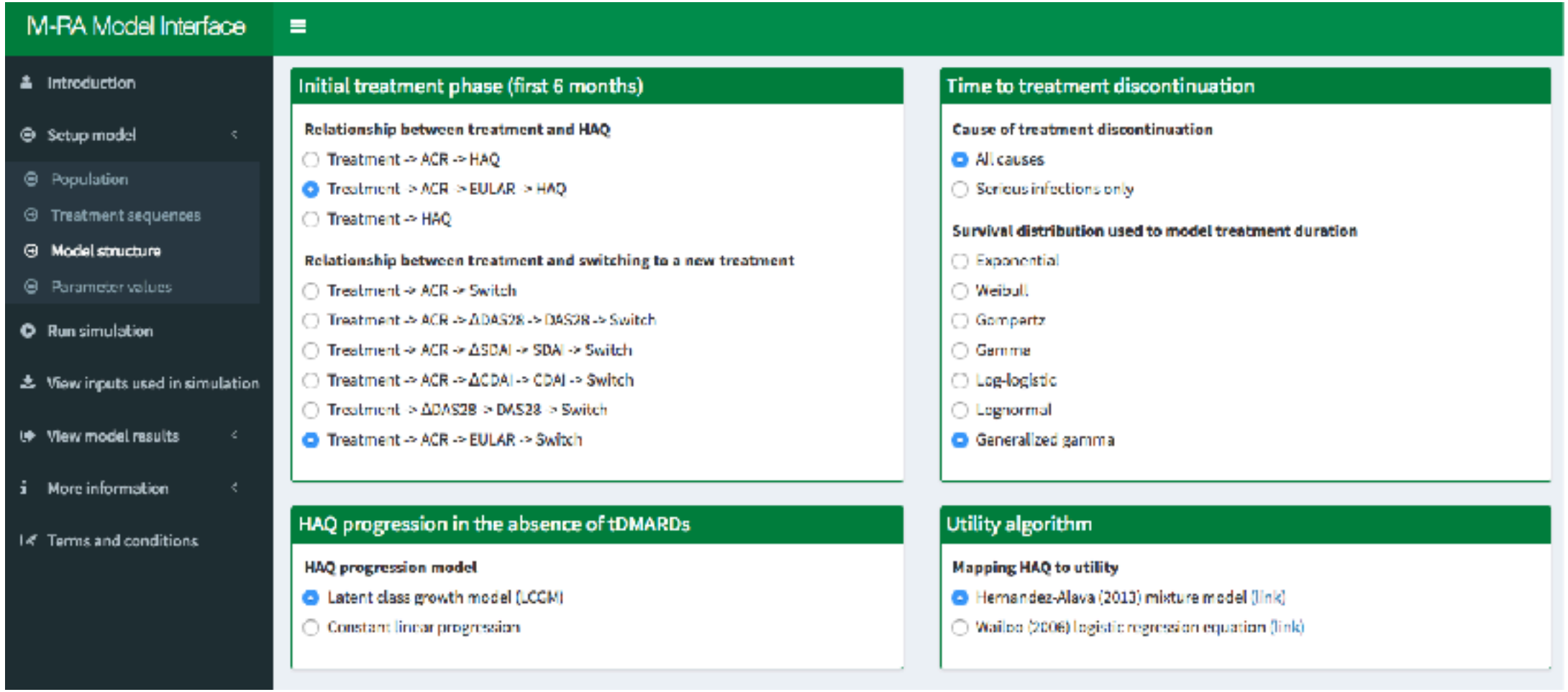
```[r]
# Input data
transmod_data <- create_transmod_data(struct, tmat, pats)
## Print first 5 rows and and 10 covariates from data
print(transmod_data[1:5, 1:10])

# 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_params$coefs$scale[1:5, 1:4]
```

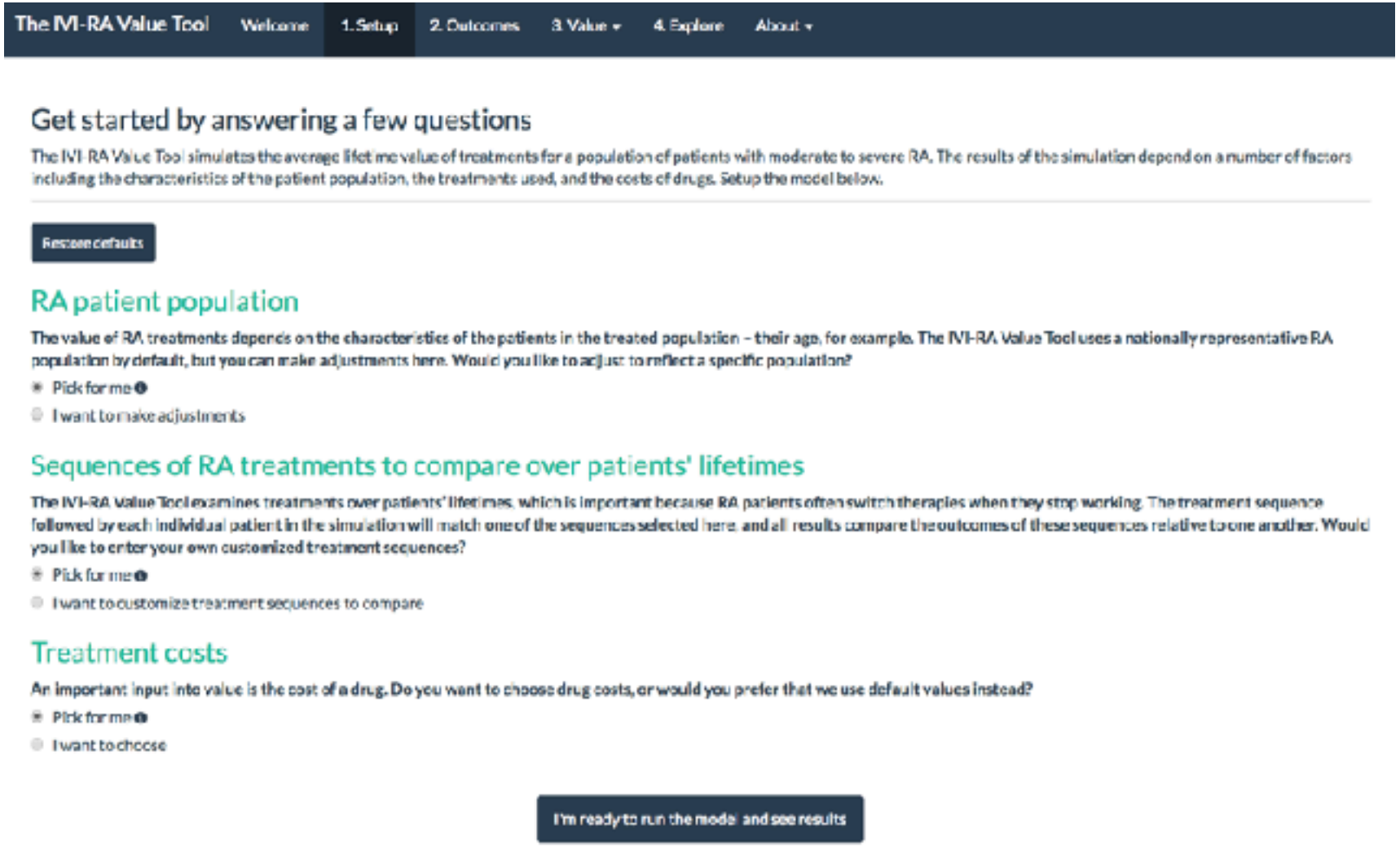
Increasing transparency with web apps

- 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

Live Content Slide

When playing as a slideshow, this slide will display live content

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
  - http://www.statistica.it/gianluca/page_software/
- Toy decision tree model
  - https://github.com/Bogdasayen/Depression-toy-decision-tree-in-R
- hesim
  - https://innovationvalueinitiative.github.io/hesim/
- IVI-RA Web apps
  - Expert (https://innovationandvalueinitiative.shinyapps.io/ivi-ra-expert/)
  - General audience (https://innovationandvalueinitiative.shinyapps.io/ivi-ra/)

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