R you seriously saying we shouldn't use Excel?

Gianluca Baio

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g.baio@ucl.ac.uk http://www.ucl.ac.uk/statistics/research/statistics-health-economics/ http://www.statistica.it/gianluca https://github.com/giabaio

(With contributions by Andrea Berardi, Andrea Gabrio, Anna Heath, Christina Ding et al)

ISPOR European Conference

Barcelona

Wednesday, 14 November 2018

http://www.statistica.it/gianluca/teaching/r-hta-workshop/

R for trial and model-based cost-effectiveness analysis

Mon, 9 Jul, 2018 · 5 min read

11 July 2018, University College London

Venue: Room G13 in 1-19 Torrington Place, University College London, United Kingdom.

Background and objectives

This one-day workshop on the use of R for trial and model-based cost-effectiveness analysis (EE) is jointy organised by a construm, or researchers at various institutions (UCL, Inventer) of York, University of Oxford and Bargor University), led by the MRC-Hades for Trials and Methodslogy and Research Construct. If the Scientific Committee include Howard Thom, Gianciae Bais, Anthomy Hatewide University, of Latewide Willow, Relate Bargor, Datewide Willow, Relate Bargor, Bargo

Funding for the workshop has been provided by the MRC Network of Hubs for Trials Methodology Research and the UCL Research Group Statistics for Health Economics.

CEA is often performed using MS. Exce. Lost, despite its ease of use, MS. Exce. Lincuis: the disadvantages of slow computational speed and a lack of transparency; our workshop aims to explore the use of R for CEA as an alternative. The aim of the workshop is to present a wide range of tenchnical aspects, including a discussion of the many analiable add-on packages to help users get the most out of R for CEA. Presentations and public discussions address the computational and transparency advantages of R ow MS. Exce. L for CEA and for easing collaboration. The packets have diverse exercised in presentation of industry.

Final Programme

Session 1: Invited talks (1) - chair: Anthony Hatswell

- · 9:30-9:45. Howard Thom, University of Bristol. Welcome.
- 9:45-10:15. Gianluca Baio. Department of Statistical Science, University College London. R you seriously saying we shouldn't use Excel?

This talk will showcase some of the R packages excently developed to add the work of modellers working in health economic evaluations. The notivation and general philosophy of a few packages will be briefly presented. Examples of their use/advantages over more established, but of the non-optimal computational tools, use at 85 Excce 1 will be demonstrated. Link to relevant web-applications.

10:15-10:35. Marta Soares. Centre for Health Economics, University of York. Using R for Markov modelling: an introduction.

This talk introduces the use of R for generic decision modelling detailing some of the advantages and disadvatages of this advances analysis. In this talk, it also present generic R code for Markov modelling, probabilistic seminitivity analyses and value of information analysis (guident carbon simulation). R code for deterministic and probabilistic seminitivity analyses.

10:35:11:15. Boby Mihaylova and iryna Schlackow. Health Economics Research Centre, Nuffield Department of Public Health, University of Oxford. A policy model of cardiovascular disease in moderate-to-advanced chronic kidney disease.

This talk will present the design and structure in R of the SHARP CXIC-CYO model, developed using the S spears followup data of 10000 patients with chronic kidney disease in the SHARP study. The model projects chronic kidney disease progression and cardiovascular complications and mortality using a set of multivariate risk, cost and QuL equations. We will demonstrate the R Shrivbased model interface to enable use by external analysts and will discuss issues reliated to model functionality and speed of -execution. Faper describing the model, model interface.

• 11:15-11:35. Coffee break.

Session 2: Participants oral presentation session (3 speakers, 15 minutes each) - chair: Marta Soares

11:35-11:55. Jeroen Jansen, Innovation and Value Initiative. An open-source cost-effectiveness simulation model for rheumatoid arthritis in R.

As part of the Open Source Value Project (OSVP), we developed a flexible open-source includual patient simulation model for rheumatoid arthritis (N+R-A model). Alternative biologic treatment sequences, parameter and structural uncertainty, and decision framework (i.e.-costeffectiveness of multi-criteria decision analysis) can be easily explored. The model facilitate dialogue between stakeholders about relevant clinical data, modeling approaches, and value perspectives. R and C++ code is available in a Github repository, along with Shtry server user intriffects for source tracking automatical section of the secti

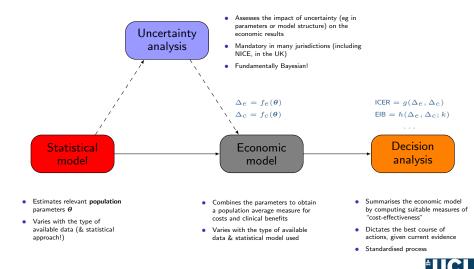
11:55-12:15. Eline Krijkamp, Erasmus MC. Introducing the Decision Analysis in R for Technologies in Health (DARTH) initiative

This talk will greent an introduction to the tools and educational materials created by the DARTH (Decision Analysis in R for Technologies in Health) collaboration. DARTH is a multi-institutional multi-inst

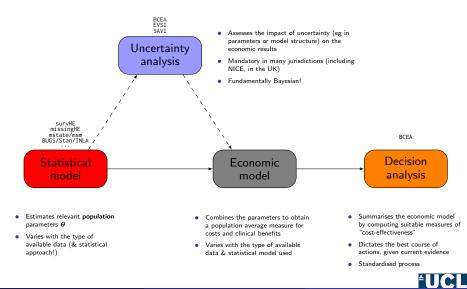


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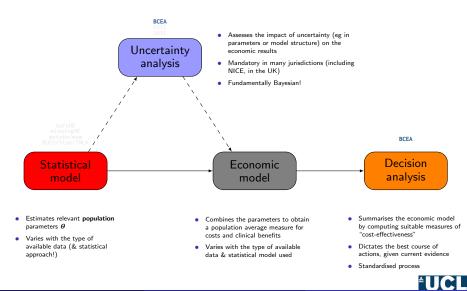
Objective: Combine costs & benefits of a given intervention into a rational scheme for allocating resources



For each module, we may need/use different/specific packages!



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BCEA & its use directly in R are designed with these objectives in mind

- O Checking the model assumptions
 - Do we mean what we mean (eg in terms of PSA simulations)?...
 - Simulation error (especially, but not only, for a Bayesian approach)





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- Produce the base-case economic evaluation
 - What's the most cost-effective intervention, given current evidence?
 - Cost-effectiveness plane, Expected Incremental Benefit (as a function of k),...



ISPOR Europe, 14 Nov 2018

Uncertainty analysis

Decision analysis

Throughout

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 - Standard PSA (mandatory): Cost-effectiveness Plane, CEAC, ...
 - Fairly easy (but not always used): CEAF
 - More advanced/ "too difficult" (rarely used): EVP(P)I/EVSI



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Standardised reporting

- Graphical tools (use excellent R facilities)
- Rmarkdown: analysis, commenting & reporting all in one go (real transparency + efficiency!)

Uncertainty analysis

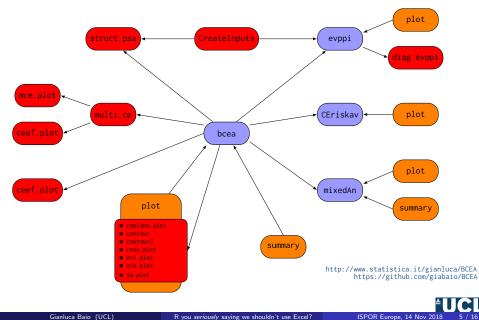
Decision analysis

Uncertainty analysis

Throughout

Throughout





Gianluca Baio (UCL)

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```
# Loads BCEA into the R workspace
> library(BCEA)
# Loads the PSA data from the R object "Vaccine"
> data(Vaccine)
# Or from an Excel spreadsheet, for example
> vaccine = read.csv("PSA_simulations.csv")
```

```
# Uses BCEA to create suitable input
> inp = CreateInputs(vaccine)
```

```
# Shows the first few rows of the PSA matrix
> head(inp$mat)
```

	Adverse.events	Death.1.1. D	eath.2.1. Dea	th.2.2.	GP.1.1.	GP.2.1.	GP.2.2.	Hospital.1.1.
1	1466	1	0	0	1664	958	230	0
2	5329	1	1	0	1414	748	276	0
3	5203	1	1	0	809	489	80	0
4	2351	2	0	0	1761	1157	261	1
5	8303	1	2	0	2472	964	432	1
6	3607	1	1	0	2224	1342	260	1
	Hospital.2.1.	Hospital.2.2.	Infected.1.1	. Infect	ted.2.1.	Infected	1.2.2. M	ild.Compl.1.1.
1	1	0	599	2	3401		876	691
2	0	1	747	1	4024		1536	570
3	0	0	671	8	4300		788	332
4	0	0	483	7	3269		702	739
5	1	0	474	9	1894		846	1049
6	0	0	493	8	2976		596	915

```
(many more rows & variables!)
```



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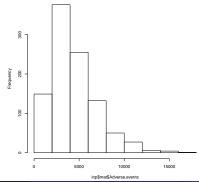
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```
> inp = CreateInputs(vaccine)
```

Checks that the intended PSA distribution gives meaningful results
> hist(inp\$mat\$Adverse.events)

Histogram of inp\$mat\$Adverse.events





R you seriously saying we shouldn't use Excel?

```
# Combines the model parameters to determine costs & effectiveness
> QALYs.inf <- QALYs.pne <- QALYs.hosp <- QALYs.adv <- QALYs.death <- matrix(0,n.sims,2)
> for (t in 1:2) {
    QALYs.inf[,t] = ((Infected[,t,1] + Infected[,t,2])*omega[,1]/365)/N
    QALYs.hosp[,t] = (((Peumonia[,t,1] + Pneumonia[,t,2])*omega[,5]/365)/N
    QALYs.hosp[,t] = ((Hospital[,t,1] + Hospital[,t,2])*omega[,5]/365)/N
    QALYs.death[,t] = ((Death[,t,1] + Death[,t,2])*omega[,6])/N
    }
    QALYs.adv[,2] = (Adverse.events*omega[,7]/365)/N
> e = -(QALYs.inf + QALYs.pne + QALYs.adv + QALYs.hosp + QALYs.death)
> ...
```

```
# Displays the first few row of the matrix for (e,c) in the two treatment arms
> head(cbind(e,c))
Control Operation Control Operation
```

Status Quo	Vaccination	Status Quo	Vaccination
-0.0010466668	-0.0008986026	10.409146	16.252537
-0.0008836105	-0.0007320416	5.834875	9.373437
-0.0008898137	-0.0006975327	5.784903	15.935623
-0.0016430238	-0.0011393237	12.208484	18.654250
-0.0013518841	-0.0009574948	9.786787	16.467321
-0.0014325715	-0.0009358231	6.560276	9.689887
	-0.001046668 -0.0008836105 -0.0008898137 -0.0016430238 -0.0013518841	Status Quo Vaccination -0.0010466668 -0.0008386026 -0.000838105 -0.0007320416 -0.0008898137 -0.0006975327 -0.0016430238 -0.0011393237 -0.00158841 -0.0005754948 -0.0013518841 -0.0009574948 -0.0014325715 -0.000358231	-0.0010466668 -0.0008986026 10.409146 -0.0008836105 -0.0007320416 5.834875 -0.0008898137 -0.0006975327 5.784903 -0.0013518841 -0.00139574948 9.786787

```
. . .
```

(many more rows!)



Enter BCEA!

```
# Uses BCEA to perform the decision analysis
> m = bcea(e,c,ref=2,interventions=c("Status Quo","Vaccination"),...)
# Summarises the results
> summarv(m)
Cost-effectiveness analysis summary
Reference intervention: Vaccination
Comparator intervention: Status Quo
Optimal decision: choose Status Quo for k<20100 and Vaccination for k>=20100
Analysis for willingness to pay parameter k = 25000
           Expected utility
Status Ouo
               -36 054
Vaccination
             -34.826
                            ETB CEAC ICER
Vaccination vs Status Ouo 1.2284 0.529 20098
Optimal intervention (max expected utility) for k=25000: Vaccination
EVPI 2.4145
```

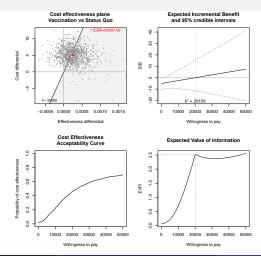


Enter BCEA!

```
# Uses BCEA to perform the decision analysis
```

```
> m = bcea(e,c,ref=2,interventions=c("Status Quo","Vaccination"),...)
```

Plots the results
> plot(m)

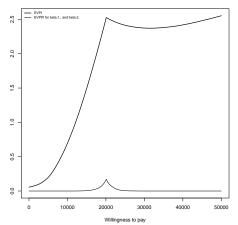




Enter BCEA!

```
# Makes the analysis of the Expected Value of Partial Perfect Information
> x = evppi(c("beta.1.","beta.2."), inp$mat, m)
# Plots the outcome
```

> plot(x)



Expected Value of Perfect Partial Information

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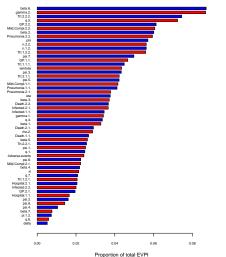
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Enter BCEA!

Summarises uncertainty in the decision making process by means of the "Info Rank" plot info.rank(inp\$parameters,inp\$mat,m)

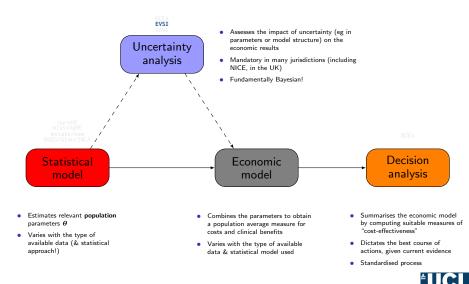
Info-rank plot for willingness to pay=20100



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R you seriously saying we shouldn't use Excel?

For each module, we may need/use different/specific packages!



- A new study will provide new data
 - Reducing (or even eliminating) uncertainty in a subset of model parameters
- Update the cost-effectiveness model
 - If the optimal decision changes, gain in monetary net benefit (NB = utility) from using new optimal treatment
 - If optimal decision unchanged, no gain in NB
- Expected VOI is the average gain in NB

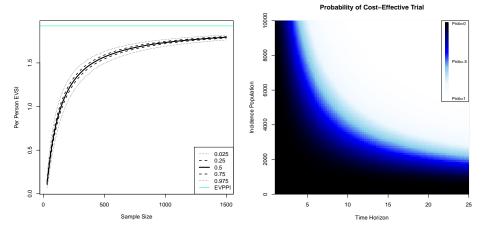
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- Expected VOI is the average gain in NB
- **O Expected Value of Perfect Information** (EVPI)
 - Value of completely resolving uncertainty in all input parameters to decision model
 - Infinite-sized long-term follow-up trial measuring everything!
 - Gives an upper-bound on the value of new study if EVPI is low, suggests we can make our decision based on existing information

2 Expected Value of Partial Perfect Information (EVPPI)

- Value of eliminating uncertainty in subset of input parameters to decision model
- Infinite-sized trial measuring relative effects on 1-year survival
- Useful to identify which parameters responsible for decision uncertainty

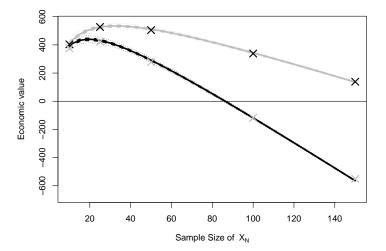
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- Value of reducing uncertainty by conducting a study of given design
- $-\,$ Can compare the benefits and costs of a study with given design
- Is the proposed study likely to be a good use of resources? What is the optimal design?

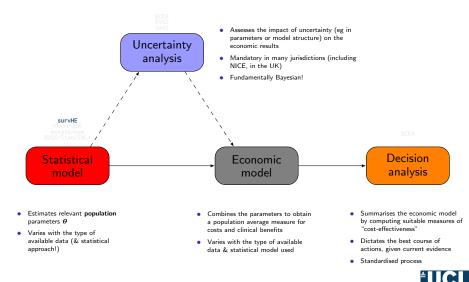


https://github.com/giabaio/EVSI https://egon.stats.ucl.ac.uk/projects/EVSI Heath et al (2018). https://arxiv.org/abs/1804.09590 Heath et al Medical Decision Making. 2017. 38(2): 163-173





For each module, we may need/use different/specific packages!



Objective: Simplify and standardise commands to fit survival analysis

- Can do MLE + bootstrap to get (possibly rough-ish!) estimates from the joint distribution of the parameters
- Can also do Bayesian models to get (usually better!) estimates from the joint posterior distribution of the parameters
 - INLA: Super fast (comparable to MLE), but currently supports only a restricted range of models
 - **MCMC**: Slower, but more generalisable survHE produces and saves the model code + data & initial values, so the user could then customise them



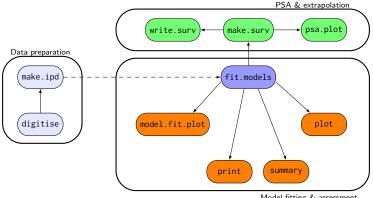
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- Automatically produce specialised graphs
 - Survival curves + model fitting statistics (AIC, BIC, DIC)
- Can produce a full PSA characterisation of the parameters and the survival curves
 - These can be directly used in the economic model!



survHE: a R package for survival analysis in HTA

Objective: Simplify and standardise commands to fit survival analysis



Model fitting & assessment

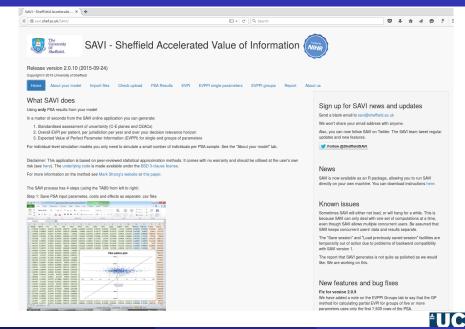
https://github.com/giabaio/survHE





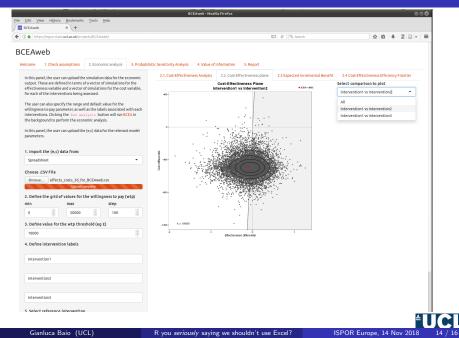
SAVI

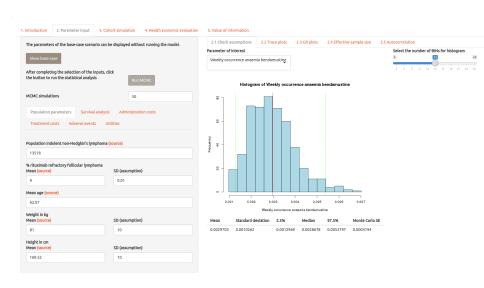
http://savi.shef.ac.uk/SAVI/



BCEAweb

https://egon.stats.ucl.ac.uk/projects/BCEAweb/





Escape (from Excel) to victory



Gianluca Baio (UCL)