R you *seriously* saying we shouldn't use Excel?

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

One-day workshop on R for trial and model-based cost-effectiveness analysis

University College London

Wednesday 11 July 2018

Health technology assessment (HTA)

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

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Statistical model

- Estimates relevant **population** parameters $\boldsymbol{\theta}$
- Varies with the type of available data (& statistical approach!)

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$$\Delta_e = f_e(\boldsymbol\theta)$$
$$\Delta_c = f_c(\boldsymbol\theta)$$

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- Combines the parameters to obtain a population average measure for costs and clinical benefits
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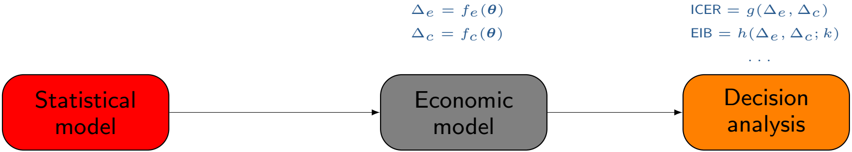

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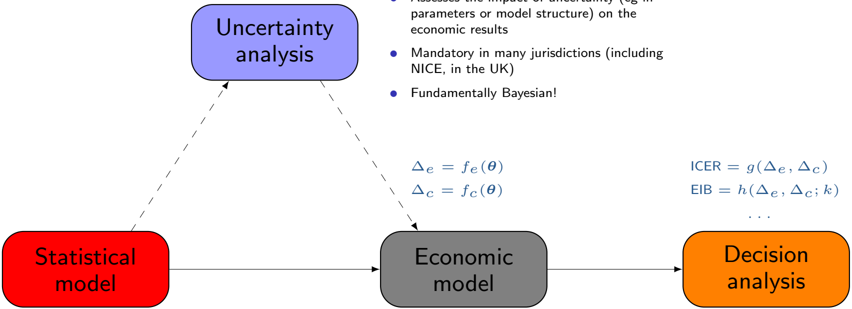

Uncertainty analysis

- Assesses the impact of uncertainty (eg in parameters or model structure) on the economic results
- Mandatory in many jurisdictions (including NICE, in the UK)
- Fundamentally Bayesian!

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$$\Delta_c = f_c(\boldsymbol\theta)$$

$$\text{ICER} = g(\Delta_e, \Delta_c)$$
$$\text{EIB} = h(\Delta_e, \Delta_c; k)$$
$$\ldots$$

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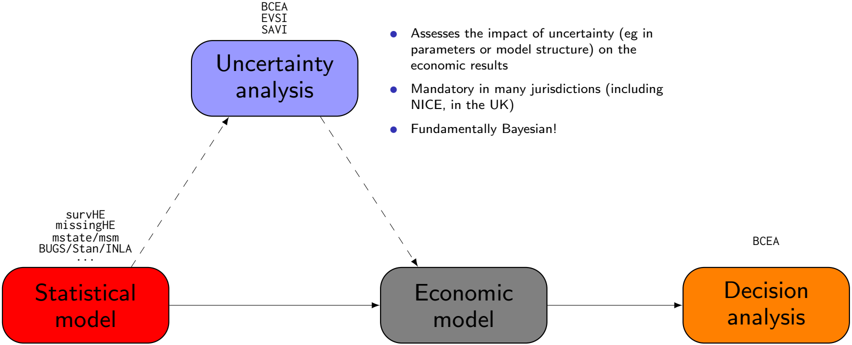
For each module, we may need/use different/specific packages!



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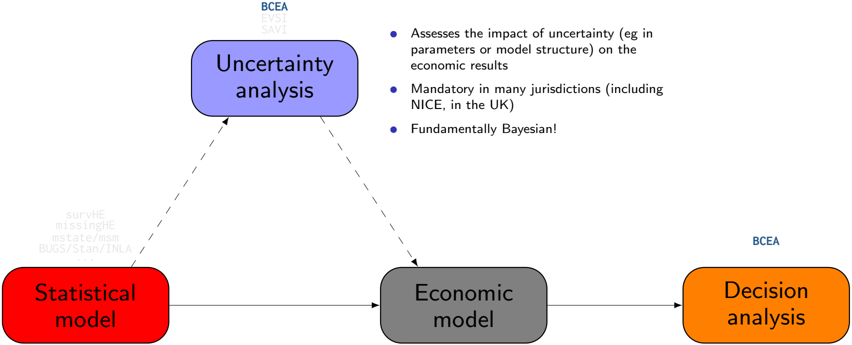

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BCEA & its use directly in R are designed with these objectives in mind

0. Checking the model assumptions — Throughout — Uncertainty analysis
   - 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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   - What's the most cost-effective intervention, given current evidence?
   - Cost-effectiveness plane, Expected Incremental Benefit (as a function of k),...

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   - Standard PSA (mandatory): Cost-effectiveness Plane, CEAC, ...
   - Fairly easy (but not always used): CEAF
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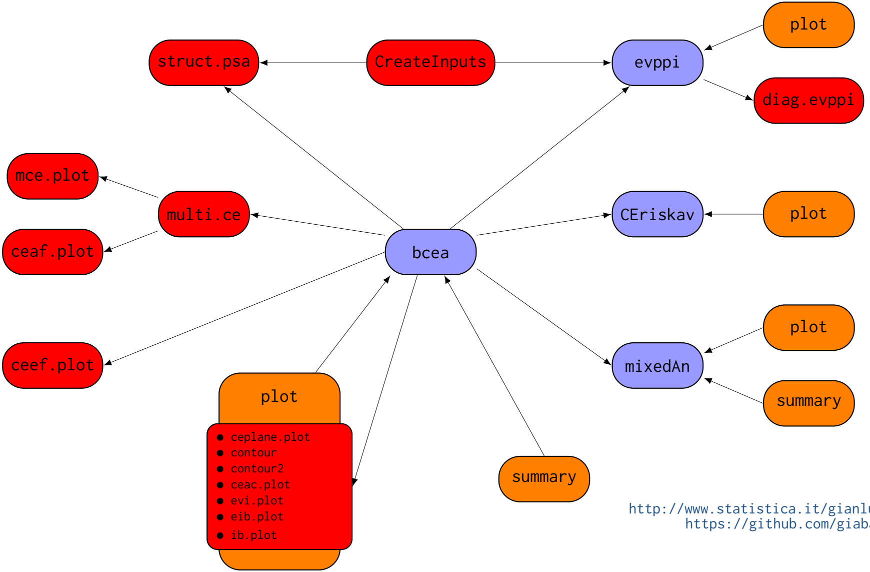
3. Standardised reporting — Throughout
   - Graphical tools (use **excellent** R facilities)



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How does BCEA work?

Param_sim.csv - LibreOffice Calc

File Edit View Insert Format Tools Data Window Help

A49 | 6145

1	Adverse.events	Death.1	Death.2	Death.3	Death.4	GP.1	GP.2	GP.3	GP.4	Hospital.1	Hospital.2	Hospital.3	Hospital.4	Infected.1	Infected.2	Infected.3	Infected.4	Mild.Compl.1	Mild.Compl.2	Mild.Compl.3	Mild.Compl.4	Pneumonia.1	Pneumonia.2	Pneumonia.3	Pneumonia.4	Repeat.GP.1
2	3670	1	2	0	0	1642	812	0	221	1	0	0	0	3051	1520	0	427	731	352	0	103	39	17	0	3	692
3	1195	0	1	0	0	1622	857	0	236	1	0	0	0	10045	5042	0	1356	650	386	0	109	9	14	0	0	641
4	3334	1	2	0	0	1792	1072	0	208	3	2	0	1	5164	3114	0	593	758	399	0	96	31	21	0	8	727
5	3828	2	0	0	0	2781	1764	0	380	0	0	0	0	7369	4695	0	984	1199	767	0	157	60	32	0	8	1139
6	442	2	0	0	0	1428	954	0	164	0	2	0	0	6189	4246	0	627	603	413	0	60	31	13	0	4	572
7	3937	1	0	0	0	1408	617	0	268	1	0	0	0	4763	2080	0	888	585	247	0	116	16	5	0	0	569
8	4913	1	0	0	0	477	238	0	72	0	0	0	0	4946	2726	0	731	215	92	0	33	3	3	0	1	212
9	4438	1	0	0	0	2683	1711	0	266	6	1	0	0	5821	3901	0	557	1067	675	0	110	37	25	0	6	1030
10	2995	2	2	0	0	3692	2451	0	355	2	0	0	1	8337	5653	0	817	1519	1050	0	154	46	35	0	4	1473
11	6528	1	0	0	0	2017	992	0	280	1	1	0	1	10409	5105	0	1420	812	402	0	114	32	18	0	1	780
12	2220	2	0	0	0	2118	1573	0	144	0	0	0	0	7629	5719	0	447	886	610	0	70	35	16	0	2	851
13	3665	2	2	0	0	1233	797	0	189	1	0	0	0	6450	4085	0	878	523	327	0	84	14	7	0	1	509
14	6460	1	0	0	0	1834	696	0	367	3	0	0	0	9485	3550	0	1977	720	269	0	139	26	9	0	6	694
15	5921	1	1	0	0	2186	1022	0	167	0	0	0	0	10334	4620	0	827	903	432	0	78	23	13	0	4	880
16	5496	3	0	0	0	1599	901	0	232	0	0	0	0	6543	3805	0	894	661	384	0	96	20	16	0	5	641
17	5067	1	0	0	0	2137	1013	0	403	1	1	0	0	6554	3184	0	1162	868	407	0	151	31	12	0	3	837
18	5328	1	0	0	0	1998	1058	0	276	1	1	0	0	7058	3759	0	994	858	454	0	109	31	8	0	4	827
19	1975	0	0	0	0	693	503	0	40	0	1	0	0	5346	4062	0	366	290	220	0	18	9	10	0	1	281
20	9162	3	1	0	0	3083	1857	0	417	0	0	0	0	8451	4940	0	1088	1264	779	0	176	44	22	0	6	1220
21	1596	0	2	0	0	1746	1133	0	138	0	0	0	0	5616	3759	0	455	706	493	0	72	35	25	0	3	671
22	2485	4	2	0	1	1518	857	0	154	0	2	0	0	6118	3651	0	663	611	355	0	64	13	12	0	5	598
23	2114	4	3	0	0	2282	1480	0	202	1	0	0	0	8003	5249	0	710	913	597	0	82	32	17	0	2	881
24	3045	0	0	0	0	1071	639	0	131	0	1	0	0	4527	2591	0	511	452	268	0	55	12	4	0	1	440
25	5305	1	1	0	0	1986	996	0	287	0	0	0	1	7978	3829	0	1055	854	434	0	125	29	10	0	7	825
26	3819	0	0	0	0	1081	578	0	89	1	0	0	0	4055	2057	0	379	419	234	0	38	15	4	0	4	404
27	5286	0	1	0	0	842	503	0	126	0	0	0	0	4713	2777	0	708	337	234	0	64	13	11	0	1	324
28	1865	0	0	0	0	1459	722	0	157	0	0	0	0	5191	2752	0	582	559	275	0	53	11	3	0	1	548
29	10761	2	0	0	0	2729	1397	0	428	1	0	0	1	6569	3427	0	1065	1131	557	0	167	35	22	0	8	1096
30	1231	1	2	0	0	3207	2027	0	322	0	1	0	0	8460	5491	0	871	1359	812	0	130	48	25	0	3	1311
31	1530	6	4	0	0	2870	1778	0	404	1	0	0	0	6907	4281	0	919	1165	715	0	170	42	22	0	4	1123
32	3412	1	1	0	0	1571	871	0	173	0	1	0	0	5719	3041	0	577	629	374	0	64	19	14	0	1	610
33	4582	3	3	0	1	2942	1346	0	521	1	0	0	0	8097	3934	0	1501	1248	569	0	225	41	20	0	8	1207
34	1520	0	2	0	0	2093	1708	0	176	3	4	0	1	8319	6656	0	823	902	708	0	67	36	35	0	2	866
35	5527	3	0	0	0	2287	1149	0	416	0	1	0	0	6910	3351	0	1228	881	465	0	165	21	11	0	6	860
36	8523	1	0	0	0	2311	1418	0	256	3	0	0	1	7019	4373	0	755	954	570	0	106	36	16	0	5	918
37	2698	0	2	0	0	2171	1040	0	391	0	0	0	0	8565	3907	0	1442	865	411	0	154	25	18	0	9	840
38	4084	2	1	0	0	1838	1097	0	152	1	0	0	0	9362	5786	0	920	716	480	0	67	30	25	0	3	686
39	8112	3	1	0	0	2706	1116	0	436	1	0	0	0	6932	2932	0	1124	1214	495	0	172	55	17	0	8	1159
40	4593	1	2	0	0	2700	1582	0	297	2	1	0	0	6303	3693	0	680	1101	665	0	122	31	12	0	3	1070
41	4659	4	4	0	1	2985	1551	0	353	2	1	0	0	10024	5430	0	1321	1244	673	0	152	32	26	0	2	1212
42	5721	1	1	0	0	1185	667	0	168	1	0	0	0	6347	3687	0	866	473	292	0	81	16	10	0	5	457
43	1229	0	0	0	0	1136	566	0	153	1	0	0	0	7654	3909	0	949	494	245	0	56	15	6	0	0	479
44	1829	1	1	0	0	1327	928	0	137	0	1	0	0	5720	4105	0	557	551	356	0	55	24	14	0	1	527
45	10450	2	0	0	0	2944	1167	0	688	1	0	0	1	8426	3267	0	1851	1263	489	0	285	26	16	0	12	1237
46	3683	1	0	0	0	1699	1008	0	224	2	0	0	0	6246	3591	0	837	732	404	0	85	21	11	0	3	711
47	7192	2	0	0	0	2117	1145	0	361	0	0	0	0	6764	3642	0	1095	856	470	0	169	23	17	0	4	833
48	5315	3	0	0	0	3255	1753	0	504	1	1	0	0	7035	3885	0	1087	1304	673	0	193	31	18	0	3	1273
49	6145	0	0	0	0	1541	890	0	126	0	0	0	0	5765	3382	0	410	618	361	0	57	9	4	0	2	609
50	6226	1	4	0	0	2411	1230	0	364	0	2	0	0	7587	3816	0	1191	950	488	0	161	20	13	0	8	930
51	3218	1	1	0	0	1624	766	0	279	0	0	0	0	6665	3347	0	1175	692	323	0	118	31	13	0	5	661
52	3809	0	1	0	0	1502	888	0	254	0	0	0	0	4592	2714	0	725	590	327	0	109	21	12	0	5	569
53	2998	1	2	0	1	1280	931	0	135	0	0	0	0	7901	5984	0	738	520	415	0	55	23	18	0	0	497
54	7735	5	0	0	0	2210	996	0	312	0	0	0	0	6930	3104	0	1021	930	423	0	142	28	12	0	9	902

Sheet 1 / 1 Default Sum=6145 100%

```
# Loads BCEA into the R workspace
> library(BCEA)

# Loads the PSA data from the R object "Vaccine"
> data(Vaccine)

# 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. Death.2.1. Death.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. Infected.2.1. Infected.2.2. Mild.Compl.1.1.
1             1             0          5992          3401           876             691
2             0             1          7471          4024          1536             570
3             0             0          6718          4300           788             332
4             0             0          4837          3269           702             739
5             1             0          4749          1894           846            1049
6             0             0          4938          2976           596             915

...

(many more rows & variables!)
```

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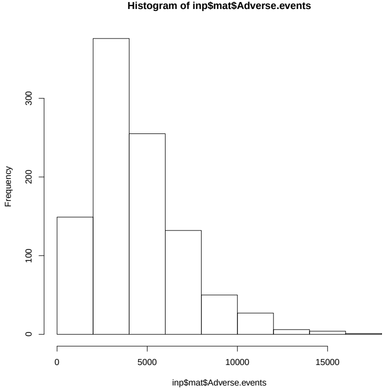
```
# Checks that the intended PSA distribution gives meaningful results
> hist(inp$mat$$Adverse.events)
```



```
# 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.pne[,t] = ((Pneumonia[,t,1] + Pneumonia[,t,2])*omega[,4]/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))

       Status Quo   Vaccination  Status Quo Vaccination
[1,] -0.0010466668 -0.0008986026  10.409146   16.252537
[2,] -0.0008836105 -0.0007320416   5.834875    9.373437
[3,] -0.0008898137 -0.0006975327   5.784903   15.935623
[4,] -0.0016430238 -0.0011393237  12.208484   18.654250
[5,] -0.0013518841 -0.0009574948   9.786787   16.467321
[6,] -0.0014325715 -0.0009358231   6.560276    9.689887

...

(many more rows!)
```

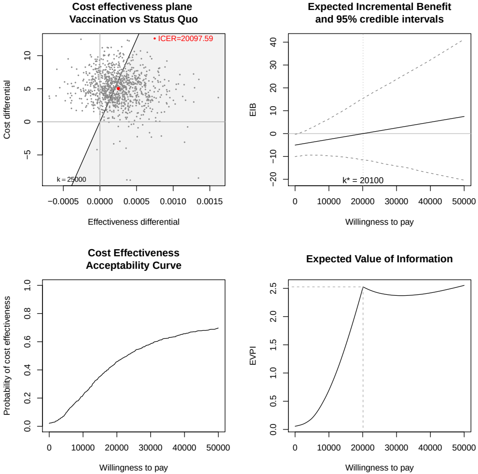
```
# Uses BCEA to perform the decision analysis
> m = bcea(e,c,ref=2,interventions=c("Status Quo","Vaccination"),...)
```

```
# Summarises the results
> summary(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 Quo           -36.054
Vaccination          -34.826

                             EIB  CEAC  ICER
Vaccination vs Status Quo 1.2284 0.529 20098

Optimal intervention (max expected utility) for k=25000: Vaccination

EVPI 2.4145
```

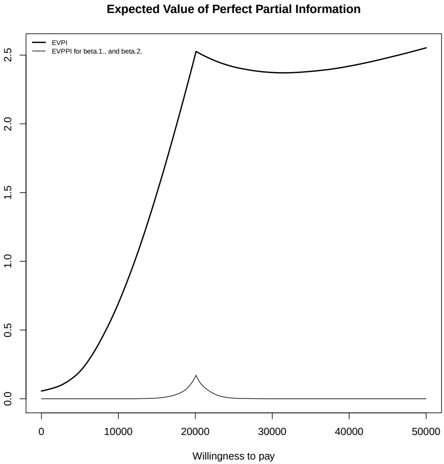
How does BCEA work?

```
# Uses BCEA to perform the decision analysis
> m = bcea(e,c,ref=2,interventions=c("Status Quo","Vaccination"),...)
```

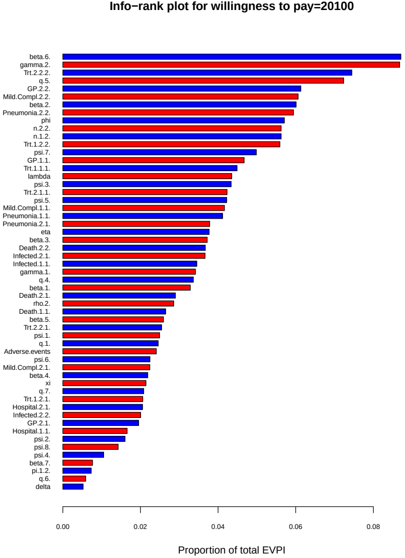
```
# Plots the results
> plot(m)
```



```
# 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)
```



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



Health technology assessment (HTA)

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BCEA
EVSI
SAVI

Uncertainty analysis

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- Mandatory in many jurisdictions (including NICE, in the UK)
- Fundamentally Bayesian!

survHE
missingHE
mstate/msm
BUGS/Stan/INLA
...

Statistical model

Economic model

BCEA

Decision analysis

- Estimates relevant **population** parameters $\boldsymbol{\theta}$
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- Combines the parameters to obtain a population average measure for costs and clinical benefits
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VoI: Basic idea

- 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

VoI: Basic idea and relevant measures

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  - 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

1. **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
3. **Expected Value of Sample Information** (EVSI)
   - 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?

Posterior given data d

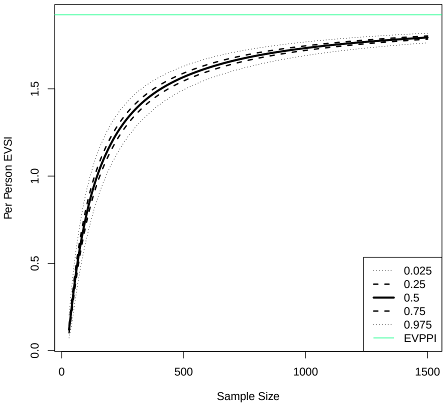
$$\text{EVSI} = \text{E}_{\boldsymbol\theta,d|\boldsymbol\theta}\left[\max_t \underbrace{\text{E}_{\boldsymbol\theta|d}\left[\text{NB}_t(\boldsymbol\theta)\right]}_{\text{Value of decision based on sample information (for a given study design)}}\right] - \underbrace{\max_t \text{E}_{\boldsymbol\theta}\left[\text{NB}_{t^*}(\boldsymbol\theta)\right]}_{\text{Value of decision based on current information}}$$

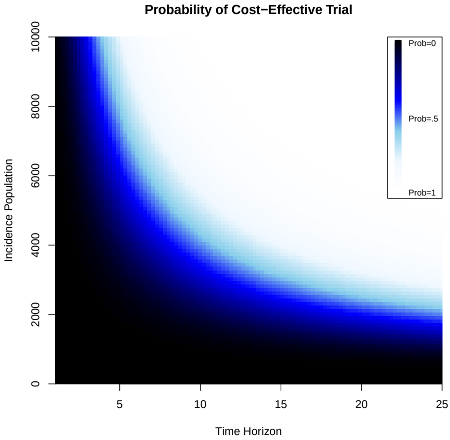
Prior predictive distribution (pre-posterior)

Value of decision based on **sample** information (for a given study design)

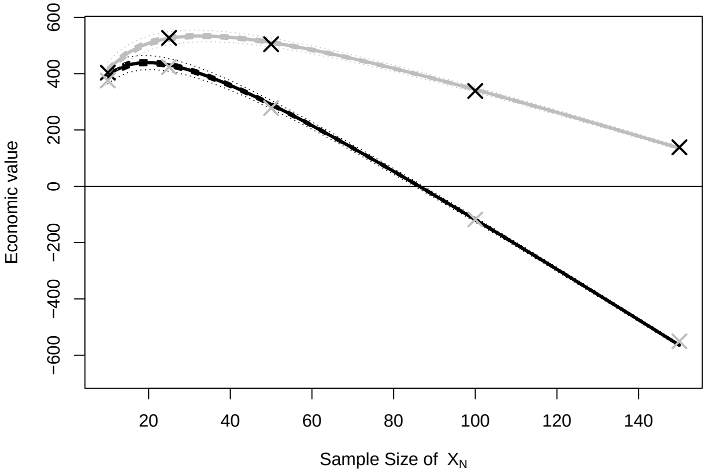
Value of decision based on **current** information

- Computationally complex
  - Requires specific knowledge of the model for (future/hypothetical) data collection
  - Again, recent methods have improved efficiency
- Can be used to drive design of new study (eg sample size calculations)
- The package EVSI can be used (with some knowledge of Bayesian modelling) to estimate the value of effectively any study design in reducing uncertainty in the corresponding decision-making process
  - Sample size calculations/study design
  - Research prioritisation



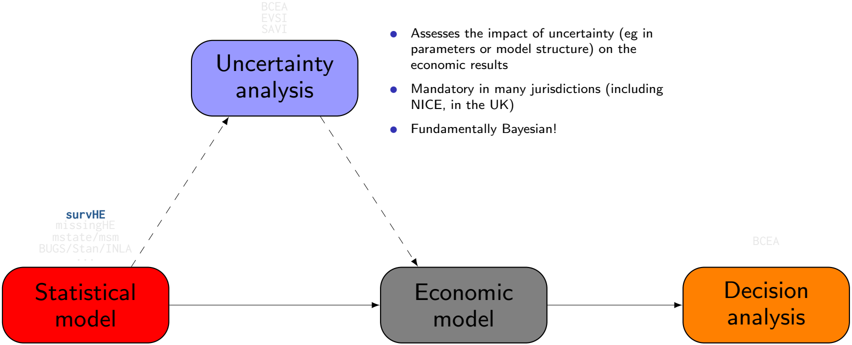


https://github.com/giabaio/EVSI
https://egon.stats.ucl.ac.uk/projects/EVSI
Heath et al (2018). https://arxiv.org/abs/1804.09590
Heath et al *Medical Decision Making*. 2017. **38(2)**: 163-173


Economic value
600
400
200
0
−200
−400
−600
20
40
60
80
100
120
140
Sample Size of X_N

Health technology assessment (HTA)

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



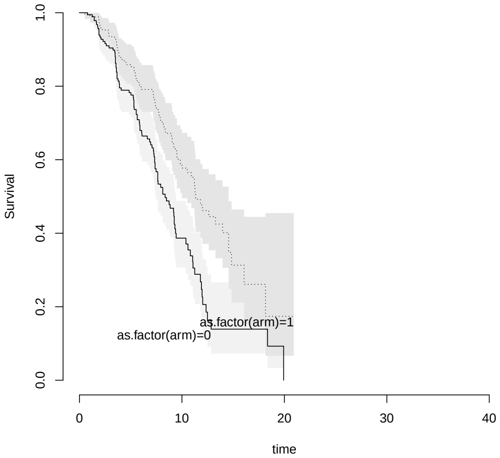
- Assesses the impact of uncertainty (eg in parameters or model structure) on the economic results
- Mandatory in many jurisdictions (including NICE, in the UK)
- Fundamentally Bayesian!

- Estimates relevant **population** parameters $\boldsymbol{\theta}$
- Varies with the type of available data (& statistical approach!)

- Combines the parameters to obtain a population average measure for costs and clinical benefits
- Varies with the type of available data & statistical model used

- Summarises the economic model by computing suitable measures of "cost-effectiveness"
- Dictates the best course of actions, given current evidence
- Standardised process

- Survival data are often the main outcome in clinical studies relevant for HTA
  - Cancer drugs (progression-free/overall survival time): ≈ 40% of NICE appraisals!
  - Need to **extrapolate**, for economic modelling purposes. **BUT**: Limited follow up from trials, not consistent with time horizon of economic model



Median time: $t : S(t) = 0.5$

- Survival data are often the main outcome in clinical studies relevant for HTA
  - Cancer drugs (progression-free/overall survival time): $\approx$ 40% of NICE appraisals!
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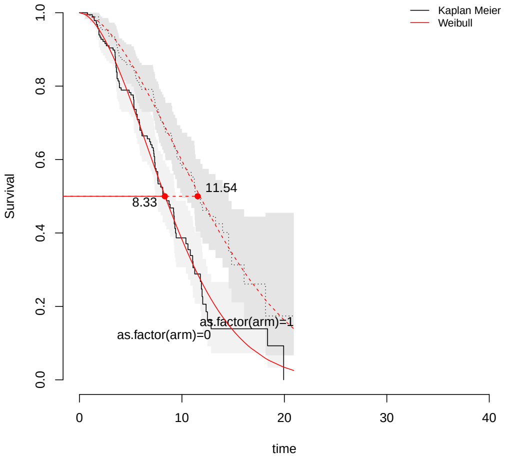

Mean time: $\int_0^\infty S(t)dt$

- Survival data are often the main outcome in clinical studies relevant for HTA
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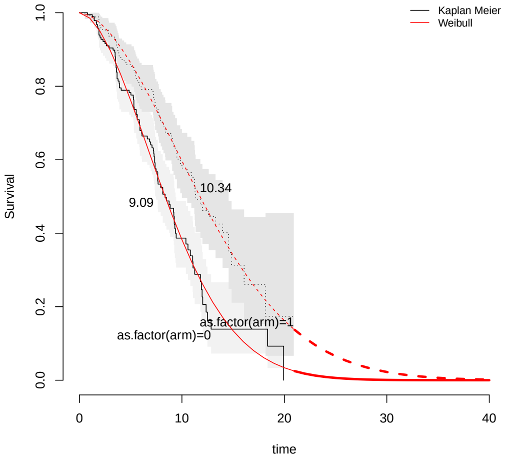

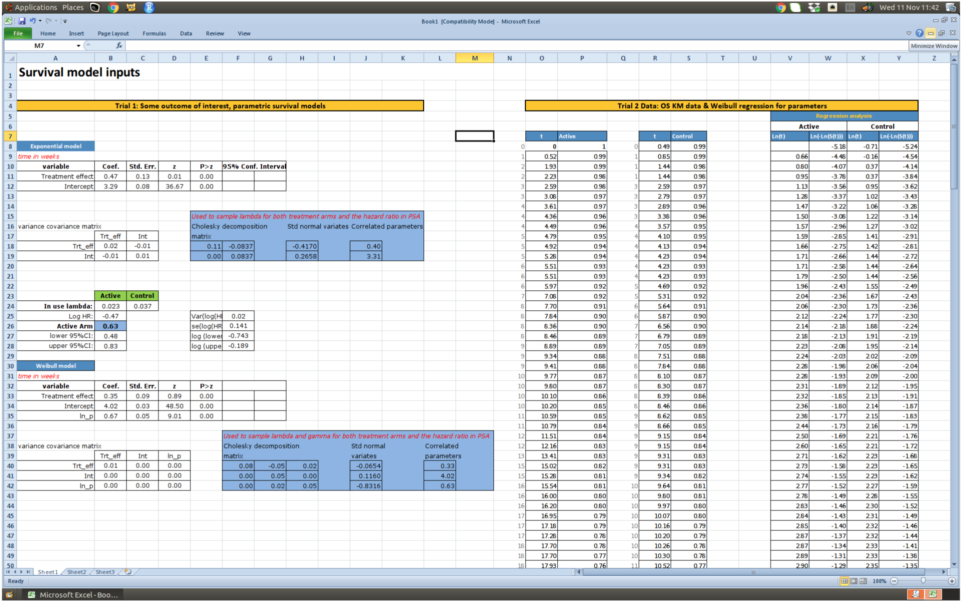

Applications Places — Wed 11 Nov 11:42

Book1 [Compatibility Mode] - Microsoft Excel

File Home Insert Page Layout Formulas Data Review View

M7 — Minimize Window

Survival model inputs

Trial 1: Some outcome of interest, parametric survival models

Exponential model

time in weeks

variable	Coef.	Std. Err.	z	P>z	95% Conf. Interval	
Treatment effect	0.47	0.13	0.01	0.00		
Intercept	3.29	0.08	36.67	0.00		

variance covariance matrix

	Trt_eff	Int
Trt_eff	0.02	-0.01
Int	-0.01	0.01

Used to sample lambda for both treatment arms and the hazard ratio in PSA

Cholesky decomposition matrix		Std normal variates	Correlated parameters
0.11	-0.0837	-0.4170	0.40
0.00	0.0837	0.2658	3.31

	Active	Control
In use lambda:	0.023	0.037
Log HR:	-0.47	
Active Arm	**0.63**	
lower 95%CI:	0.48	
upper 95%CI:	0.83	

Var(log(H	0.02
se(log(HR	0.141
log (lower	-0.743
log (uppe	-0.189

Weibull model

time in weeks

variable	Coef.	Std. Err.	z	P>z		
Treatment effect	0.35	0.09	0.89	0.00		
Intercept	4.02	0.03	48.50	0.00		
ln_p	0.67	0.05	9.01	0.00		

variance covariance matrix

	Trt_eff	Int	ln_p
Trt_eff	0.01	0.00	0.00
Int	0.00	0.00	0.00
ln_p	0.00	0.00	0.00

Used to sample lambda and gamma for both treatment arms and the hazard ratio in PSA

Cholesky decomposition matrix			Std normal variates	Correlated parameters
0.08	-0.05	0.02	-0.0654	0.33
0.00	0.05	0.00	0.1160	4.02
0.00	0.02	0.05	-0.8316	0.63

Trial 2 Data: OS KM data & Weibull regression for parameters

	t	Active		t	Control	Regression analysis: Active Ln(t)	Active Ln(-Ln(S(t)))	Control Ln(t)	Control Ln(-Ln(S(t)))
0	0	1	0	0.49	0.99		-5.18	-0.71	-5.24
1	0.52	0.99	1	0.85	0.99	0.66	-4.48	-0.16	-4.54
2	1.93	0.99	1	1.44	0.98	0.80	-4.07	0.37	-4.14
2	2.23	0.98	1	1.44	0.98	0.95	-3.78	0.37	-3.84
3	2.59	0.98	3	2.59	0.97	1.13	-3.56	0.95	-3.62
3	3.08	0.97	3	2.79	0.97	1.28	-3.37	1.02	-3.43
4	3.61	0.97	3	2.89	0.96	1.47	-3.22	1.06	-3.28
4	4.36	0.96	3	3.38	0.96	1.50	-3.08	1.22	-3.14
4	4.49	0.96	4	3.57	0.95	1.57	-2.96	1.27	-3.02
5	4.79	0.95	4	4.10	0.95	1.59	-2.85	1.41	-2.91
5	4.92	0.94	4	4.13	0.94	1.66	-2.75	1.42	-2.81
5	5.28	0.94	4	4.23	0.94	1.71	-2.66	1.44	-2.72
6	5.51	0.93	4	4.23	0.93	1.71	-2.58	1.44	-2.64
6	5.51	0.93	4	4.23	0.93	1.79	-2.50	1.44	-2.56
6	5.97	0.92	5	4.69	0.92	1.96	-2.43	1.55	-2.49
7	7.08	0.92	5	5.31	0.92	2.04	-2.36	1.67	-2.43
8	7.70	0.91	6	5.64	0.91	2.06	-2.30	1.73	-2.36
8	7.84	0.90	6	5.87	0.90	2.12	-2.24	1.77	-2.30
8	8.36	0.90	7	6.56	0.90	2.14	-2.18	1.88	-2.24
8	8.46	0.89	7	6.79	0.89	2.18	-2.13	1.91	-2.19
9	8.89	0.89	7	7.05	0.89	2.23	-2.08	1.95	-2.14
9	9.34	0.88	8	7.51	0.88	2.24	-2.03	2.02	-2.09
9	9.41	0.88	8	7.84	0.88	2.28	-1.98	2.06	-2.04
10	9.77	0.87	8	8.10	0.87	2.28	-1.93	2.09	-2.00
10	9.80	0.87	8	8.30	0.87	2.31	-1.89	2.12	-1.95
10	10.10	0.86	8	8.39	0.86	2.32	-1.85	2.13	-1.91
10	10.20	0.85	8	8.46	0.86	2.36	-1.80	2.14	-1.87
11	10.59	0.85	9	8.62	0.85	2.38	-1.77	2.15	-1.83
11	10.79	0.84	9	8.66	0.85	2.44	-1.73	2.16	-1.79
12	11.51	0.84	9	9.15	0.84	2.50	-1.69	2.21	-1.76
12	12.16	0.83	9	9.15	0.84	2.60	-1.65	2.21	-1.72
13	13.41	0.83	9	9.31	0.83	2.71	-1.62	2.23	-1.68
15	15.02	0.82	9	9.31	0.83	2.73	-1.58	2.23	-1.65
15	15.28	0.81	9	9.34	0.82	2.74	-1.55	2.23	-1.62
16	15.54	0.81	10	9.64	0.81	2.77	-1.52	2.27	-1.59
16	16.00	0.80	10	9.80	0.81	2.78	-1.49	2.28	-1.55
16	16.20	0.80	10	9.97	0.80	2.83	-1.46	2.30	-1.52
17	16.95	0.79	10	10.07	0.80	2.84	-1.43	2.31	-1.49
17	17.18	0.79	10	10.16	0.79	2.85	-1.40	2.32	-1.46
17	17.28	0.78	10	10.20	0.79	2.87	-1.37	2.32	-1.44
18	17.70	0.78	10	10.26	0.78	2.87	-1.34	2.33	-1.41
18	17.70	0.77	10	10.30	0.78	2.89	-1.31	2.33	-1.38
18	17.93	0.76	11	10.52	0.77	2.90	-1.29	2.35	-1.35

Sheet1 Sheet2 Sheet3

Ready — 100%

Microsoft Excel - Boo...


Dr.Oetker
Ristorante
PIZZA PASTA

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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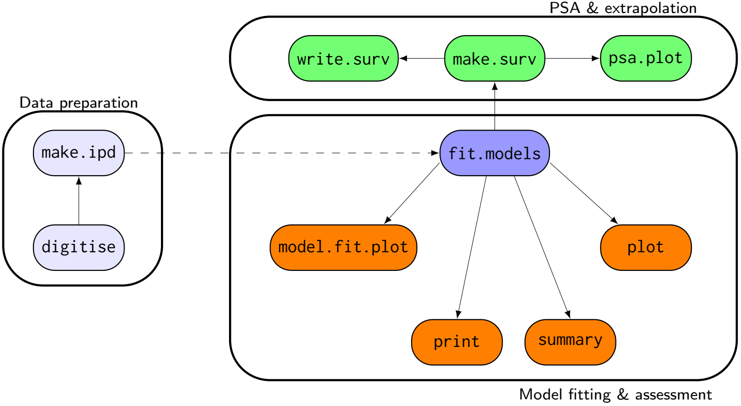
- Automatically produce specialised graphs
  - Survival curves + model fitting statistics (AIC, BIC, DIC)

- Can produce a full PSA characterisation of the parameters **and** the survival curves
  - These can be directly used in the economic model!

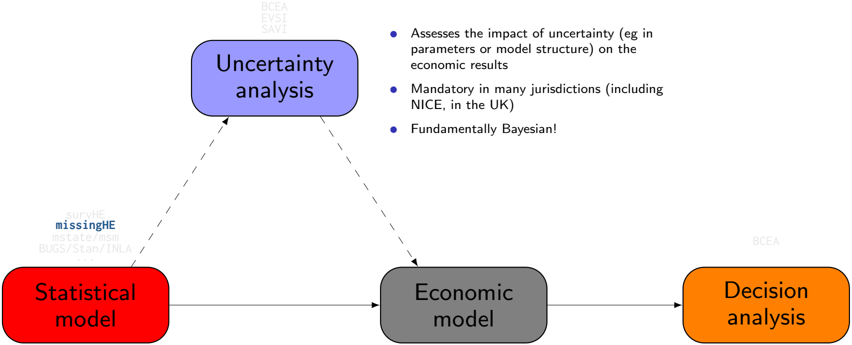
Objective: Simplify and standardise commands to fit survival analysis



https://github.com/giabaio/survHE

Health technology assessment (HTA)

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



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- The MenSS pilot RCT evaluates the cost-effectiveness of a new digital intervention to reduce the incidence of STI in young men with respect to the SOC
  - QALYs calculated from utilities (EQ-5D 3L)
  - Total costs calculated from different components (no baseline)

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  - Total costs calculated from different components (no baseline)

Time	Type of outcome	observed (%)	observed (%)
		Control (n_1=75)	Intervention (n_2=84)
Baseline	utilities	72 (96%)	72 (86%)
3 months	utilities and costs	34 (45%)	23 (27%)
6 months	utilities and costs	35 (47%)	23 (27%)
12 months	utilities and costs	43 (57%)	36 (43%)
Complete cases	utilities and costs	27 (44%)	19 (23%)

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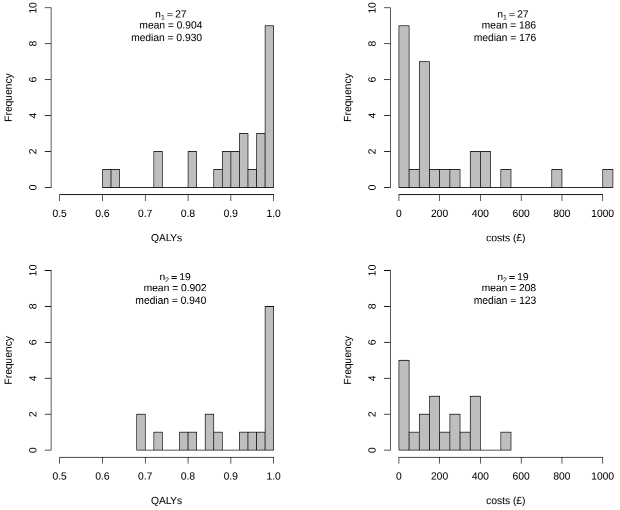
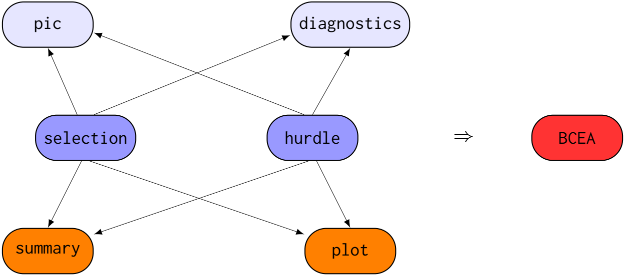
  - Total costs calculated from different components (no baseline)

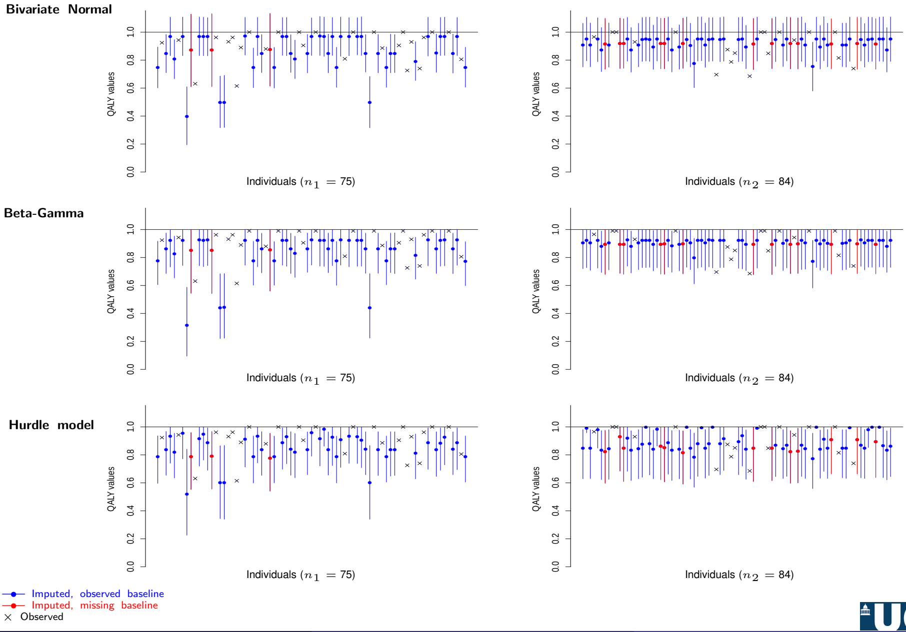


Objective: Run a set of complex models to account for different level of complexity & missingness

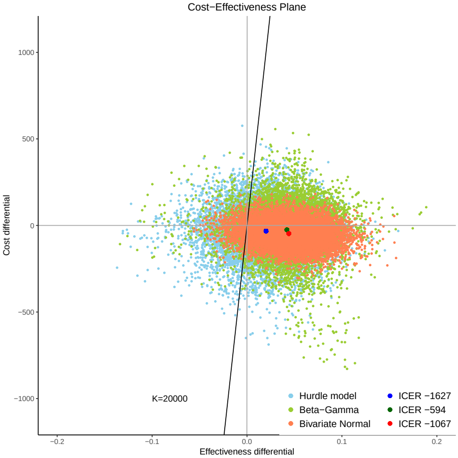


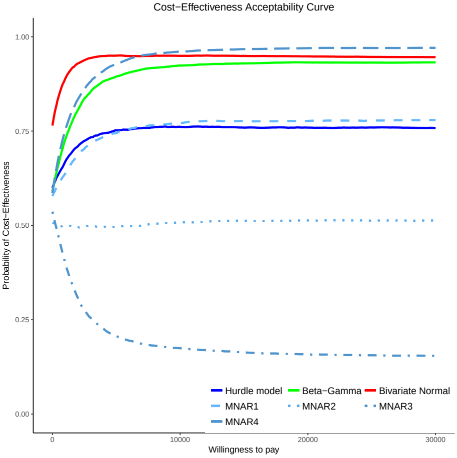
Gabrio et al. (2018). https://arxiv.org/abs/1801.09541
https://github.com/giabaio/missingHE

Bayesian multiple imputation (under MAR)



Cost-effectiveness analysis





All in!

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SAVI - Sheffield Accelerated Value of Information

Funded by NIHR

Release version 2.0.10 (2015-09-24)

Home | About your model | Import files | Check upload | PSA Results | EVPI | EVPPI single parameters | EVPPI groups | Report | About us

What SAVI does

Using **only** PSA results from your model

In a matter of seconds from the SAVI online application you can generate:

1. Standardised assessment of uncertainty (C-E planes and CEACs)
2. Overall EVPI per patient, per jurisdiction per year and over your decision relevance horizon
3. Expected Value of Perfect Parameter Information (EVPPI) for single and groups of parameters

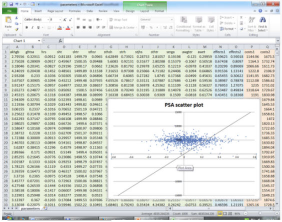
For individual-level simulation models you only need to simulate a small number of individuals per PSA sample. See the "About your model" tab.

Disclaimer: This application is based on peer-reviewed statistical approximation methods. It comes with no warranty and should be utilised at the user's own risk (see here). The underlying code is made available under the BSD 3-clause license.

For more information on the method see Mark Strong's website or this paper.

The SAVI process has 4 steps (using the TABS from left to right)

Step 1: Save PSA input parameters, costs and effects as separate .csv files



Sign up for SAVI news and updates

Send a blank email to savi@sheffield.ac.uk

We won't share your email address with anyone.

Also, you can now follow SAVI on Twitter. The SAVI team tweet regular updates and new features.

Follow @SheffieldSAVI

News

SAVI is now available as an R package, allowing you to run SAVI directly on your own machine. You can download instructions here.

Known issues

Sometimes SAVI will either not load, or will hang for a while. This is because SAVI can only deal with one set of computations at a time, even though SAVI allows multiple concurrent users. Be assured that SAVI keeps concurrent users' data and results separate.

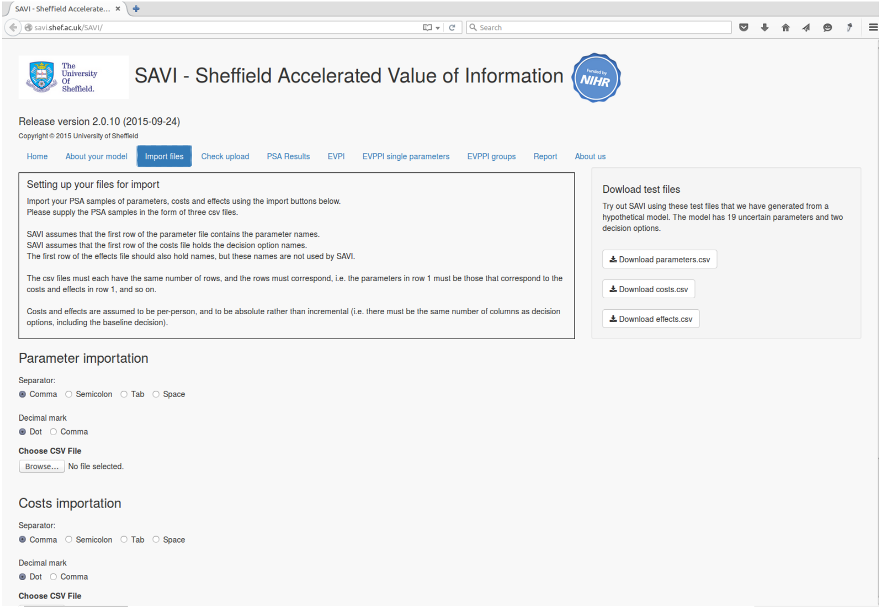
The "Save session" and "Load previously saved session" facilities are temporarily out of action due to problems of backward compatibility with SAVI version 1.

The report that SAVI generates is not quite as polished as we would like. We are working on this.

New features and bug fixes

Fix for version 2.0.9

We have added a note on the EVPPI Groups tab to say that the GP method for calculating partial EVPI for groups of five or more parameters uses only the first 7,500 rows of the PSA.


SAVI - Sheffield Accelerate...
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Search
The University Of Sheffield.
SAVI - Sheffield Accelerated Value of Information
Funded by NIHR
Release version 2.0.10 (2015-09-24)
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Home
About your model
Import files
Check upload
PSA Results
EVPI
EVPPI single parameters
EVPPI groups
Report
About us
Setting up your files for import
Import your PSA samples of parameters, costs and effects using the import buttons below.
Please supply the PSA samples in the form of three csv files.
SAVI assumes that the first row of the parameter file contains the parameter names.
SAVI assumes that the first row of the costs file holds the decision option names.
The first row of the effects file should also hold names, but these names are not used by SAVI.
The csv files must each have the same number of rows, and the rows must correspond, i.e. the parameters in row 1 must be those that correspond to the costs and effects in row 1, and so on.
Costs and effects are assumed to be per-person, and to be absolute rather than incremental (i.e. there must be the same number of columns as decision options, including the baseline decision).
Dowload test files
Try out SAVI using these test files that we have generated from a hypothetical model. The model has 19 uncertain parameters and two decision options.
Download parameters.csv
Download costs.csv
Download effects.csv
Parameter importation
Separator:
Comma
Semicolon
Tab
Space
Decimal mark
Dot
Comma
Choose CSV File
Browse...
No file selected.
Costs importation
Separator:
Comma
Semicolon
Tab
Space
Decimal mark
Dot
Comma
Choose CSV File

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Funded by NIHR

Release version 2.0.10 (2015-09-24)

Home | About your model | Import files | Check upload | PSA Results | EVPI | EVPPI single parameters | EVPPI groups | Report | About us

Overall Expected Value of Perfect Information

The overall EVPI per person affected by the decision is estimated to be £0.8687. This is equivalent to 4.343e-05 QALYs per person on the health effects scale.

If the number of people affected by the decision per year is 1000, then the overall EVPI per year is £868.70 for England.

When thinking about the overall expected value of removing decision uncertainty, one needs to consider how long the current comparison will remain relevant. If the decision relevance horizon is 10 years, then the overall expected value of removing decision uncertainty for England would be £8686.96.

Research or data collection exercises costing more than this amount would not be considered an efficient use of resources. This is because the return on investment from the research – as measured by the health gain and cost savings resulting from enabling the decision maker to better identify the best decision option – is expected to be no higher than £8686.96.

The EVPI estimates in the table below quantify the expected value to decision makers within England of removing all current decision uncertainty at a threshold of £20000 per QALY. This will enable comparison against previous analyses to provide an idea of the scale of decision uncertainty in this topic compared with other previous decisions. The EVPI estimate for a range of willingness-to-pay thresholds are illustrated in the figures below the table.

Overall EVPI

The Expected Value of Removing all Current Decision Uncertainty

	Overall EVPI (£)	Overall EVPI (QALY)
Per Person Affected by the Decision	1	0.00
Per Year in England Assuming 1000 Persons Affected per Year	869	0.04
Over 5 Years	4343	0.22
Over 10 Years	8687	0.43
Over 15 Years	13030	0.65
Over 20 years	17370	0.87
Over Specified Decision Relevance Horizon (10 years)	8687	0.43

Download table as a csv file

Download table

Overall EVPI (on costs scale) versus lambda

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

BCEAweb - Mozilla Firefox

File Edit View History Bookmarks Tools Help

BCEAweb

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

BCEAweb

Welcome | 1. Check assumptions | 2. Economic analysis | 3. Probabilistic Sensitivity Analysis | 4. Value of information | 5. Report

In this panel, the user can upload the simulations for the relevant model parameters.

1. Import parameters simulation data from:

Spreadsheet

Choose CSV File

Browse... parameters.csv

Upload complete

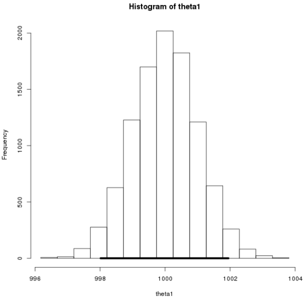
2. Select parameter of interest for checking

theta1

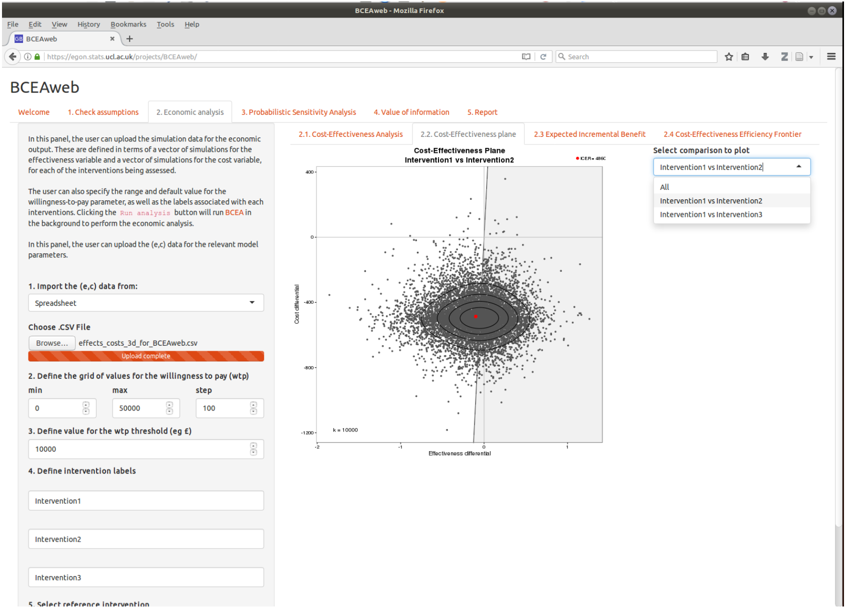
3. Select the number of bins for histogram

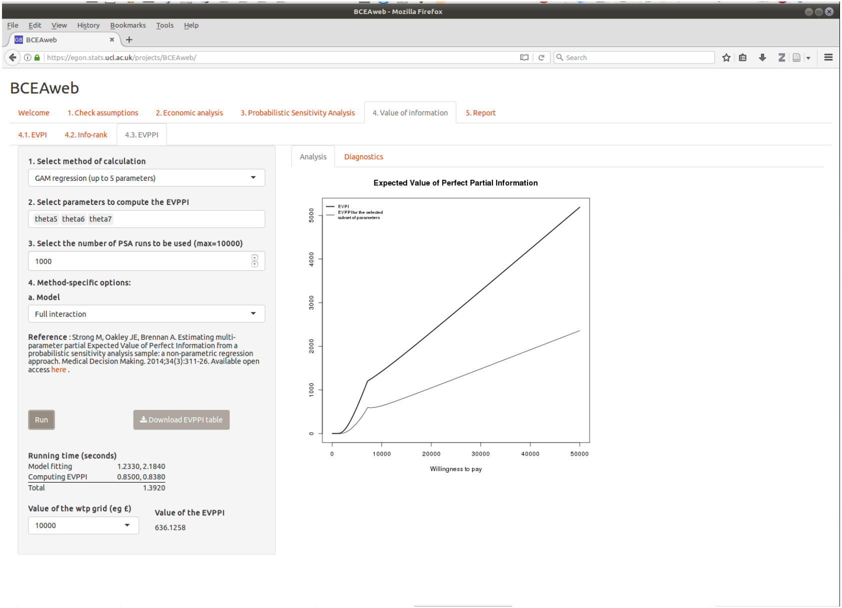
5 15 25

1.1. Plot and summary | 1.2. Trace plots



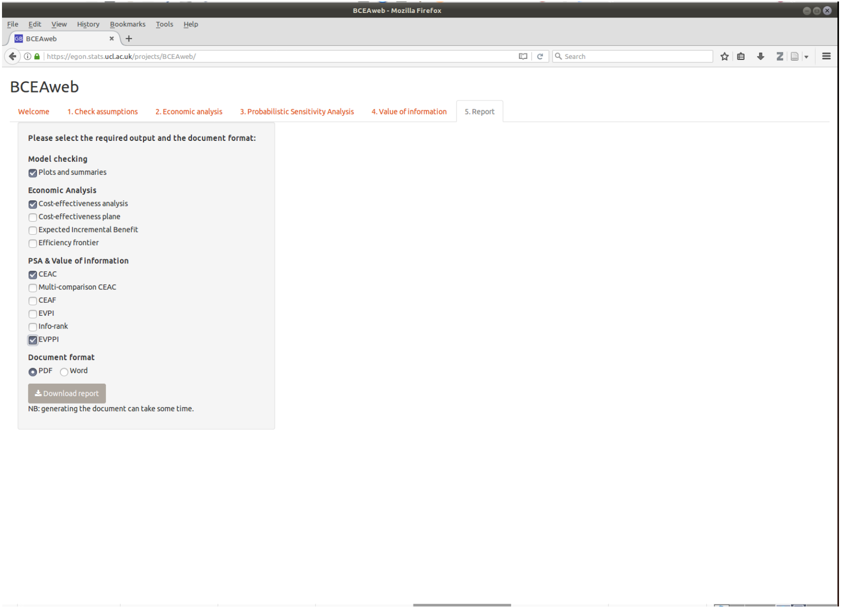
	Mean	Standard deviation	2.5%	Median	97.5%	Monte Carlo SE
theta1	999.994	0.99863	998.017	1000.011	1001.946	0.0099858


BCEAweb - Mozilla Firefox
File Edit View History Bookmarks Tools Help
BCEAweb
https://egon.stats.ucl.ac.uk/projects/BCEAweb/
Search
BCEAweb
Welcome
1. Check assumptions
2. Economic analysis
3. Probabilistic Sensitivity Analysis
4. Value of information
5. Report
In this panel, the user can upload the simulation data for the economic output. These are defined in terms of a vector of simulations for the effectiveness variable and a vector of simulations for the cost variable, for each of the interventions being assessed.
The user can also specify the range and default value for the willingness-to-pay parameter, as well as the labels associated with each interventions. Clicking the Run analysis button will run BCEA in the background to perform the economic analysis.
In this panel, the user can upload the (e,c) data for the relevant model parameters.
1. Import the (e,c) data from:
Spreadsheet
Choose .CSV File
Browse...
effects_costs_3d_for_BCEAweb.csv
Upload complete
2. Define the grid of values for the willingness to pay (wtp)
min
max
step
0
50000
100
3. Define value for the wtp threshold (eg £)
10000
4. Define intervention labels
Intervention1
Intervention2
Intervention3
5. Select reference intervention
2.1. Cost-Effectiveness Analysis
2.2. Cost-Effectiveness plane
2.3 Expected Incremental Benefit
2.4 Cost-Effectiveness Efficiency Frontier
Cost-Effectiveness Plane
Intervention1 vs Intervention2
ICER= 486C
Cost differential
Effectiveness differential
k = 10000
400
0
-400
-800
-1200
-2
-1
0
1
Select comparison to plot
Intervention1 vs Intervention2
All
Intervention1 vs Intervention2
Intervention1 vs Intervention3


BCEAweb - Mozilla Firefox
File Edit View History Bookmarks Tools Help
BCEAweb
https://egon.stats.ucl.ac.uk/projects/BCEAweb/
Search
BCEAweb
Welcome
1. Check assumptions
2. Economic analysis
3. Probabilistic Sensitivity Analysis
4. Value of information
5. Report
4.1. EVPI
4.2. Info-rank
4.3. EVPPI
1. Select method of calculation
GAM regression (up to 5 parameters)
2. Select parameters to compute the EVPPI
theta5 theta6 theta7
3. Select the number of PSA runs to be used (max=10000)
1000
4. Method-specific options:
a. Model
Full interaction
Reference : Strong M, Oakley JE, Brennan A. Estimating multi-parameter partial Expected Value of Perfect Information from a probabilistic sensitivity analysis sample: a non-parametric regression approach. Medical Decision Making. 2014;34(3):311-26. Available open access here .
Run
Download EVPPI table
Running time (seconds)
Model fitting 1.2330, 2.1840
Computing EVPPI 0.8500, 0.8380
Total 1.3920
Value of the wtp grid (eg £)
10000
Value of the EVPPI
636.1258
Analysis
Diagnostics
Expected Value of Perfect Partial Information
EVPI
EVPPI for the selected subset of parameters
0
1000
2000
3000
4000
5000
0
10000
20000
30000
40000
50000
Willingness to pay

BCEAweb

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



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

1. Introduction | 2. Parameter input | 3. Cohort simulation | 4. Health economic evaluation | 5. Value of information

The parameters of the base-case scenario can be displayed without running the model.

Show base-case

After completing the selection of the inputs, click the button to run the statistical analysis

Run MCMC

MCMC simulations: 50

Population parameters | Survival analysis | Administration costs | Treatment costs | Adverse events | Utilities

Population indolent non-Hodgkin's lymphoma (source)

13518

% rituximab refractory follicular lymphoma

Mean (source): 9 | SD (assumption): 0.01

Mean age (source)

62.07

Weight in kg

Mean (source): 81 | SD (assumption): 10

Height in cm

Mean (source): 169.52 | SD (assumption): 10

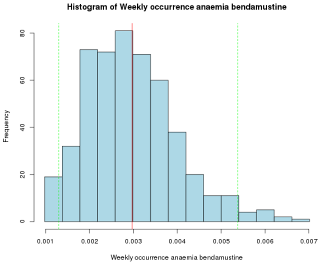
2.1 Check assumptions | 2.2 Trace plots | 2.3 GR plots | 2.4 Effective sample size | 2.5 Autocorrelation

Parameter of interest

Weekly occurrence anaemia bendamustine

Select the number of BINs for histogram

5 — 15 — 25



Mean	Standard deviation	2.5%	Median	97.5%	Monte Carlo SE
0.0029703	0.0010262	0.0012969	0.0028678	0.0053797	0.0004194

Escape (from `Excel`) to victory