Introduction to R for Health Economics using BCEA

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Health Economic Modeling in R: A Hands-on Introduction
ISPOR Europe 2022, Vienna, Austria

6 November 2022

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UCL Statistical Science

Disclaimer...

...Just so you know what you're about to get into... 😉

Health technology assessment (HTA)

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- Estimates relevant **population** parameters θ
- Varies with the type of available data (& statistical approach!)

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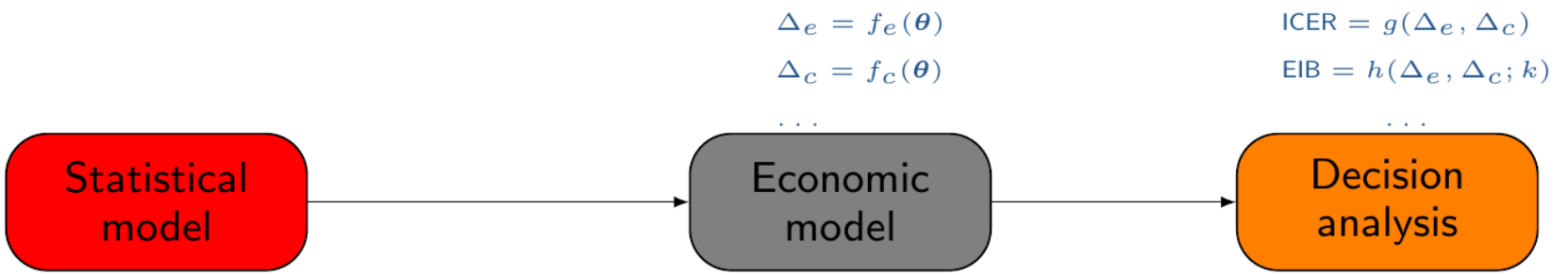

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- Standardised process

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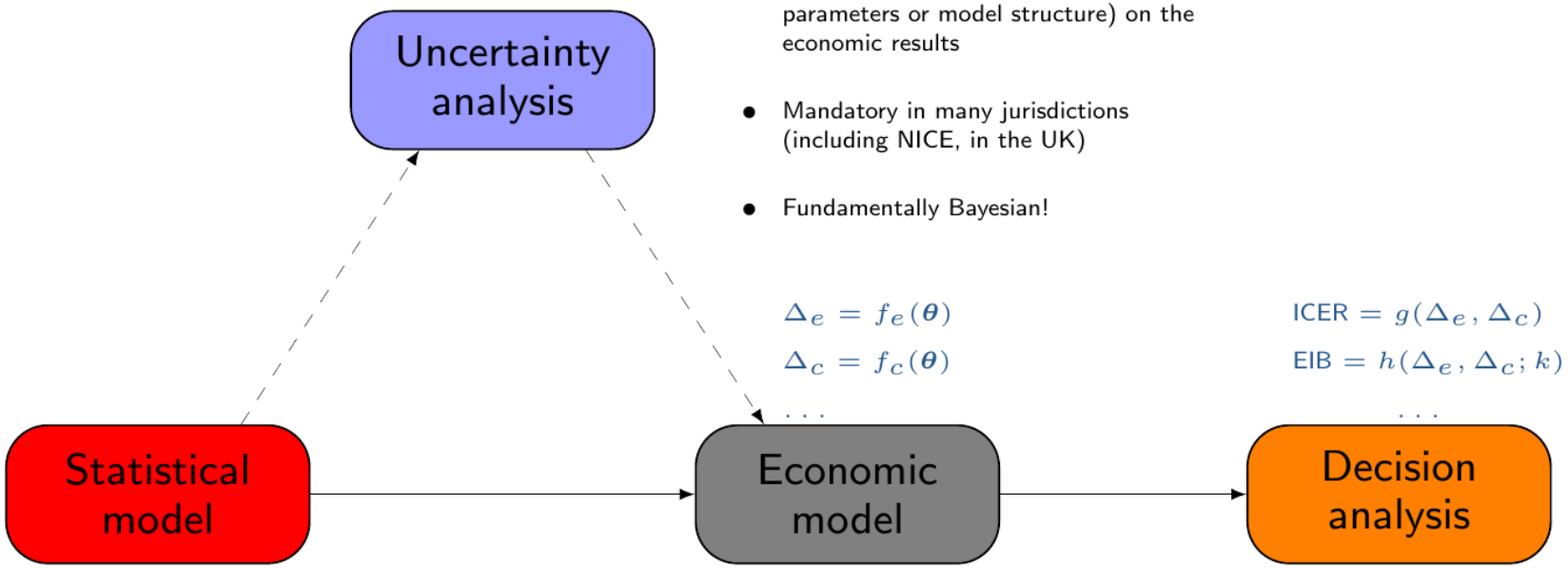

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- Mandatory in many jurisdictions (including NICE, in the UK)
- Fundamentally Bayesian!

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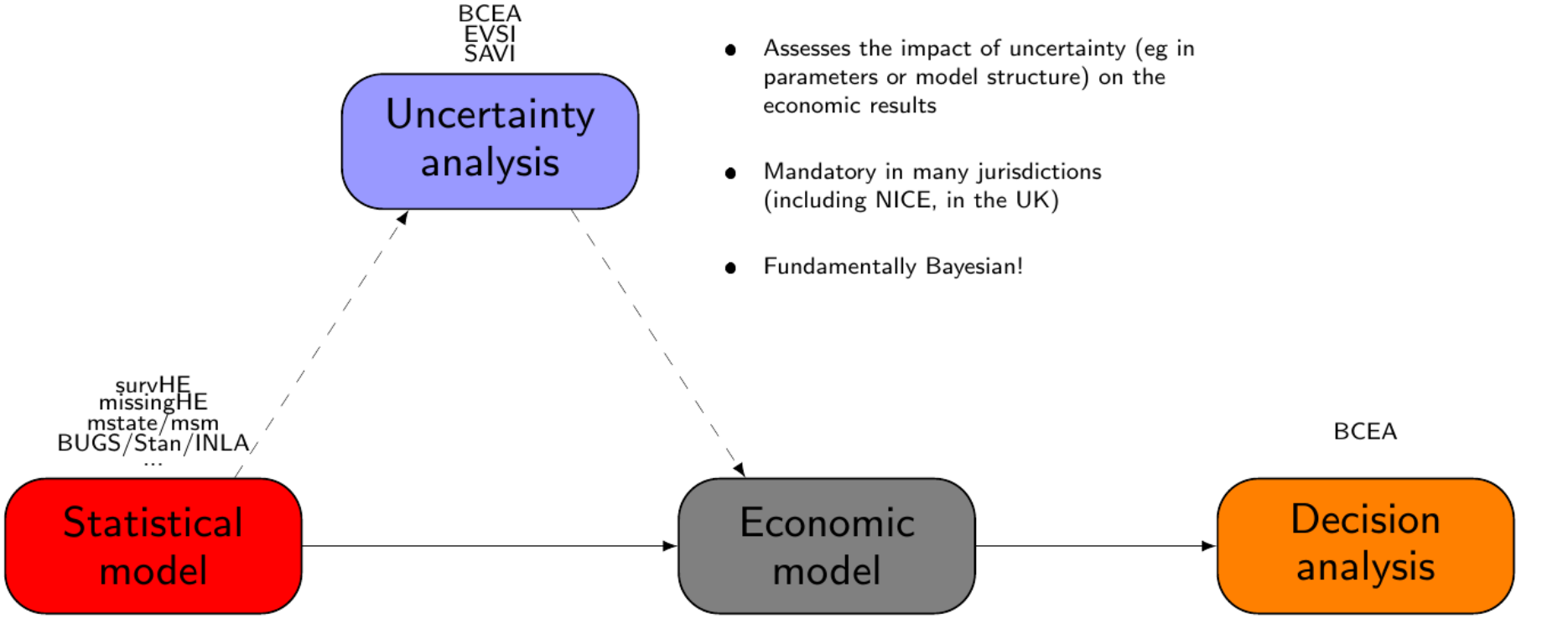

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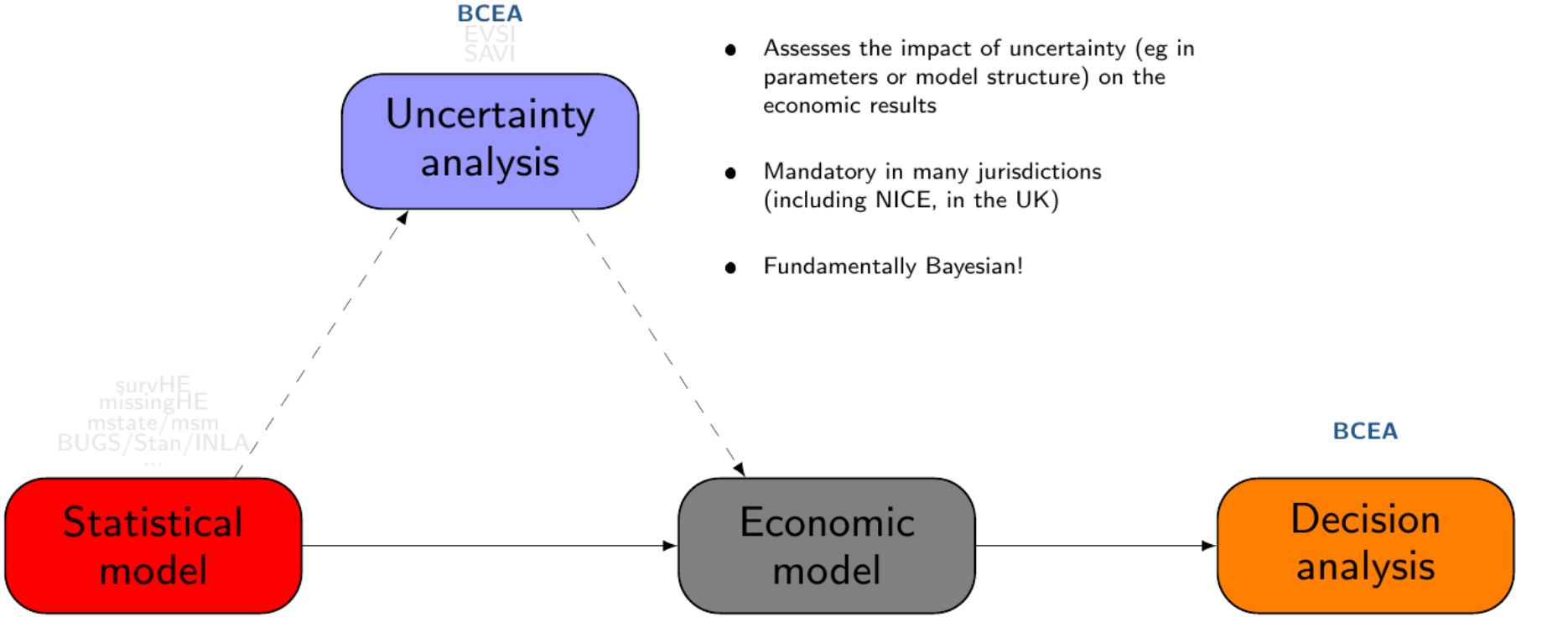

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What is R?

- R is a very powerful **statistical software**
  – Specifically designed for statistical analysis
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  – **Open source and free**

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Why use R?

- Everything can be (and almost invariably is) scripted
- This helps with:
  – Reproducibility
  – Sharing your work with colleagues
  – Reusing templates for "similar" projects
  – **"Transparency"**!
- **Fantastic** graphical capability
  – Especially with new `tidyverse` packages (`ggplot2`)
- Generally **fit for purpose**
  – You **need** advanced tools for many (most??) of the models you do...

Section added to the site with Tutorials!

We have added a new section to the website, with a view of collating tutorials on tools for economic evaluation based on R. The first one is an online tutorial on creating a Shiny interface for Markov models by Robert Smith and Paul Schneider from University of Sheffield. Shiny allows you to create user friendly and web-accessible graphical user interfaces for your R models. More details here"

But...

> "*Transparency is in the eye of the beholder*"
> (Andy Briggs at the R-HTA workshop – October 2020)

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- There **is** an entry cost
- And more importantly, the effort goes hand in hand with sophistication in the statistical modelling associated with the economic evaluation!


Totally worth it.

BCEA

A R package for (Bayesian) cost-effectiveness analysis

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

1. 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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   - 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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3. Perform uncertainty analysis
   - 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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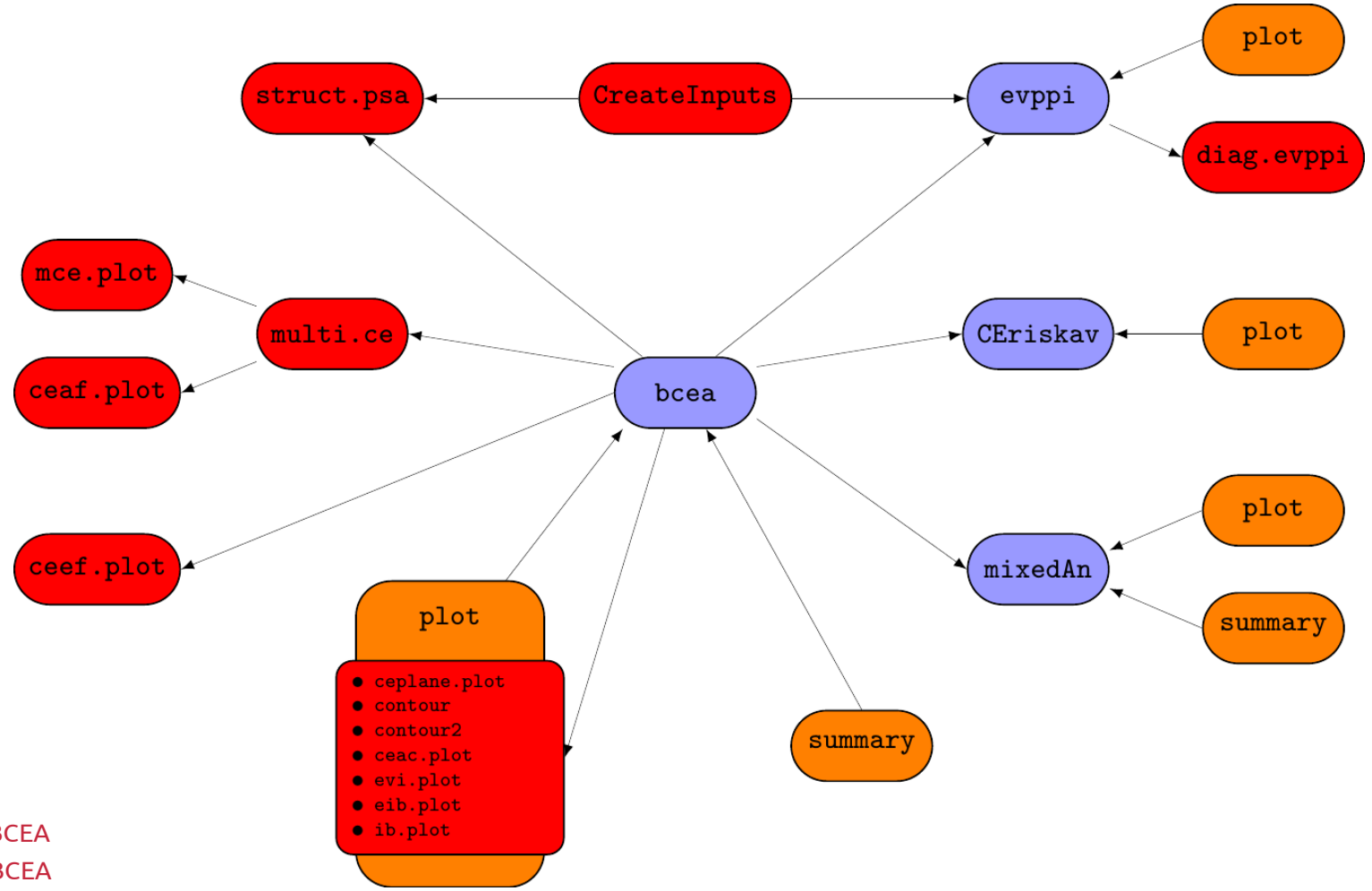
4. Standardised reporting
   - Graphical tools (use **excellent** R facilities)
   - Embed code in structured reports (docx/pdf)

A R package for (Bayesian) cost-effectiveness analysis



www.statistica.it/gianluca/BCEA
https://github.com/giabaio/BCEA

Using BCEA to summarise outputs of an economic model

How does BCEA work?

- BCEA is available from CRAN
  - Current *stable* version: 2.4-2 (3 September 2022)
- But it is also under constant development in the GitHub repository
  - Current *stable* version: 2.4-2 (3 September 2022)
  - Current *development* version: 2.4-2 (ongoing development, until integrated in the next stable release)

```
> # Install BCEA (only required once and needs an internet connection!).
>
> # You can either get the "official" version from CRAN
> install.packages("BCEA")
>
> # Or the development version from the GitHub repository
> remotes::install_github("giabaio/BCEA")              # stable version (2.4-2)
>
> remotes::install_github("giabaio/BCEA",ref="dev")    # development version (2.4-2)
```

NB: The beauty of the GitHub version is that it can be updated on the fly and be immediately available for users!

How does BCEA work?


```
> library(dplyr)  # (Not necessary - helpful for data manipulation!)
>
> library(BCEA)   # Then loads the package (so you can access its functions)
> data(Vaccine)   # Loads an example dataset
```

- The "Vaccine" example is a fictional cost-effectiveness model for and influenza vaccine, based on evidence synthesis (and a real case)
- 2 treatment options ("Standard of care" vs "Vaccination") and overall 63 parameters
- Discussed in details in 📖 Baio et al, 2017 and Baio and Dawid, 2011
- In this case, PSA simulations obtained from a full Bayesian model, but could be done in a spreadsheet and imported into R

How does BCEA work?


```
> # The object 'Vaccine' contains a matrix 'vaccine_mat', with all the simulated values for the many model
> # parameters BCEA can create a matrix with the underlying model simulations starting from various formats
> # (BUGS/R/Excel) and can get rid of "redundant" columns (those that are linear combination of each other...)
> inp = createInputs(vaccine_mat, print_is_linear_comb = FALSE)
>
> # Visualise the output: "piping" ('%>%') + nicer visualisation
> inp$mat %>% as_tibble()
```

NB: There are various R packages/tools to work with tables

- kable and kableExtra

How does BCEA work?

Installation | Using BCEA | Show. Me. The. Data! | ... | Economic model | Cost & effects

```
# A tibble: 1,000 × 56
   Adverse.e…¹ Death…² Death…³ Death…⁴ GP.1.1. GP.2.1. GP.2.2. Hospi…⁵ Hospi…⁶ Hospi…⁷ Infec…⁸ Infec…⁹ Infec…ˣ Mild…
         <dbl>   <dbl>   <dbl>   <dbl>   <dbl>   <dbl>   <dbl>   <dbl>   <dbl>   <dbl>   <dbl>   <dbl>   <dbl>   <db
 1        1466       1       0       0    1664     958     230       0       1       0    5992    3401     876      6
 2        5329       1       1       0    1414     748     276       0       0       1    7471    4024    1536      5
 3        5203       1       1       0     809     489      80       0       0       0    6718    4300     788      3
 4        2351       2       0       0    1761    1157     261       1       0       0    4837    3269     702      7
 5        8303       1       2       0    2472     964     432       1       1       0    4749    1894     846     10
 6        3607       1       1       0    2224    1342     260       1       0       0    4938    2976     596      9
 7        6304       4       1       1    3478    1107     591       2       1       0   11080    3547    2045     15
 8        4337       1       1       1    1483     799     189       0       0       0    3867    2164     525      6
 9        5482       0       0       0    1587     798     279       0       0       0    5163    2532     910      6
10        3125       2       2       0    2578    1681     243       0       0       0    7265    4766     700     10
# … with 990 more rows, 38 more variables: Pneumonia.2.2. <dbl>, Trt.1.1.1. <dbl>, Trt.2.1.1. <dbl>, Trt.1.2.1. <dbl
#   Trt.1.2.2. <dbl>, Trt.2.2.2. <dbl>, beta.1. <dbl>, beta.2. <dbl>, beta.3. <dbl>, beta.4. <dbl>, beta.5. <dbl>, b
#   delta <dbl>, eta <dbl>, gamma.1. <dbl>, gamma.2. <dbl>, lambda <dbl>, n.1.2. <dbl>, n.2.2. <dbl>, phi <dbl>, pi.
#   psi.2. <dbl>, psi.3. <dbl>, psi.4. <dbl>, psi.5. <dbl>, psi.6. <dbl>, psi.7. <dbl>, psi.8. <dbl>, q.1. <dbl>, q.
#   q.7. <dbl>, rho.2. <dbl>, xi <dbl>, and abbreviated variable names ¹Adverse.events, ²Death.1.1., ³Death.2.1., ⁴D
#   ⁶Hospital.2.1., ⁷Hospital.2.2., ⁸Infected.1.1., ⁹Infected.2.1., ˣInfected.2.2., ˣMild.Compl.1.1., ˣMild.Compl.2.
#   ˣPneumonia.1.1., ˣPneumonia.2.1.
```

How does BCEA work?


```
> # Defines the number of simulations considered
> n.sims=inp$mat %>% nrow()
> # applies the function 'nrow' (number of rows) to the object 'inp$mat'
> # NB: Since R 4.1.0, can also use 'native' pipe ('|>')
> # (probably a bit quicker, but in most cases, may be immaterial...)
>
> # Aggregates the model inputs to compute (e,c)
> 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) + ...
```

- NB: The data stored in the `Vaccine` object (built-in in `BCEA`) already contains the objects `e`,`c` that can be used to run the decision analysis...
- So, this step is actually not needed (but documented in 🕮 Baio et al, 2017)

How does BCEA work?


```
> cbind(eff,cost) %>% as_tibble(.name_repair="universal")      # ensures that the columns are named
```

```
# A tibble: 1,000 × 4
   Status.Quo...1 Vaccination...2 Status.Quo...3 Vaccination...4
            <dbl>           <dbl>          <dbl>           <dbl>
 1      -0.00105        -0.000899          10.4            16.3
 2      -0.000884       -0.000732           5.83            9.37
 3      -0.000890       -0.000698           5.78           15.9
 4      -0.00164        -0.00114           12.2            18.7
 5      -0.00135        -0.000957           9.79           16.5
 6      -0.00143        -0.000936           6.56            9.69
 7      -0.000960       -0.00105            8.45           11.3
 8      -0.00181        -0.00139            6.76            9.99
 9      -0.000842       -0.000556           3.60           10.1
10      -0.00168        -0.00105            4.09           11.0
# … with 990 more rows
```

- These calculations *can* be done also in a spreadsheet (nothing more than algebra, **once you have the simulations**)

How does BCEA work?

- At this point, we are ready to call the function `bcea` that runs the economic analysis, for example something like

```
> treats = c("Status quo","Vaccination")
> m = bcea(e=eff,c=cost,ref=2,interventions=treats,Kmax=50000)
```

- The inputs to the function are
  - `eff`: a **matrix** containing the simulations for the clinical benefits (that is $n_{\text{sim}} \times n_{\text{int}}$ values)
  - `cost`: a **matrix** containing the simulations for the costs (that is $n_{\text{sim}} \times n_{\text{int}}$ values)
  - `ref`: an indication of which intervention is to be taken as reference (default: the intervention in the first column of `e` or `c`)
  - `interventions`: a vector of labels for the interventions being compared
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- The output is an object `m` containing several elements

```
> names(m)
```

```
 [1] "n_sim"          "n_comparators" "n_comparisons" "delta_e"       "delta_c"       "ICER"          "Kmax"
[10] "ib"             "eib"           "kstar"         "best"          "U"             "vi"            "Ustar"
[19] "ref"            "comp"          "step"          "interventions" "e"             "c"
```

How does BCEA work?

Can visualise the output in various formats (tables/graphs)

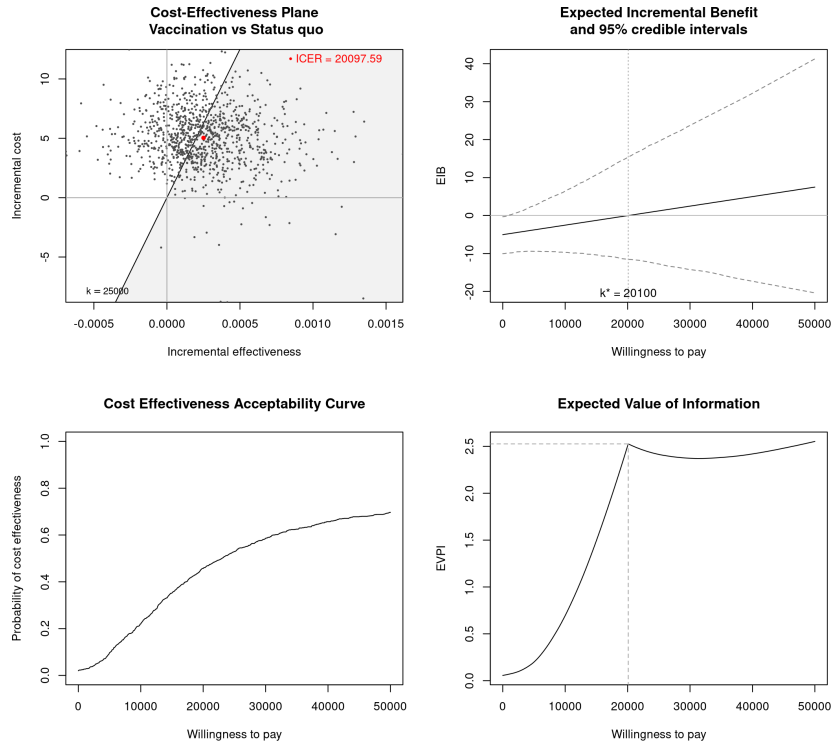
```
> # The 'summary' "method" produces a tabular output
> summary(m)
```

```
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 net benefit
Vaccination                -36.054
Status quo                 -34.826

                            EIB  CEAC  ICER
Vaccination vs Status quo 1.2284 0.529 20098

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

EVPI 2.4145
```

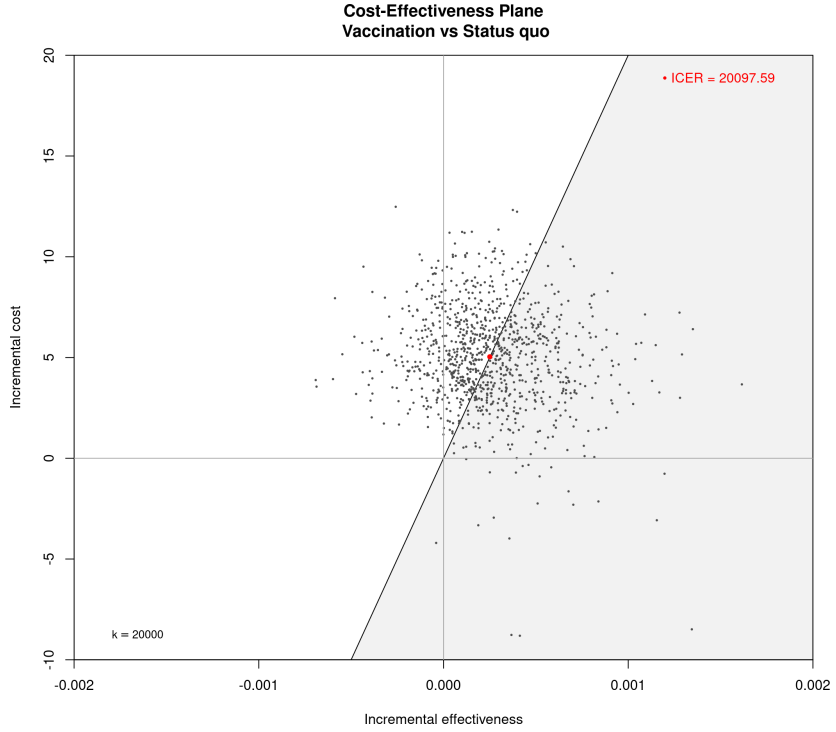
How does BCEA work?

Can visualise the output in various formats (tables/graphs)

```
> # The 'plot' "method" produces a *specific*
> # version of graphical output
> plot(m)
```

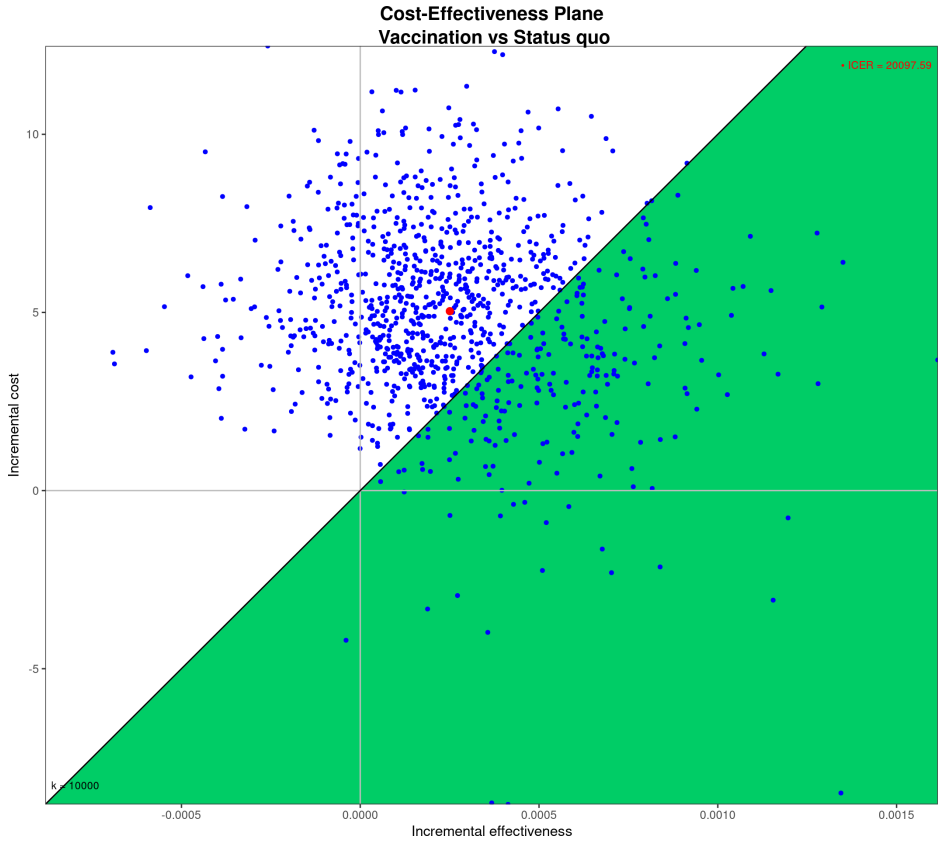



```
> ceplane.plot(
+   m,wtp=20000,xlim=c(-.002,.002),ylim=c(-10,20)
+ )
```



How does BCEA work?

```
> # Using 'ggplot', you can go crazy with customisation...
> ceplane.plot(m,wtp=10000,graph="gg",point=list(color="blue",size=1.8),area=list(fill="springgreen3"))
```



- https://ggplot2.tidyverse.org/
- https://n8thangreen.github.io/BCEA/

BCEA

> Perform Bayesian Cost-Effectiveness Analysis in R.

🚀 **Version 2.4.1 out now!** Check out the release notes here.

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Links

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Report a bug

License

Full license

GPL-3

Community

Contributing guide

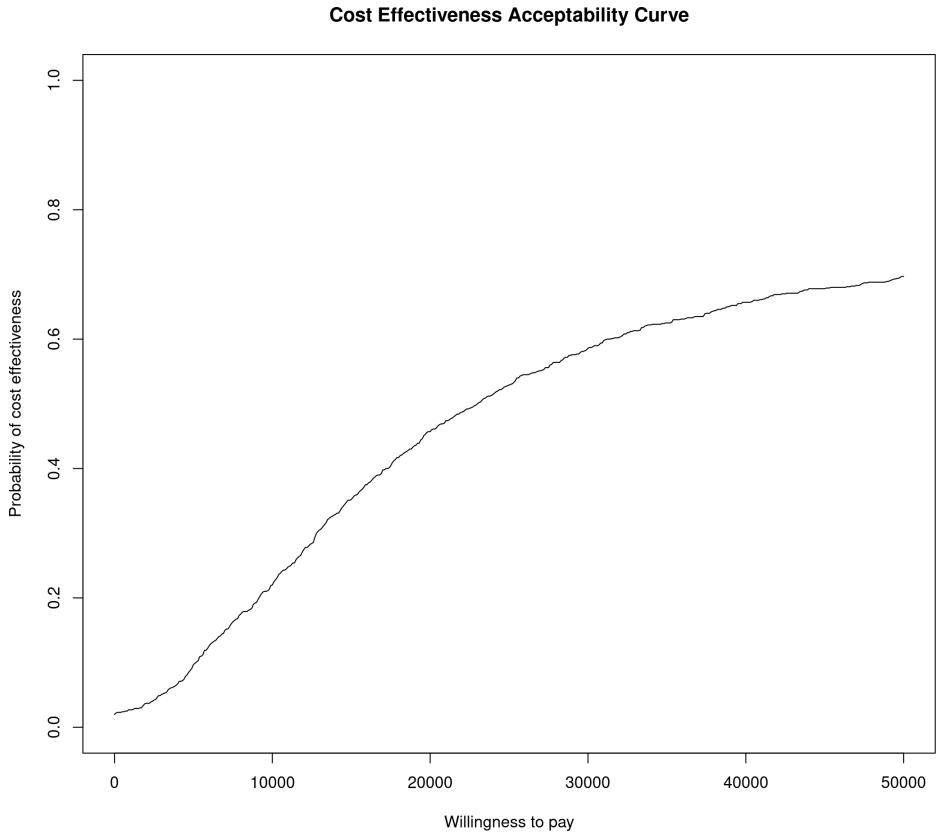
Citation

Citing BCEA

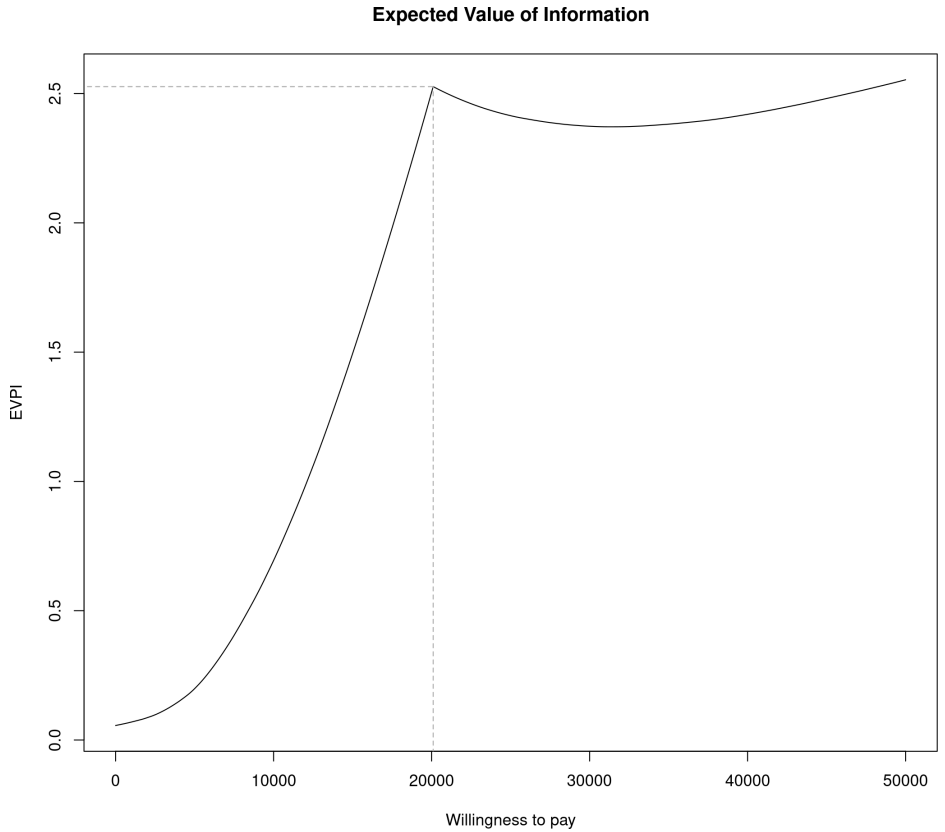
Developers

How does BCEA work?

```
> # Plots the Cost-Effectiveness Acceptability Curve
> ceac.plot(m)
```



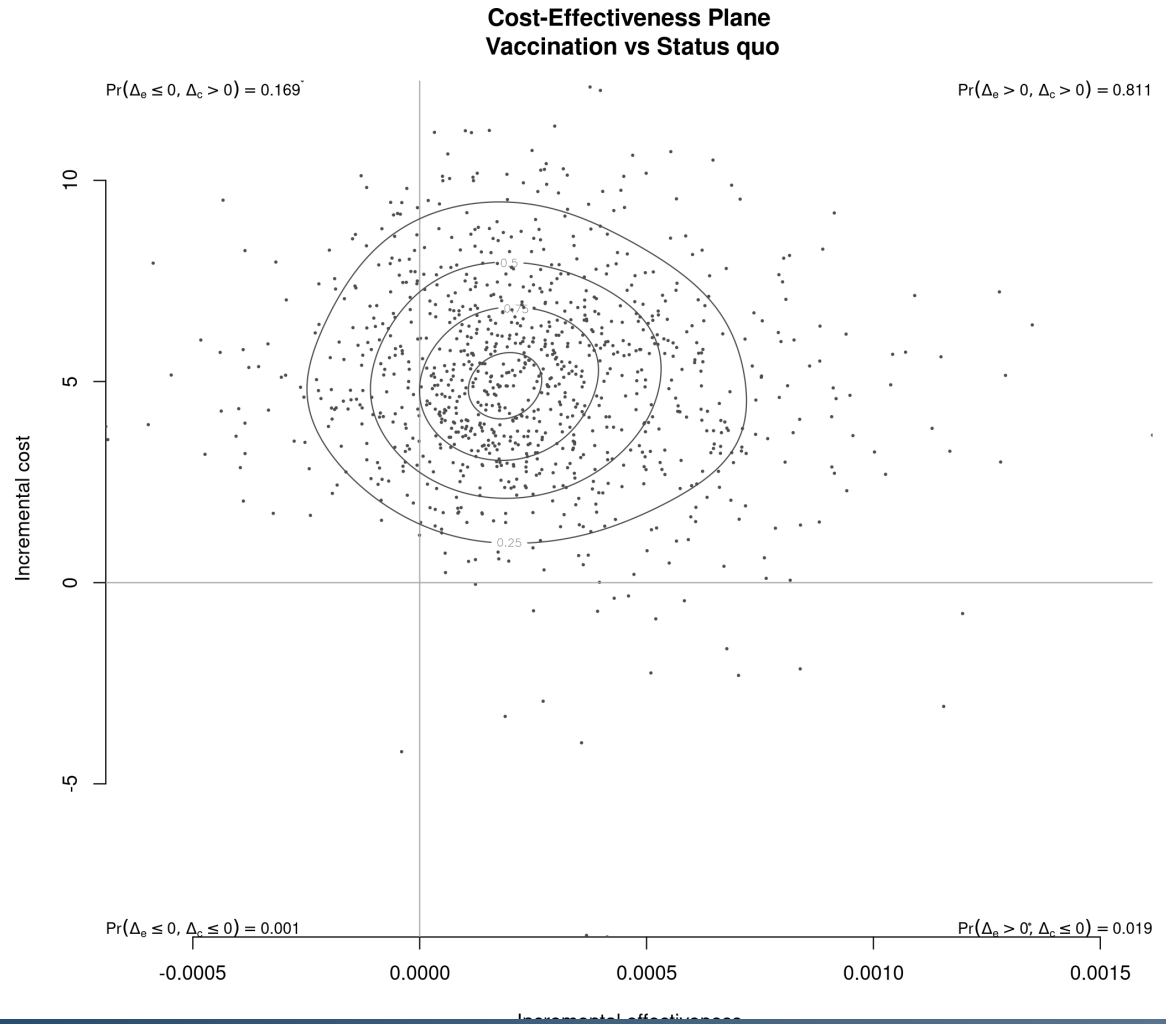

```
> # Plots the Expected Value of Partial Information (
> evi.plot(m)
```



Specialised plots

- Can generate a *contour* plot of the cost-effectiveness plane and estimate the proportion of points in each quadrant

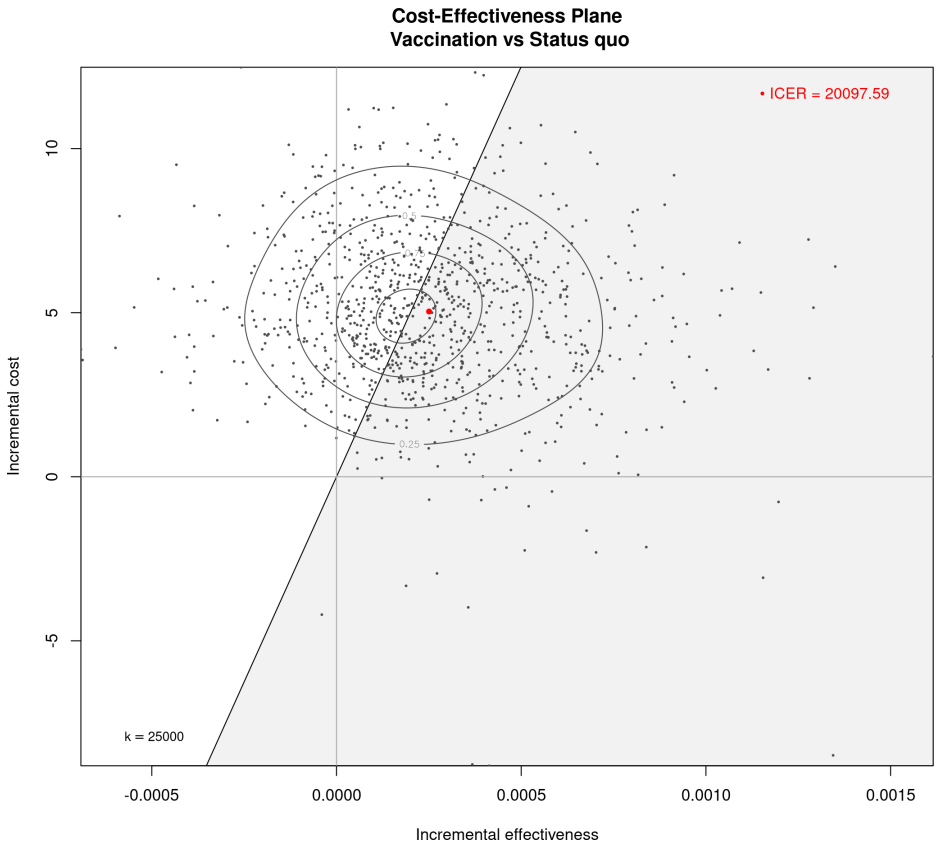
```
> # "Basic" contourplot
> contour(m)
```



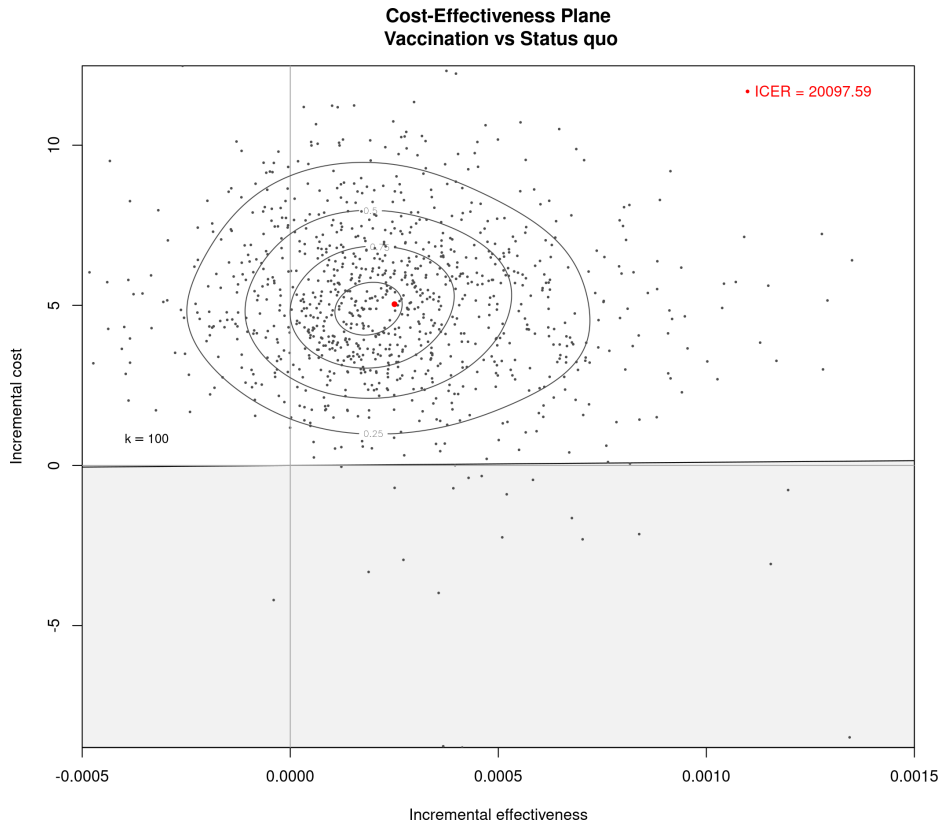
Specialised plots

The specialised function `contour2` also shows the **sustainability area**

```
> contour2(m)
```




```
> contour2(m,wtp=100,xlim=c(-.0005,0.0015))
```



Cost-effectiveness efficiency frontier

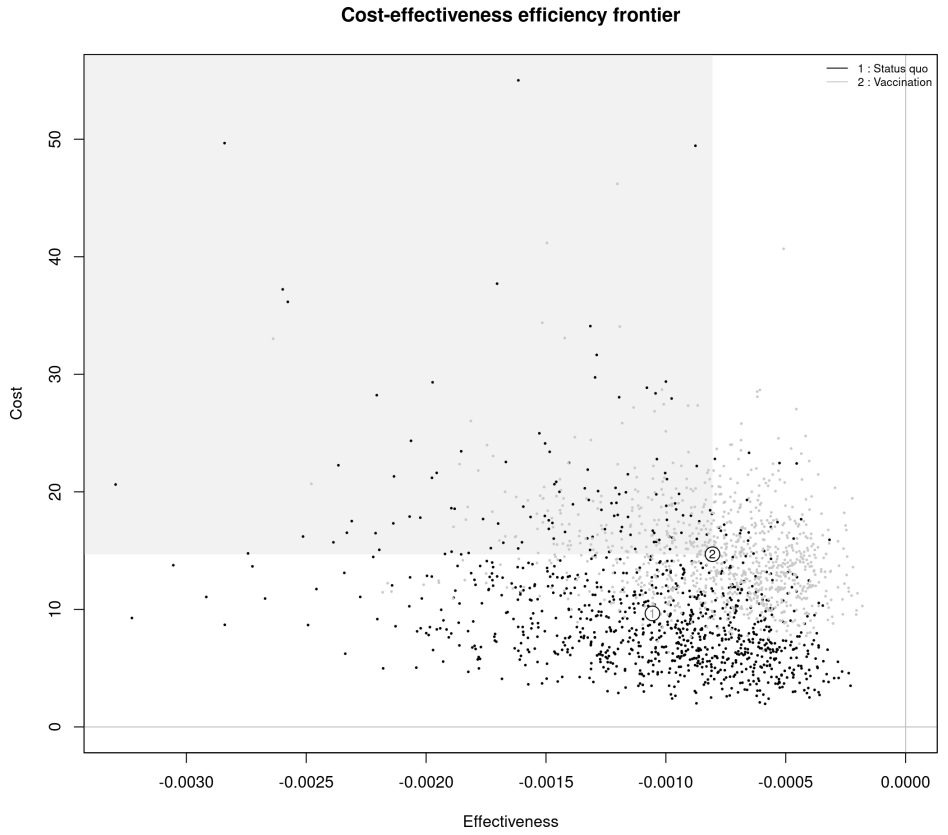
```
> ceef.plot(m,print.plot=FALSE)
```

```
Cost-effectiveness efficiency frontier summary

Interventions on the efficiency frontier:
            Effectiveness  Costs Increase slope Increas
Vaccination   -0.00080537 14.691             NA

Interventions not on the efficiency frontier:
           Effectiveness  Costs     Dominance type
Status quo    -0.0010559 9.6555 Extended dominance
```

```
> ceef.plot(m,print.summary=FALSE)
```



Exporting graphical output

- R has excellent graphical facilities and the graphs produced by BCEA can be easily exported to many different formats

```
> # "Opens" the graphical device
> pdf("NAME_OF_THE_FILE",width=8,height=8)      # for 'pdf', units are in inches
> # Makes the plot
> ceplane.plot(BCEA_OBJECT)                     # of course, specify whatever name you've
>                                                 #  chosen when creating the object...
> # "Closes" the graphical device
> dev.off()
>
>
> # "Open" the graphical device"
> jpeg("NAME_OF_FILE.jpg",width=480,height=480)  # for 'jpeg' units are in px
> # Makes the plot
> ceplane.plot(BCEA_OBJECT)
> # "Closes" the graphical device
> dev.off()
```

NB: Rstudio and rmarkdown can do even more – that's for another time...

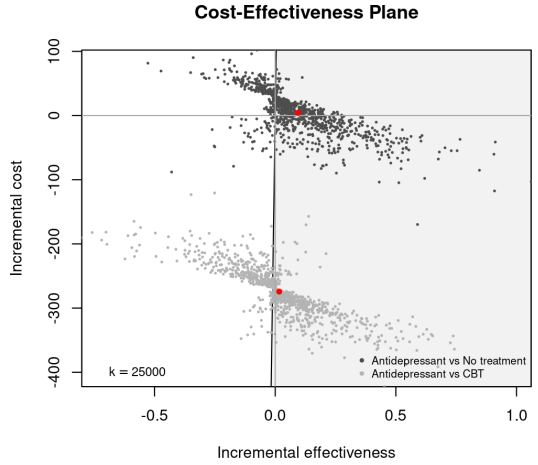
Advanced use of BCEA

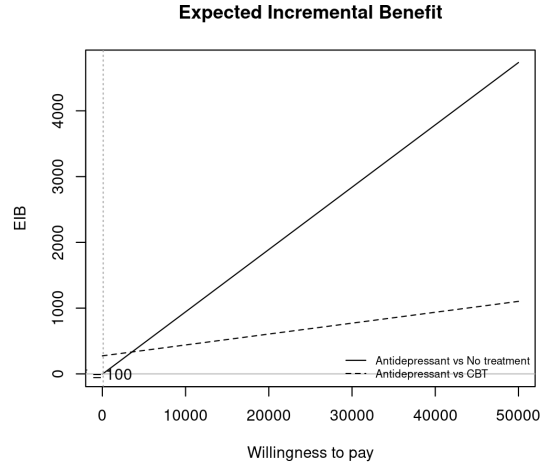
Probabilistic "depression model"

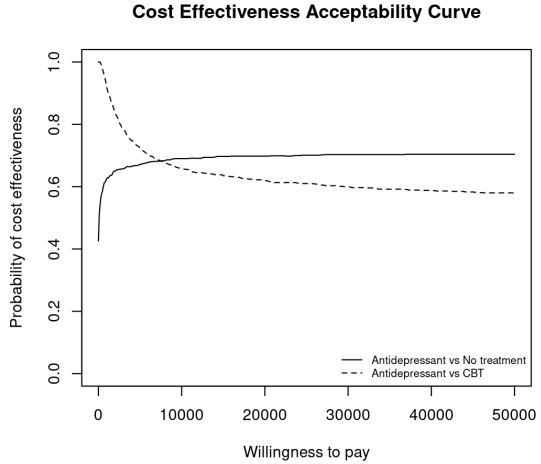
- Fictional model comparing antidepressants to cognitive behaviour therapy (CBT) and no treatment in people with depression
- Statistical modelling based on evidence synthesis
  - Benefits: based on QALYs
  - Costs: associated with treatments and various resources use
- Economic modelling: two matrices with relevant population summaries
  - `effects`
  - `costs`
- NB: The details of the actual modelling are *not* important for the purposes of demonstrating the example...

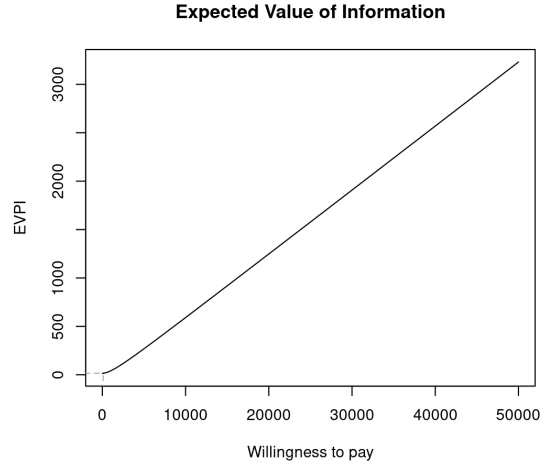
Probabilistic "depression model"

```
> # Intervention labels
> t.names<-c("No treatment","CBT","Antidepressant")
>
> # "Standard" analysis: pairwise comparisons
> depression.bcea = bcea(effects,costs,
+                        interventions=t.names,ref=3)
> # the third intervention is the reference
>
> # Plots the results
> plot(depression.bcea)
```





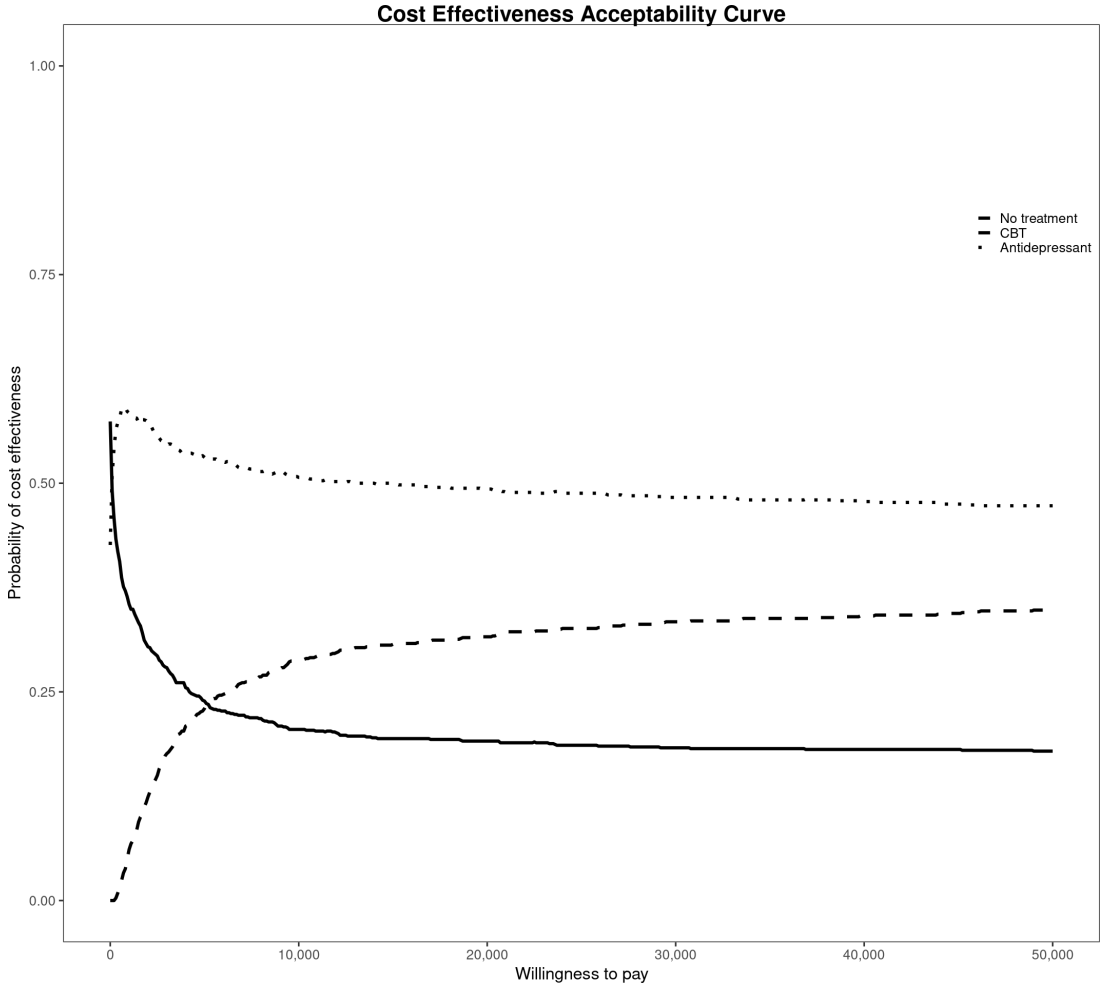




Probabilistic "depression model"

```
> # For multiple treatment comparison
> depression.multi.ce = multi.ce(depression.bcea)
>
> # Specialised plot method
> ceac.plot(
+   depression.multi.ce,pos=c(1,0.8),
+   graph="ggplot2"
+ )
```

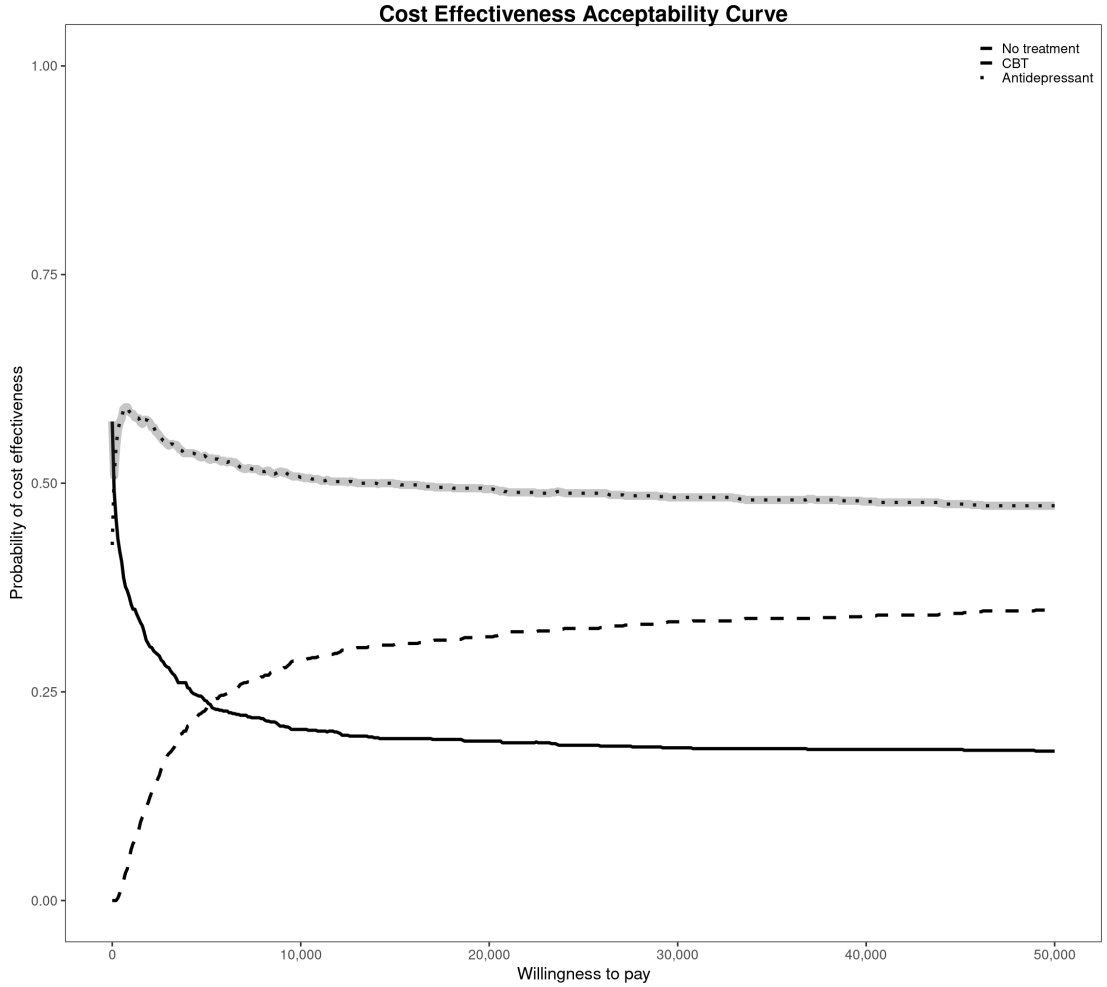
NB: In older releases of BCEA, this graph was done using the **deprecated** function `mce.plot`



Probabilistic "depression model"

- Can use `ggplot` to customise the graph

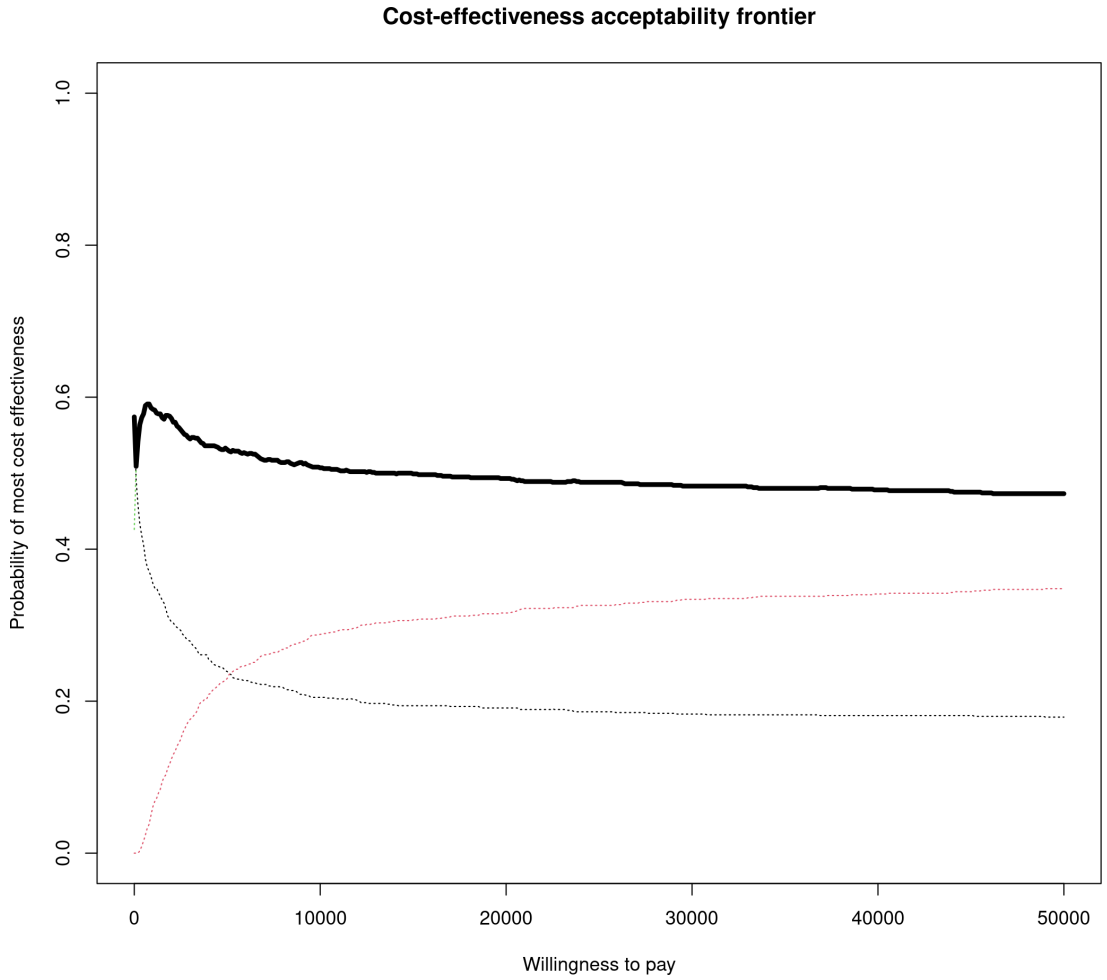
```
> ceac.plot(
+   depression.multi.ce,pos=c(1,1),
+   graph="ggplot2"
+ ) +
+   ggplot2::stat_summary(
+     fun=max, geom="line",
+     colour="grey25",
+     alpha=.3, lwd=2.5
+   )
```



Probabilistic "depression model"

- Can also use the specialised function `ceaf.plot`

```
> # Specialised plot
> ceaf.plot(depression.multi.ce)
```



- Inspired by similar projects – eg SAVI
- Create a web interface to use BCEA without even opening R (or even having it installed on your computer!)

- Inspired by similar projects – eg SAVI
- Create a web interface to use BCEA without even opening R (or even having it installed on your computer!)

- Typical work flow
  1. Design the economic model (eg Markov model, decision tree, ...)
  2. Run the statistical analysis to estimate the quantities of interest (eg survival analysis, evidence synthesis, ...)
  3. Run the economic model and obtain "PSA samples"
  4. Upload "PSA samples", including values for (e, c) to `BCEAweb`
  5. Use `BCEA` in the background to do **all** the economic analysis
  6. Create reports that can be used as the basis for papers, reimbursement files, ...

```
> # Creates a matrix with the underlying model simulations
> inp = createInputs(vaccine_mat, print_is_linear_comb=FALSE)
>
> # Runs BCEAweb
> BCEAweb(e=e,                  # matrix of simulations for the effectiveness
+         c=c,                  # matrix of simulations for the costs
+         parameters=inp$mat    # matrix of simulations for all the model parameters
+        )
```

```
> # Creates a matrix with the underlying model simulations
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>
> # Runs BCEAweb
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+         c=c,                  # matrix of simulations for the costs
+         parameters=inp$mat    # matrix of simulations for all the model parameters
+        )
```

- BCEAweb exists as a standalone webapp
  - Can access it here
- **Or**, you can launch your own "local" version from the BCEA package (as in the code above)!
  - This will launch a web page from which you can manipulate your output (➔ Live Demo)


THANK YOU SO MUCH.