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Decision tree models in R

Howard Thom

London, 8-July-2019

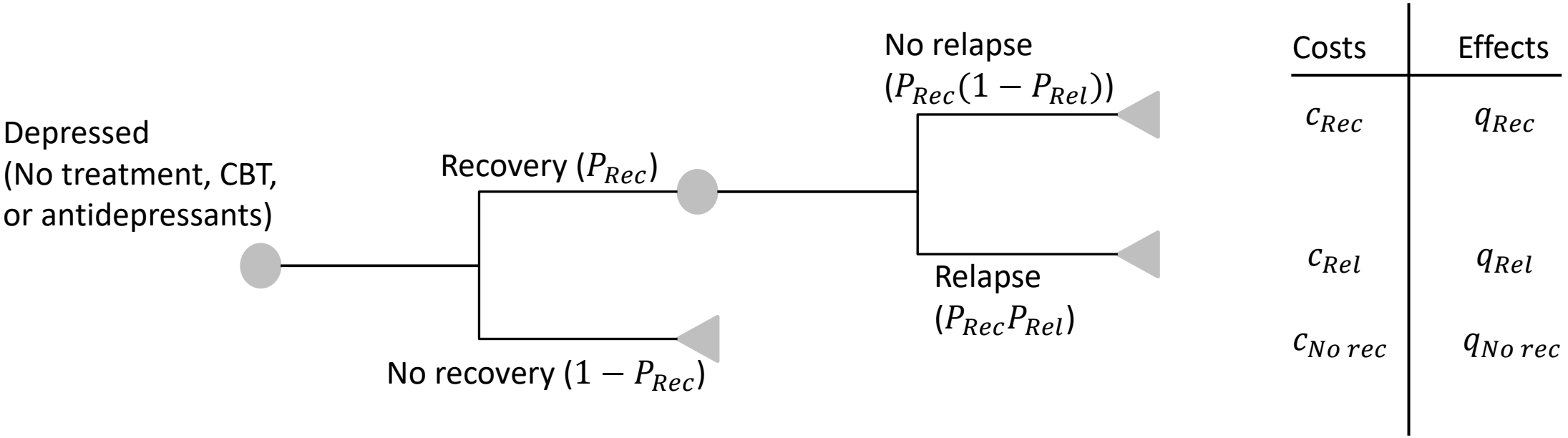
Two steps

- Implementing a (deterministic) decision tree in R
  - Code in “depression.decision.tree.deterministic.R"
- Making the decision tree probabilistic
  - Code in “depression.decision.tree.probabilistic.R"

A deterministic decision tree in R

Open “depression.decision.tree.deterministic.R"

Simple decision tree in R



- Consider this simple decision tree with artificial input parameters.
- Probabilities of recovery and relapse for no treatment (option 1), cognitive behavioural therapy (option 2), and antidepressants (option 3).
- In addition to costs of outcomes, there is a treatment cost TC_k for treatment k

Initial set-up

- Number and names of treatments

```
# Number and names of treatments
n.treat<-3
t.names<-c("No treatment","CBT","Antidepressant")
```

Defining the costs and QALYS of each outcome

- Costs and QALYs for recovery, relapse, and no recovery.

```
# Over a 30 year time horizon
# Costs for recovery, relapse, and no recovery
c.rec<-1000
c.rel<-2000
c.norec<-2500

# Cost of treatment
c.treat<-c(0,300,30)

# Over a 30 year time horizon
# QALYs for recovery, relapse, and no recovery
q.rec<-26
q.rel<-23
q.norec<-20
```

Probabilities of recovery and relapse

```
# Probabilities of recovery and relapse following recover
p.rec<-p.rel<-rep(NA,n.treat)

# Probabilities for no treatment
p.rec[1]<-0.029
p.rel[1]<-0.019
```

- These are 3 element vectors with a probability of the outcome for each of 3 treatments
- Use the same format for probabilities on CBT and antidepressant

Probabilities for CBT and antidepressants

```
# Probabilities for CBT
# Higher recovery probability than no treatment
p.rec[2]<-0.044
# Lowest probability of relapse
p.rel[2]<-0.010

# Probabilities for antidepressant
# Highest probability of recovery
# Higher relapse probability than CBT
p.rec[3]<-0.047
p.rel[3]<-0.017
```

- Names the elements of these vectors after the treatments

```
# Name the vectors
names(p.rec)<-names(p.rel)<-t.names
```

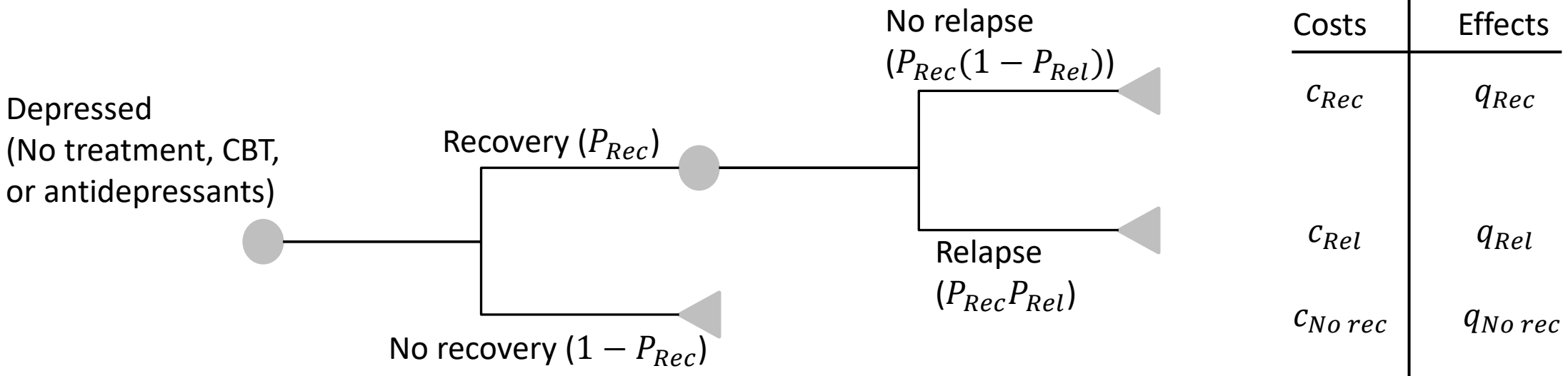
Final set up before generating results

```
# Willingness to pay threshold
lambda.target<-20000

# Create structures to save the incremental costs, effects, and net benefits,
# as well as # absolute costs, effects, and net benefits
incremental.costs<-incremental.effects<-incremental.nb<-
  costs<-effects<-net.benefit<-rep(NA,n.treat)
# Now name these vectors
incremental.costs<-incremental.effects<-incremental.nb<-
  names(c.treat)<-names(costs)<-names(effects)<-t.names
```

- Willingness-to-pay threshold is £20,000
- Set up vectors to store results and name them after the treatments

Total costs and effects for treatment k



Treatment costs

Costs if recover, no relapse

Costs if recover, then relapse

Costs if no recovery

$$Total\ costs_k = TC_k + P_{Rec,k} \times (1 - P_{Rel,k}) \times c_{Rec} + P_{Rec,k} \times P_{Rel,k} \times c_{Rel} + (1 - P_{Rec,k}) \times c_{No\ rec}$$

$$Total\ effects_k = P_{Rec,k} \times (1 - P_{Rel,k}) \times q_{Rec} + P_{Rec,k} \times P_{Rel,k} \times q_{Rel} + (1 - P_{Rec,k}) \times q_{No\ rec}$$

QALYs if recover, no relapse

QALYs if recover, then relapse

QALYs if no recovery

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Total costs and effects in R

$$Total\ costs_k = TC_k + P_{Rec,k} \times \left(1 - P_{Rel,k}\right) \times c_{Rec} + P_{Rec,k} \times P_{Rel,k} \times c_{Rel} + \left(1 - P_{Rec,k}\right) \times c_{No\ rec}$$

$$Total\ effects_k = P_{Rec,k} \times \left(1 - P_{Rel,k}\right) \times q_{Rec} + P_{Rec,k} \times P_{Rel,k} \times q_{Rel} + \left(1 - P_{Rec,k}\right) \times q_{No\ rec}$$

```
costs<-c.treat+p.rec*(1-p.rel)*c.rec+p.rec*p.rel*c.rel+(1-p.rec)*c.norec
effects<-p.rec*(1-p.rel)*q.rec+p.rec*p.rel*q.rel+(1-p.rec)*q.norec
```

Results of the model

```
# Net benefit
net.benefit<-lambda.target*effects-costs

# Incremental results relative to no treamtent
incremental.costs<-costs-costs[1]
incremental.effects<-effects-effects[1]
incremental.net.benefit<-lambda.target*incremental.effects-incremental.costs

# Incremental cost effectiveness ratios relative to no treatment
icer<-incremental.costs/incremental.effects
```

- Use above code to generate cost-effectiveness comparative results

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And what do they say?

- Costs higher on CBT but about the same on antidepressants
- QALYs higher on both CBT and antidepressants
- Net benefit highest on antidepressants.
- CBT cost-effective at willingness-to-pay £20,000.
- But antidepressants have lowest ICER

```
> # Calculate the total costs and effects
> (costs<-c.treat+p.rec*(1-p.rel)*c.rec+p.rec*p.rel*c.rel+(1-p.rec)*c.norec)
  No treatment            CBT Antidepressant
      2457.051       2734.440       2460.299
> (effects<-p.rec*(1-p.rel)*q.rec+p.rec*p.rel*q.rel+(1-p.rec)*q.norec)
  No treatment            CBT Antidepressant
      20.17235       20.26268       20.27960
>
> # Net benefit
> (net.benefit<-lambda.target*effects-costs)
  No treatment            CBT Antidepressant
      400989.9       402519.2       403131.8
>
> # Incremental results relative to no treamtent
> (incremental.costs<-costs-costs[1])
  No treatment            CBT Antidepressant
         0.000        277.389          3.248
> (incremental.effects<-effects-effects[1])
  No treatment            CBT Antidepressant
      0.000000       0.090333       0.107256
> (incremental.net.benefit<-lambda.target*incremental.effects-incremental.costs)
  No treatment            CBT Antidepressant
         0.000       1529.271       2141.872
>
> # Incremental cost effectiveness ratios relative to no treatment
> (icer<-incremental.costs/incremental.effects)
  No treatment            CBT Antidepressant
           NaN     3070.73827       30.28269
```

Making the decision tree probabilistic

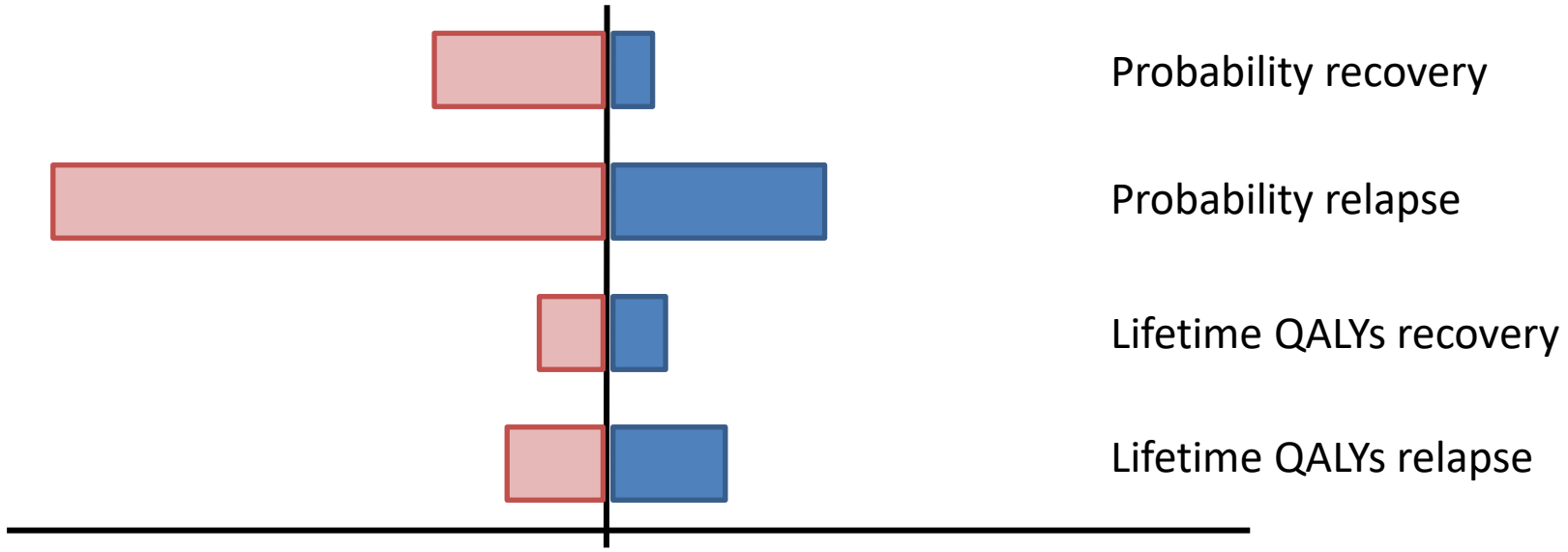
Open “depression.decision.tree.probabilistic.R"

Parameter uncertainty

- In practice, parameter inputs to our models can be uncertain
- They are estimated using small studies or elicited from expert opinion
  - Probabilities of recovery or relapse based on trial data
  - Lifetime QALYs based on patient surveys
  - Lifetime costs estimated based on hospital statistics
  - Treatment costs (e.g. dose monitoring) based on cohort studies
- This leads to uncertainty in the total costs, QALYs, and the estimated ICER

Deterministic sensitivity analysis

- Sets parameters to extreme but plausible limits
- Highlights parameters to which decision is most sensitive



Net benefit antidepressants vs no treatment (illustrative only)

Probabilistic sensitivity analysis

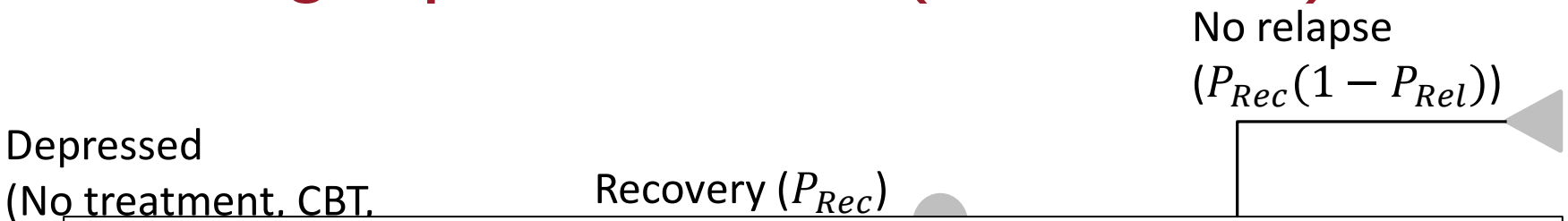
- An alternative is to put a probability distribution on the parameters
- In depression we previously assumed lifetime cost of recovery was £1000
- Could use normal distribution Normal(mean=1000,sd=50) to represent uncertainty…

Initial set-up

- You'll notice a new line of code towards the start of the file that sets the number of PSA samples
- We can set this to whatever number we want but 1000 is sufficient for stability for this simple model.

```
# Number of PSA samples
n.samples<-1000
```

Making it probabilistic (core code)



See any difference?

R performs the same calculations whether the p.rec and other variables are vectors or scalars

However, we need to define these parameters as probabilistic.

```
effects<-p.rec*(1-p.rel)*q.rec+p.rec*p.rel*q.rel+(1-p.rec)*q.norec
costs<-c.treat+p.rec*(1-p.rel)*c.rec+p.rec*p.rel*c.rel+(1-p.rec)*c.norec
net.benefit<-lambda*effects-costs
incremental.nb<-net.benefit-net.benefit[,1]
```

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Making it probabilistic (Costs, Utilities)

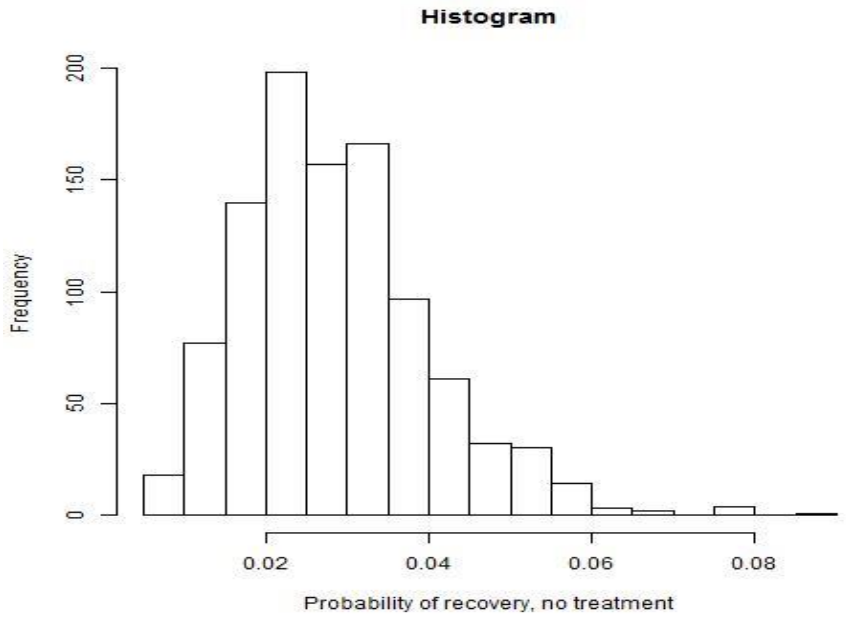
Outcome	Costs	QALYS
Recovery, no relapse	$C_{rec} = N(\mu = 1000, \sigma = 50)$	$Q_{rec} = N(\mu = 26, \sigma = 2)$
Recovery, relapse	$C_{rel} = N(\mu = 2000, \sigma = 100)$	$Q_{rel} = N(\mu = 23, \sigma = 3)$
No recovery	$C_{no\ rec} = N(\mu = 2500, \sigma = 125)$	$Q_{no\ rec} = N(\mu = 20, \sigma = 4)$

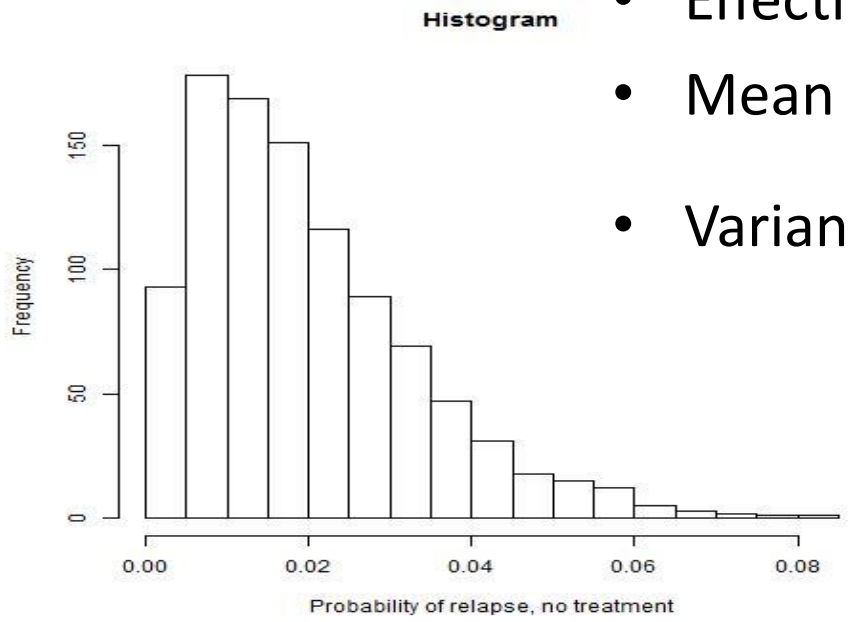
```
# Costs for recovery, relapse, and no recovery
c.rec<-rnorm(n=n.samples, mean=1000, sd=50)
c.rel<-rnorm(n=n.samples, mean=2000, sd=100)
c.norec<-rnorm(n=n.samples, mean=2500, sd=125)

# QALYs for recovery, relapse, and no recovery
q.rec<-rnorm(n=n.samples, mean=26, sd=2)
q.rel<-rnorm(n=n.samples, mean=23, sd=3)
q.norec<-rnorm(n=n.samples, mean=20, sd=4)
```

Beta distributions for probability recovery and relapse

Parameter	No Treatment (Option 1)
P_{rec}	$P_{1,rec} = Beta(\alpha = 6, \beta = 200)$
P_{rel}	$P_{1,rel} = Beta(\alpha = 2, \beta = 100)$





- Bounded between 0 and 1.
- Parameter relate to number of events, number of non-events.
- Effective sample size is $\alpha + \beta$
- Mean is α/β
- Variance is $\frac{\alpha\beta}{(\alpha+\beta)^2(\alpha+\beta+1)}$

Making it probabilistic (Reference probabilities)

Parameter	No Treatment (Option 1)	Mean (SD)
P_{rec}	$P_{1,rec} = Beta(\alpha = 6, \beta = 200)$	0.03 (0.01)
P_{rel}	$P_{1,rel} = Beta(\alpha = 2, \beta = 100)$	0.02 (0.0002)

- The beta distribution is another of many implemented in base R.
- Note naming convention of the parameters: α is *shape1* and β is *shape2*.

p.rec[,1]<-rbeta(n=n.samples, shape1=6, shape2=200)

p.rel[,1]<-rbeta(n=n.samples, shape1=2, shape2=100)

Probabilities for comparators

	Parameter	No Treatment (Option 1)	Mean (SD)
CBT	P_{rec}	$P_{2,rec} = Beta(\alpha = 6, \beta = 130)$	0.046 (0.0003)
	P_{rel}	$P_{2,rel} = Beta(\alpha = 2, \beta = 200)$	0.01 (0.00005)
Antidepressants	P_{rec}	$P_{3,rec} = Beta(\alpha = 6, \beta = 120)$	0.05 (0.0004)
	P_{rel}	$P_{3,rel} = Beta(\alpha = 2, \beta = 120)$	0.017 (0.0001)

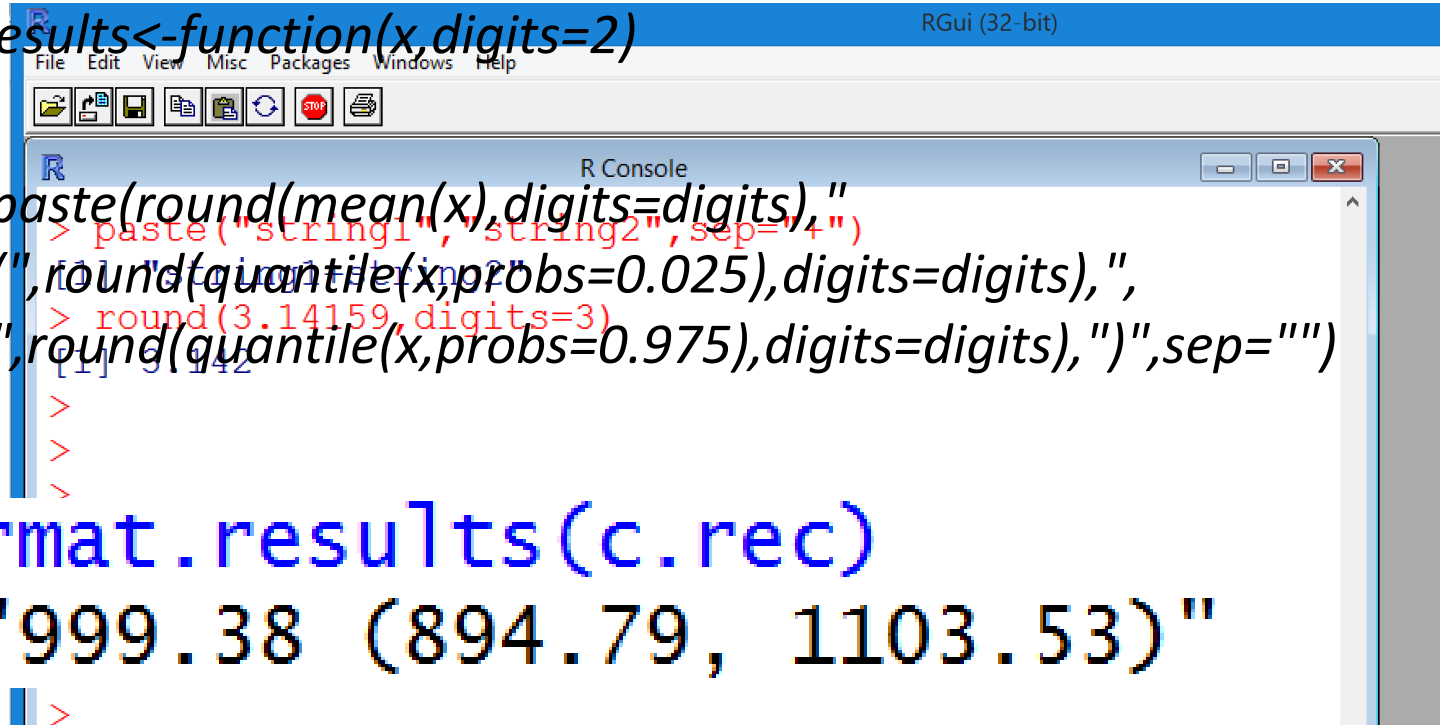
```
# Probabilities for CBT
# Probability of recovery higher than on no treatment
p.rec[,2]<-rbeta(n=n.samples, shape1=6, shape2=130)
# Probability of relapse lower than on no treatment
p.rel[,2]<-rbeta(n=n.samples, shape1=2, shape2=200)

# Probabilities for antidepressant
# Probability of recovery lower than no treatment or CBT
p.rec[,3]<-rbeta(n=n.samples, shape1=6, shape2=120)
# Probability relase lower than no treatment, higher than CBT
p.rel[,3]<-rbeta(n=n.samples, shape1=2, shape2=120)
```

Formatting results

- Recall *paste("string1", "string2")* function for string concatenation
- Recall *round(x,digits=3)* for numeric formatting

```
format.results<-function(x,digits=2)
{
        paste(round(mean(x),digits=digits),"
        (",round(quantile(x,probs=0.025),digits=digits),",
        ",round(quantile(x,probs=0.975),digits=digits),")",sep="")
}
```




```
> format.results(c.rec)
[1] "999.38 (894.79, 1103.53)"
```

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Decision tree results

- Build a results matrix

results.matrix<-matrix(NA, nrow=4,ncol=n.treat)

- Name the rows and columns

rownames(results.matrix)<-c("Total costs","Total QALYs", "Net Benefit","Incremental NB")

colnames(results.matrix)<-t.names

- Then calculate summaries

```
for(i.treat in 1:n.treat)
{
        results.matrix["Total costs",i.treat]<-format.results(x=costs[,i.treat])
        results.matrix["Total QALYs",i.treat]<-format.results(x=effects[,i.treat])
        results.matrix["Net Benefit",i.treat]<-format.results(x=net.benefit[,i.treat])
        results.matrix["Incremental NB",i.treat]<-format.results(x=incremental.nb[,i.treat])
}
```

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Exporting the results matrix to Excel

- Export as a csv, which is readable in Excel

write.csv(results.matrix, file="depression.results.csv")

	No treatment	CBT	Antidepressant
Total costs	2451.07 (2210.36, 2691.42)	2729.25 (2497, 2975.34)	2451.69 (2220.78, 2697.22)
Total QALYs	20.18 (12.88, 27.48)	20.26 (13.13, 27.49)	20.29 (13.19, 27.41)
Net Benefit	0 (0, 0)	278.18 (218.85, 334.57)	0.61 (-75.5, 60.12)
Incremental NB	0 (0, 0)	0.09 (-0.16, 0.48)	0.12 (-0.15, 0.62)

Summary

- We have implemented a very simple decision model in R
- We then made it probabilistic to conduct probabilistic sensitivity analysis
- Gianluca will now show how to analyse the results using BCEA...