

WP-2

Final workshop

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Deliverables

- A review of methods used to extrapolate RCT outcomes using real world data
- • Validation of the DICE modelling technique and speeding up execution of the DICE simulation macro
- Training modules and manuals for HTA staff, reviewers, and modelers.

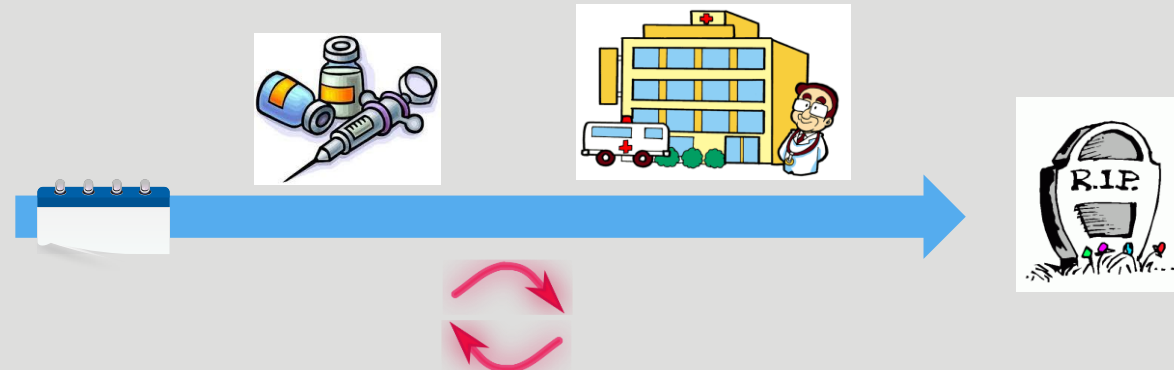
The core of a DICE model

For each contemplated intervention, a decision maker wants to know, given the conditions at the time of the decision, what will happen to these and when those events will occur

Dynamic
Conditions



Events



DICE is specified in lists

Profiles frame

ID	Group
1	Older men
2	Younger men
3	Older women
4	Younger women

Conditions list

Name	Initial value
ProgFree	100
Progressed	0
Dead	0
OnTmt	Yes
Time	0
Interval	iCycle
NextEventTime	
NextEvent	



For each contemplated intervention, a decision maker wants to know, given the conditions at the time of the decision, what will happen to these and when those events will occur

All events list

Events	Initial Time	Table
Start	Now	tblStart
Partition	Never	tblPartition
End	iTimeHorizon	tblEnd
TmtInit	Now	tblTmtInit
Progress	Never	tblProgress
Dead	Never	tblDead

Event: Partition

Type	Name	Expression
Output	QALYs	$QALYs + Interval * (ProgFree * uProgFree + Progress * uProgress)$
Output	Cost	$Cost + Interval * (ProgFree * uProgFree + Progress * uProgress)$
Condition	Dead	$Exp(-((Exp(-Lambda) * Time)^(1/Gamma)))$
Condition	ProgFree	= eqPFS
Condition	Progressed	Dead – ProgFree
Event	Partition	Time + iCycle

Interventions frame

IntervNum	Name	HR
1	SoC	1
2	Newmab	0.8
3

Outputs list

Forecast	Initial value
QALYs	0
Cost	0
CostTmt	0
dQALYs	0
dCosts	0

What is the next time?

Conditions list	
Name	Initial value
Now	0
Never	999999
TimeHorizon	20
CycleLength	0.5
Time	0
Interval	
NextEventTime	
NextEvent	

All events list			
Events	Current Time	Initial Time	Table
Start	999999	Now	tblStart
Partition	20.5	CycleLength	tblPartition
End	20	TimeHorizon	tblEnd

Event: Start		
Type	Name	Expression
Condition	Time	Start
Event	Start	Never
Output	Tmt	CHOOSE(IntervNum,"SoC","UpUpMab")
Condition	lambda	lambda*CHOOSE(IntervNum,1,RR)
Output	CostTmt	CHOOSE(IntervNum,0,CostInterv)
Condition	NextEventTime	MIN(CurEventTime)
Condition	NextEvent	MATCH(NextEventTime,CurEventTime,0)

Event: Partition		
Type	Name	Expression
Output	QALYs	QALYs + Interval*(ProgFree*uProgFree+Progressed*uProgress)
Output	Cost	Cost + Interval*(ProgFree*uProgFree+Progressed*uProgress)
Condition	OverallSurv	Exp(-((Exp(-Lambda)*Time)^(1/Gamma)))
Condition	ProgFree	= eqPFS
Condition	Progressed	OverallSurv-ProgFree
Event	Partition	Time+Cycle

RUN

Set counters

Read profile

Read Conditions

Read Events

Add 1 to RepNum

Add 1 to ID

Add 1 to IntervNum

Core loop

Set Time=MIN(Event times)
Find matching event

Read matching tblEvent
Execute expressions

End event?

Another Intervention?

Another Profile?

Another Rep?

Another Scenario?

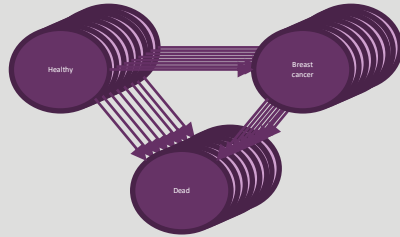
Report Raw results



Validation: breast cancer model

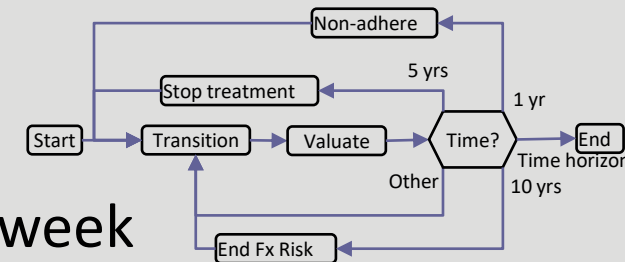
Standard method: cohort Markov

- 32 Markov models to handle
 - 4 strategies,
 - 4 age strata,
 - 2 risk groups
- Handling of non-persistence, treatment stop, end of AE risk via additional states & many formulas
- 2 large files (17 MB)
- Implementation 18 weeks



DICE approach

- Single hybrid model
 - 1 intervention variable for strategies
 - 8 profiles for age/risk strata
 - 3 conditions for states
- Handled via 3 events set to occur at appropriate times
- 1 small file (116 KB)
- Implementation <1 week



Same results!

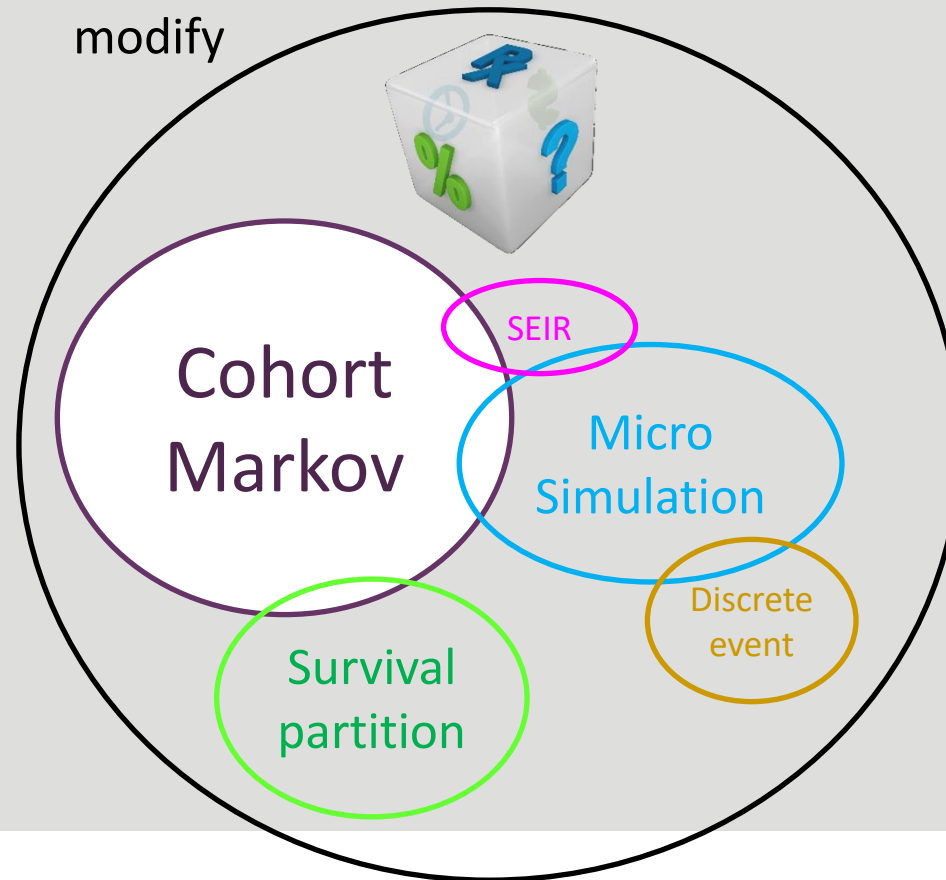
DICE is a simulation method that facilitates HTA

1. Specification of a DICE model is done in a text *Blueprint* that enumerates :

- Dynamic conditions
- Outputs
- Events
- Static conditions
 - Profiles
 - Interventions
 - Settings and constants
 - Other inputs

2. Implementation of a DICE model:

- Lists all elements in simple MS Excel tables
- This makes it very transparent, flexible and easy to modify



3. Execution of a DICE simulation is done by:

- A simple VBA macro that reads the lists and carries out the instructions
- The VBA “engine” is free to download
- No special software is required but can use other software (e.g., C#, Python, R).

Next steps

- Continue to improve the engine
- Further training for HTA agencies and modellers
- Finalize publications

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