TSD15: Cost-effectiveness modelling using patient-level simulation

Appendix C: Simul8 documentation

The text to the right of the # symbols is annotation that has been added to the documentation produced by Simul8.

NB: The visual logic is used to process one event after another in the order they occur and to accrue outcomes according to the time elapsing between events rather than the simulation clock being used to hold entities in queues until the time of their next event.

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SIMUL8 Documentation for: DSU_DES_example_for_web

Created by: DSU

Last opened by: DSU

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General Simulation Information

Warm Up Time: 0 Results Collection Time: 10 (Minutes) # set to be high enough that all patients have reached death state before end of simulation

Start of day: 540 Length of day: 480 , Days per week: 5 #not relevant as the simulation clock isn't used in this example

Current Random Stream Set: 1 #this can be changed to provide results based on a different random number stream

Data display when simulation stopped: Work Item Count

****

Distributions # this block defines named distributions

Dist Hip Fracture # details below for time to hip fracture distribution

Named Distribution

Distribution Detail:

Weibull 4 10 0 0

Dist Vert Fracture # details below for time to vertebral fracture distribution

Named Distribution

Distribution Detail:

Weibull 2 8 0 0

Dist Death # details below for time to death distribution

Named Distribution

Distribution Detail:

Normal 12 3 0 0

Labels # this block defines labels to be attached to patients. It doesn't set their values.

Time of Vert Fracture # time from start of simulation to next vertebral fracture. This is re-set after first vertebral fracture to give time to second one

(Number)

Time of Death # time from start of simulation to death (all-cause mortality)

(Number)

Time of Hip Fracture # time from start of simulation to hip fracture

(Number)

Utility # current patient utility used when calculating QALYs accrued between previous event and current event

(Number)

Router # variable used to route patients from one work center to the next according to the event due to happen next

(Number)

Time of Last Event # used to accrue costs and QALYs over period from last event to current event

(Number)

Vert Fracture # used to record the fact that a vertebral fracture has happened

(Number)

Hip Fracture # used to record that hip fracture has happened

(Number)

Images # this block can be ignored as these are all default settings.

Default Image Entry

Width: 32 Height: 32

Transparent Color: 16711935

Default Image Storage Bin

Width: 32 Height: 32

Transparent Color: 16711935

Default Image Work Center

Width: 32 Height: 32

Transparent Color: 16711935

Default Image Exit

Width: 32 Height: 32

Transparent Color: 16711935

Default Image Resource

Width: 32 Height: 32

Transparent Color: 16711935

Default Image Conveyor

Width: 32 Height: 32

Transparent Color: 16777215

Default Image Tank

Width: 32 Height: 32

Transparent Color: 16777215

Default Image Rotz

Width: 32 Height: 32

Transparent Color: 16777215

Default Image Process

Width: 32 Height: 32

Transparent Color: 16777215

Default Image Loader

Width: 32 Height: 32

Transparent Color: 16777215

Default Image Vehicle

Width: 32 Height: 32

Transparent Color: 16777215

Default Image Component

Width: 32 Height: 32

Transparent Color: 255

Default Image 3D Light

Width: 32 Height: 32

Transparent Color: 16777215

Default Image 3D Object

Width: 32 Height: 32

Transparent Color: 16777215

SIMUL8 Windows and sub-windows # can be ignored as these are standard settings

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Open

Icon Location X:840 Y:510 W:32 H:32

Window Location X:196 Y:104 W:1698 H:874

Color 16777215

Work Item Types # these are the simulation entities, in this case patients

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Main Work Item Type

Length 1

Attached Labels: # attaching labels to patients

Hip Fracture

Time of Death

Time of Vert Fracture

Time of Hip Fracture

Utility

Vert Fracture

Router

Time of Last Event

****

Simulation Objects

Work Entry # entry points are used to bring patients into the simulation

Work Entry Point 1 # there is just one work entry point in this simulation

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Display Parameters 4

X:172 Y:251 W:32 H:32

Xinc -10 Yinc 0

Show Count

Show Image

Work Item Type: Main Work Item Type # this entry point is bringing in patients

Inter-arrival time # set inter-arrival time such that all patients arrive at the start

Distribution Detail:

Fixed 0 0 0 0 # all patients arrive at start of simulation

Route Out Objects # entry point routes out to queues for each fracture type based on router variable

Queue for Next Event Vert

Queue for Next Event Hip

Queue for Next Event Death

On Label Action Visual Logic: # this is the visual logic which is used to process the simulation in this case

VL SECTION: Work Entry Point 1 Entry Logic

IF Work Entry Point 1.Arrived Count = NumPats

SET Work Entry Point 1.Interarrival Time = Large Number # this logic stops more patients arriving once the required number have arrived

IF Intervention = 1 # i.e only apply this logic if intervention arm and not control arm is being processed

SET Time of Vert Fracture = Time of Vert Fracture*2 # intervention doubles time to first vertebral fracture

SET Time of Hip Fracture = Time of Hip Fracture*2 # intervention doubles time to hip fracture

SET Temp = Time of Vert Fracture # this block of logic sets the router according to the event with the lowest sampled time

SET Router = 1

IF Time of Hip Fracture < Temp

SET Temp = Time of Hip Fracture

SET Router = 2

IF Time of Death < Temp

SET Temp = Time of Death

SET Router = 3 #end of block of logic setting router according to next event.

Label Actions # sets the attributes of the individual patients to be sampled from the named distributions

Time of Death

Set

Distribution Detail:

Uses: Dist Death

Named Distribution

Distribution Detail:

Normal 12 3 0 0

Time of Vert Fracture

Set

Distribution Detail:

Uses: Dist Vert Fracture

Named Distribution

Distribution Detail:

Weibull 2 8 0 0

Time of Hip Fracture

Set

Distribution Detail:

Uses: Dist Hip Fracture

Named Distribution

Distribution Detail:

Weibull 4 10 0 0

Utility

Set

Distribution Detail:

Fixed 0.7 0 0 0 # sets starting utility

Vert Fracture

Set

Distribution Detail:

Fixed 0 0 0 0 # records that no previous vertebral fractures at start of simulation

Hip Fracture

Set

Distribution Detail:

Fixed 0 0 0 0 # records that no previous hip fractures at start of simulation

Storage Bin # storage bins are needed to hold patients until a work centre is free to process their next event

Queue for Next Event Vert # this holds patients whose next event is a vert fracture until work center is free to process that event

---

Display Parameters 5

X:318 Y:119 W:32 H:32

Xinc -10 Yinc 0

Show Count

Show Image

Capacity: -1

Input Objects # defines how patients arrive at this queue i.e from work entry point at start of simulation, or after hip or vertebral fracture events.

Work Entry Point 1

Next Event Hip

Next Event Vert

Output Objects

Next Event Vert # defines where patients go from this queue, i.e to vertebral fracture event

Storage Bin

Queue for Next Event Hip # this holds patients whose next event is a hip fracture until work center free to process that event

---

Display Parameters 5

X:316 Y:251 W:32 H:32

Xinc -10 Yinc 0

Show Count

Show Image

Capacity: -1

Input Objects #defines how patients arrive at this queue i.e from work entry point at start of simulation, or after hip or vertebral fracture events

Work Entry Point 1

Next Event Vert

Output Objects

Next Event Hip # defines where patients go from this queue ie. to hip fracture event

Storage Bin

Queue for Next Event Death # holds patients whose next event is death until work center free to process that event

---

Display Parameters 5

X:309 Y:353 W:32 H:32

Xinc -10 Yinc 0

Show Count

Show Image

Capacity: -1

Input Objects # defines how patients arrive at this queue i.e from work entry point at start of simulation, or after hip or vertebral fracture events.

Work Entry Point 1

Next Event Vert

Next Event Hip

Output Objects

Next Event Death # defines where patients go from this queue ie. to death event

Work Center

Next Event Death # this work center processes the death event.

Display Parameters 4

X:425 Y:361 W:32 H:32

Xinc -10 Yinc 0

Show Title

Show Count

Show Image

Replicate 1

Priority 50

Routing In

Priority

Route In Objects

Queue for Next Event Death #routes in from the queue which holds patients whose next event is death

Require resources before collecting any work items

Routing Out

Circulate

Preference only

Route Out Objects

Work Complete 1 # go to work exit point for all-cause mortality (i.e non hip fracture related)

Release resources as soon as task complete

Operation Time

Distribution Detail:

Average 0 0 0 0 # no time elapses during event processing

On Work Complete Visual Logic:

VL SECTION: Next Event Death Work Complete Logic

IF Time of Death < 0 # this line and next ensures that time of death is never <0 as this impacts on QALY and cost calculation

```
    SET Time of Death  =  0
   SET Total QALYs  =  Total QALYs+[Utility*[Time of Death-Time of Last Event]]  #accrues QALYs from last event till death
   SET Temp  =  EXP[Time of Death*[0-DRBi]]  # this line and next three lines calculate discounted QALYs
   SET Temp  =  Temp-EXP[Time of Last Event*[0-DRBi]]
   SET Temp  =  Temp/[0-DRBi]
   SET Total DQALYs  =  Total DQALYs+[Utility*Temp]
   IF Intervention  =  1 # do this logic only for intervention arm and not for control arm
    SET Total Cost  =  Total Cost+[Time of Death*InterventionCost] # drug costs accrued from start of simulation to death for those having intervention
    SET Temp  =  EXP[Time of Death*[0-DRCi]] # this line and next three lines calculate discounted intervention costs
    SET Temp  =  Temp-EXP[0*[0-DRCi]]
    SET Temp  =  Temp/[0-DRCi]
    SET Total DCost  =  Total DCost+[InterventionCost*Temp]

Work Exit Point
  Work Complete 1  # exit point for all cause (non-hip fracture related) death
  ----------
   Display Parameters 4
   X:544 Y:364 W:32 H:32
```

Xinc -10 Yinc 0

Show Count

Show Image

Input Objects

Next Event Death # patients enter this work center from the death event work centre

Work Center

Next Event Vert # this work centre processes the vertebral fracture events

---

Display Parameters 4

X:430 Y:120 W:32 H:32

Xinc -10 Yinc 0

Show Title

Show Count

Show Image

Replicate 1

Priority 50

Routing In

Priority

Route In Objects

Queue for Next Event Vert #patients route in here from the queue for this work center

Require resources before collecting any work items

Routing Out

Label

On label: Router # route out according to this variable using list below

Preference only

Route Out Objects

Queue for Next Event Hip #go here if router =1

Queue for Next Event Death #go here if router =2

Queue for Next Event Vert #go here if router =3

Release resources as soon as task complete

Operation Time

Distribution Detail:

Fixed 0 0 0 0 # no time elapses during event processing

On Work Complete Visual Logic:

VL SECTION: Next Event Vert Work Complete Logic

```
SET Total Cost  =  Total Cost+Vert Fracture Cost # accrue cost of vertebral fracture

SET Total DCost  =  Total DCost+[Vert Fracture Cost/[[1+DRC]^Time of Vert Fracture]] # accrue discounted cost of vertebral fracture

SET Total QALYs  =  Total QALYs+[[Time of Vert Fracture-Time of Last Event]*Utility] # accrue QALYs from last event till vertebral fracture

SET Temp  =  EXP[Time of Vert Fracture*[0-DRBi]] # this line and next three accrue discounted QALYs from last event till vertebral fracture

SET Temp  =  Temp-EXP[Time of Last Event*[0-DRBi]]

SET Temp  =  Temp/[0-DRBi]

SET Total DQALYs  =  Total DQALYs+[Utility*Temp]

SET Time of Last Event  =  Time of Vert Fracture # record time of vertebral fracture as time of last event

IF Vert Fracture  =  0 # only if this is the first one experienced

  SET Temp  =  Dist Vert Fracture # resample time from this event to the next vertebral fracture

IF Intervention  =  1 #apply this code for intervention arm but not control arm

    SET Temp  =  Temp      # here we assume no impact of intervention on second vertebral fracture but this line could be used to double time to

                                # second vertebral fracture if efficacy were to be applied to both first and second vertebral fractures

  SET Time of Vert Fracture  =  Time of Vert Fracture+Temp # time to event must be time since simulation start not time since last event

  SET Utility  =  Utility*Utility Multiplier Vert # apply utility multiplier to patient's current utility which will affect  QALYs accrued after vert fracture

ELSE # do this logic when vert fracture not equal to zero, i.e when processing second vertebral fracture

  SET Time of Vert Fracture  =  Large Number # ensures no third vertebral fracture can occur.

SET Vert Fracture  =  1 # record that vertebral fracture has occurred
```

SET Temp = Time of Vert Fracture # this is start of block of code which determines next event and sets router accordingly

SET Router = 3

IF Time of Hip Fracture < Temp

SET Temp = Time of Hip Fracture

SET Router = 1

IF Time of Death < Temp

SET Temp = Time of Death

SET Router = 2 # this is end of block of code which determines next event and sets router accordingly

Work Center

Next Event Hip # this work centre processes the vertebral fracture events

---

Display Parameters 4

X:428 Y:251 W:32 H:32

Xinc -10 Yinc 0

Show Title

Show Count

Show Image

Replicate 1

Priority 50

Routing In

Priority

Route In Objects

Queue for Next Event Hip # bring patients in from the queue holding those whose next event is a hip fracture

Require resources before collecting any work items

Routing Out

Label

On label: Router # route out using variable named ‘router’ according to list below

Preference only

Route Out Objects

Queue for Next Event Vert # go here if router =1

Queue for Next Event Death # go here if router =2

Work Complete 2 # go here if router =3

Release resources as soon as task complete

Operation Time

Distribution Detail:

Average 0 0 0 0 # no time elapses during event processing

On Work Complete Visual Logic:

VL SECTION: Next Event Hip Work Complete Logic

SET Hip Fracture = 1 # records that hip fracture has occurred

SET Total Cost = Total Cost+Hip Fracture Cost # accrues cost of hip fracture

SET Total DCost = Total DCost+[Hip Fracture Cost/[[1+DRC]^Time of Hip Fracture]] # accrues discounted cost of hip fracture

SET Total QALYs = Total QALYs+[[Time of Hip Fracture-Time of Last Event]*Utility] # accrues QALYs from last event to hip fracture

SET Temp = EXP[Time of Hip Fracture*[0-DRBi]] # this line and next three accrue discounted QALYs from last event to hip fracture

SET Temp = Temp-EXP[Time of Last Event*[0-DRBi]]

SET Temp = Temp/[0-DRBi]

SET Total DQALYs = Total DQALYs+[Utility*Temp]

SET Utility = Utility*Utility Multiplier Hip # update patient's current utility to reflect hip fracture, which alters QALYs accrued after hip fracture

SET Time of Last Event = Time of Hip Fracture # record hip fracture time as time of last event.

SET Time of Hip Fracture = Large Number # prevents additional fracture occurring.

IF RANDOM[0] < MortPropHip # determine whether hip fracture is fatal

SET Router = 3 # if fatal, route patient to fatal hip exit point

IF Intervention = 1 # do this logic for intervention but not for control

SET Total Cost = Total Cost+[Time of Last Event*InterventionCost] # accrue intervention costs from start to time of fatal hip fracture

```
      SET Temp  =  EXP[Time of Last Event*[0-DRCi]] # this line and next three does same for discounted intervention costs
      SET Temp  =  Temp-EXP[0*[0-DRCi]]
      SET Temp  =  Temp/[0-DRCi]
      SET Total DCost  =  Total DCost+[Temp*InterventionCost]
    ELSE IF Time of Vert Fracture  <  Time of Death  # this block of logic determines next event for those having non-fatal hip fracture and route accordingly
     SET Router  =  1
    ELSE
     SET Router  =  2 # end of block of logic determining next event

Work Exit Point  # go here if fatal hip fracture
 Work Complete 2
 ---------------
  Display Parameters 4
  X:535 Y:248 W:32 H:32
   Xinc -10 Yinc 0
  Show Count
  Show Image
  Input Objects
```

Next Event Hip # route patients in from hip fracture event

Information Store # values are set here for numbers used by the simulation (e.g costs of fracture) and for variables which record simulation outcomes

---

Simulation Time

SIMUL8 Data

Current Value 10 # simulation time increases until it hits 10 at which point the simulation ends

Warm Up Period

SIMUL8 Data

Current Value 0 # warm up period set to zero as not relevant in this scenario

Results Collection Period

SIMUL8 Data

Current Value 10 #whole simulation time is used for results collection

Current Work Item

SIMUL8 Data

Current Value 0

Overhead Cost # not relevant to this example

SIMUL8 Data

Current Value 0

Overhead Revenue # not relevant to this example

SIMUL8 Data

Current Value 0

Graph Sync Interval # not relevant to this example

SIMUL8 Data

Current Value 5

Large Number # used within visual logic

Number

Current Value 1000000

Reset Value 1000000

Total Cost # undiscounted costs (used as running total during simulation, then averaged over cohort at end of simulation)

Number

Current Value 9022.74

Reset Value 0

Total QALYs # undiscounted QALYs (used as a running total during simulation, then averaged over cohort at end of simulation)

Number

Current Value 7.36584

Reset Value 0

Hip Fracture Cost # cost applied for each fracture, value is fixed for whole simulation

---

Number

Current Value 7000

Reset Value 7000

Vert Fracture Cost # cost applied for each fracture, value is fixed for whole simulation

---

Number

Current Value 3000

Reset Value 3000

Utility Multiplier Hip #multiplier applied after hip fracture, value is fixed for whole simulation

---

Number

Current Value 0.75

Reset Value 0.75

Utility Multiplier Vert #multiplier applied after vertebral fracture, value is fixed for whole simulation

---

Number

Current Value 0.9

Reset Value 0.9

Temp # used at various points in visual logic to hold data temporarily

---

Number

Current Value 2.38544

Reset Value 0

Intervention # set to zero for control and 1 for intervention

---

Number

Current Value 0

Reset Value 0

InterventionCost # cost per annum of intervention

Number

Current Value 500

Reset Value 500

NumPats # number of patients to be simulated

Number

Current Value 50000

Reset Value 50000

MortPropHip # likelihood of death when hip fracture occurs. value is fixed for whole simulation

---

Number

Current Value 0.05

Reset Value 0.05

Total DCost # discounted cost (used for running total during simulation, then averaged over cohort at end of simulation)

Number

Current Value 6904.12819

Reset Value 0

Total DQALYs #discounted QALYs (used for running total during simulation, then averaged over cohort at end of simulation)

Number

Current Value 6.07771

Reset Value 0

DRB # annual discount rate for benefits

Number

Current Value 0.035

Reset Value 0.035

DRC #annual discount rate for costs

Number

Current Value 0.035

Reset Value 0.035

DRBi #instantaneous discount rate for benefits

Number

Current Value 0.0344

Reset Value 0.0344

DRCi #instantaneous discount rate for costs

Number

Current Value 0.0344

Reset Value 0.0344

End Run Visual Logic: # this calculates averages across cohort from running totals

VL SECTION: End Run Logic

'Obeyed when the simulation reaches end of "Results Collection Period"

SET Work Entry Point 1.Interarrival Time = 0

SET Total Cost = Total Cost/NumPats

SET Total QALYs = Total QALYs/NumPats

SET Total DCost = Total DCost/NumPats

SET Total DQALYs = Total DQALYs/NumPats

****

SIMUL8 Profit Financial Information # not relevant as user defined variables used to track costs.

Currency: £

Fixed Cost: 0

Fixed Revenue: 0

****

Carbon Emissions Information # not relevant

Carbon Footprint Unit: CO2e

Fixed Carbon Footprint: 0

Fixed Carbon Offset: 0

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