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York Health Economics Consortium

UNIVERSITY of York

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Investigating Input Correlation in Probabilistic Sensitivity Analysis

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Background

PSA is used to characterise uncertainty in cost-effectiveness models.

Inputs in PSA are often varied independently even when they may be correlated[1]. As a result, PSA results could be misestimating uncertainty.

Uncertainty is a key factor for HTA agencies when deciding whether to approve an intervention.

[1]Lanitis T, Muszbek N, Tichy E. The Probability of a Successful Probabilistic Sensitivity Analysis. *The Evidence Forum*. 2014:30-33

Methods

Eight-state Markov model to compare a hypothetical treatment and comparator.

R and Shiny used for ease of programming and user-friendly interface.

Parameters varied in PSA (per health state)

- Five costs
- One QALY value
- Eight transition probabilities

Correlation options

- No correlation
- Partial correlation (within but not between costs, QALYs and transition matrices)
- Perfect correlation

R model

Function to generate n PSA samples of a single cost

No correlation: costs are i.i.d. gamma

Partial/perfect correlation: lognormal multiplier applied to the mean

Partial: multiplier shared by all costs for iteration i

Perfect: multiplier shared by all costs, QALYs, and transition probabilities for iteration i

```
cost_function <- function(n_samples, cost_mean, se, scenario, multiplier) {

  if (scenario == "base_case" | cost_mean == 0) {

    # FOR DETERMINISTIC

    state_costs <- rep(cost_mean, n_samples)

  } else if(scenario == "independent") {

    # FOR NO CORRELATION

    # Estimate gamma parameters

    cost_se <- cost_mean * se
    gamma_para <- gamma_function(cost_mean, cost_se^2)

    # Generate costs from gamma distribution

    state_costs <- rgamma(n_samples, shape = gamma_para$shape, scale = gamma_para$scale)

  } else if(scenario %in% c("part_correlation", "part_correlation2", "full_correlation")) {

    # FOR PARTIAL/PERFECT CORRELATION

    # Generate costs by applying a multiplier

    state_costs <- cost_mean * multiplier

  }

  state_costs %<>%
    pmax(0)

  return(state_costs)
}
```

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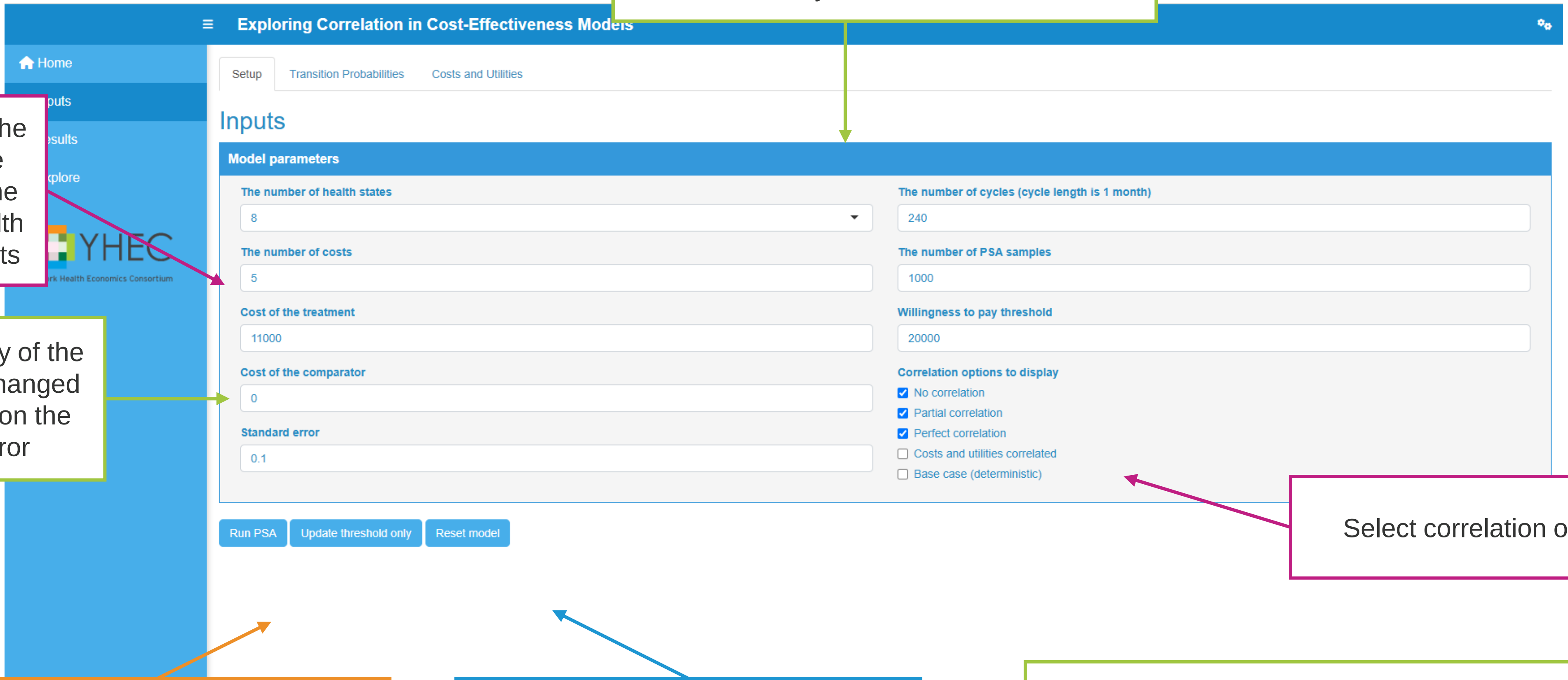
Shiny model

Dashboard layout with shinydashboard and shinydashboardPlus

Complexity of the model can be changed via the number of health states and costs

Overall variability of the model can be changed via a multiplier on the standard error



Select correlation options

Option to run the PSA or update the willingness-to-pay threshold

Reset button with shinyjs

Not pictured: editable tables with DT, informative popovers with shinyBS, loading screens with waiter

https://shiny.york.ac.uk/PSA_Correlation/

Results

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Exploring Correlation in Cost-Effectiveness Models

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Summary | Cost-Effectiveness Plane | CEAC | CEAF | EVPI

PSA results by correlation option

Means

Scenario	Treatment Cost	Comparator Cost	Treatment QALYs	Comparator QALYs	Incremental Cost	Incremental QALYs	ICER	NMB	CE %
No Correlation	£29,494	£14,481	2.52	1.61	£15,013	0.91	£16,420	£3,273	93.6%
Partial Correlation	£29,244	£14,455	2.53	1.62	£14,789	0.91	£16,262	£3,399	65.2%
Perfect Correlation	£29,221	£14,477	2.50	1.63	£14,743	0.86	£17,080	£2,520	62.9%

Standard Deviations

Scenario	Treatment Cost	Comparator Cost	Treatment QALYs	Comparator QALYs	Incremental Cost	Incremental QALYs	ICER	NMB	CE %
No Correlation	£1,463	£1,180	0.08	0.04	£1,714	0.09		£2,125	
Partial Correlation	£1,015	£1,361	0.40	0.22	£1,367	0.42		£7,372	
Perfect Correlation	£1,010	£1,356	0.21	0.29	£1,806	0.50		£8,167	

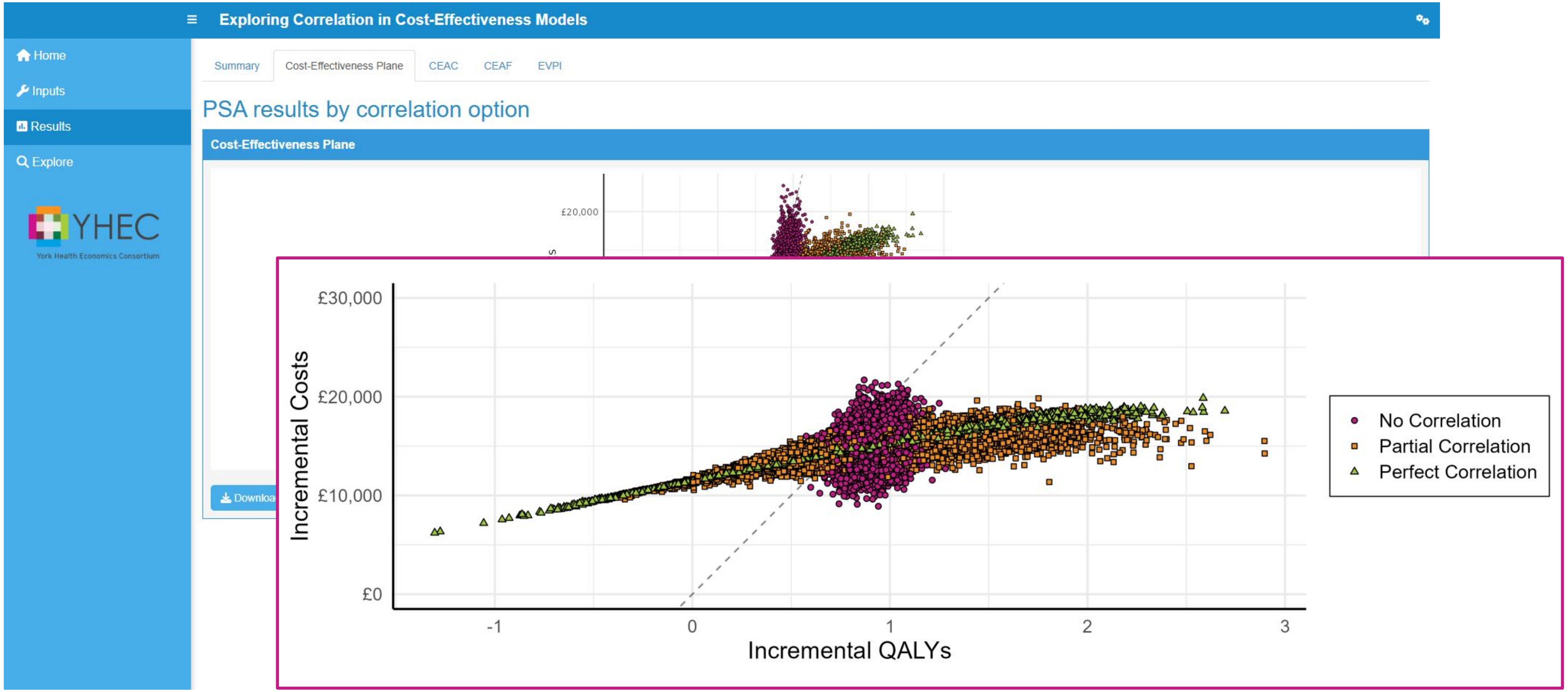
Download as .csv

	ICER	NMB	CE %
No Correlation	16420	3273	0.936
Partial Correlation	16262	3399	0.652
Perfect Correlation	17080	2520	0.629

https://shiny.york.ac.uk/PSA_Correlation/

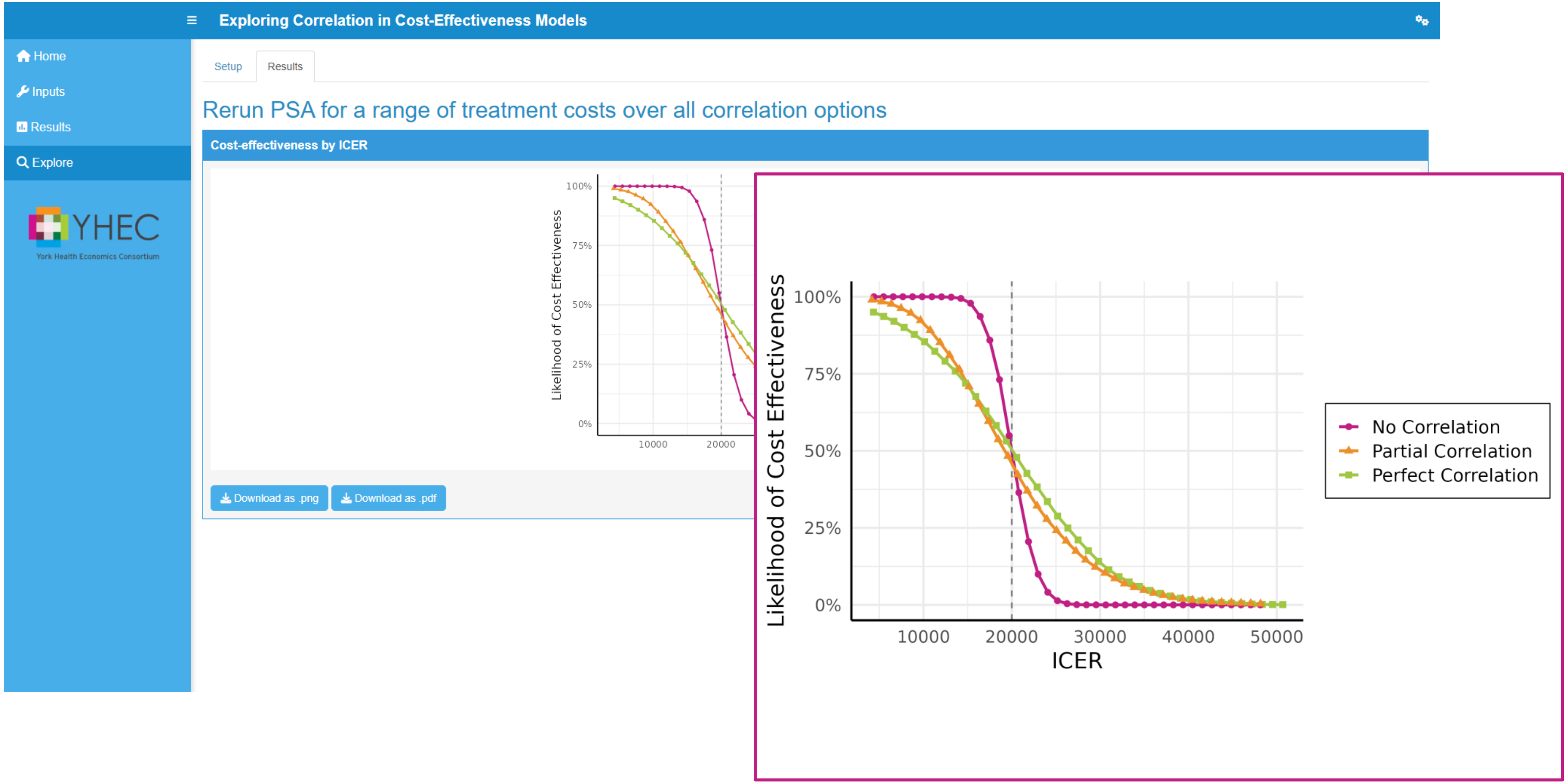
BCEA and hesim packages used under the hood to summarise results and generate plot data

Results (CE plane)



https://shiny.york.ac.uk/PSA_Correlation/

Explore



https://shiny.york.ac.uk/PSA_Correlation/

Limitations

No alternative model structures.

Fixed variation for all inputs.

One shape of scatter plot.

No real-world data.

Challenges

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Preload base case results	▪ Display saved results if the run button is null ▪ Caching – storage concerns
Manage arbitrary health states, costs and correlation options	▪ Functional programming with purrr::map ▪ Long data format and ggplot2
Keep codebase under control	▪ Re-use code: Single module for transitions, costs and QALYs, generic plot module with download button
Speed up computations	▪ Check speed with microbenchmark ▪ Move code out of loops and avoid dataframes/tibbles

Thank you

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