

A large, diagonal photograph of a rugged mountain landscape, likely in the Lake District, showing green slopes, rocky peaks, and a valley with a stream and stone walls.

# assertHE: R model reviewer

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**R-HTA 24 | Robert Smith & Tom Ward | June 2024**



[rsmith@darkpeakanalytics.com](mailto:rsmith@darkpeakanalytics.com)



<https://github.com/dark-peak-analytics>



<https://www.linkedin.com/company/dark-peak-analytics>

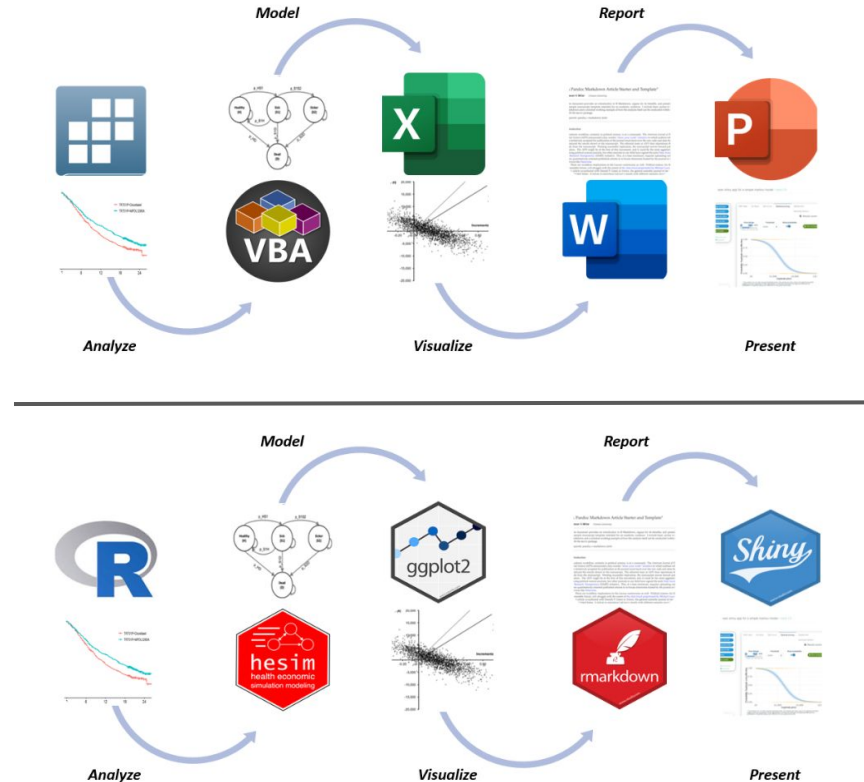
# Acknowledgements

Authors: **Robert A Smith (Dark Peak Analytics, University of Sheffield)**, Yevgeniy Samyshkin (GSK), Wael Mohammed (Dark Peak Analytics, University of Sheffield), **Tom Ward (GSK)**, Alan Martin (GSK), Sarah-Jane Anderson (GSK), Paul Schneider (Dark Peak Analytics, University of Sheffield), Baris Deniz (employee of GSK at time of writing), Dawn Lee (University of Exeter), Prof. Gianluca Baio (University College London), Howard Thom (University of Bristol), Nathan Green (University College London), Felicity Lamrock (Queens University Belfast), Brett McQueen (University of Colorado at Denver), Marina Richardson (Institute for Clinical and Economic Review), Mohamed El Alili (Zorginstituut Nederland), Xavier Pouwels (University of Twente).

Package contributors: **RobertASmith** (Robert Smith), Smit-tay (Jack Smith), W-Mohammed (Wael Mohammed), nialldavison (Niall Davison)

# Overarching aim

*Shifting the modelling pipeline from spreadsheet software (e.g. MS Excel) to script-based programming languages (e.g. R).*



# Related publications

2019

2020

2021

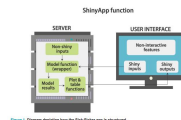
2022

2023

2024

## Making Health Economic Models Shiny: A tutorial

**Smith RA** and **Schneider PP**. Making health economic models Shiny: A tutorial. *Wellcome Open Res* 2020, **5**:69 (<https://doi.org/10.12688/wellcomeopenres.15807.2>)



covid-19 work

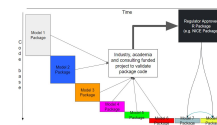
## Living HTA: Automating Health Economic Evaluation with R

**Smith RA, Schneider PP** and **Mohammed W**. Living HTA: Automating Health Economic Evaluation with R. *Wellcome Open Res* 2022, **7**:194 (<https://doi.org/10.12688/wellcomeopenres.17933.2>)



## Packaging cost-effectiveness models in R: A tutorial.

**Smith RA, Mohammed W** and **Schneider PP**. R Packaging cost-effectiveness models in R: A tutorial. 2023. (<https://wellcomeopenresearch.org/articles/8-419>)

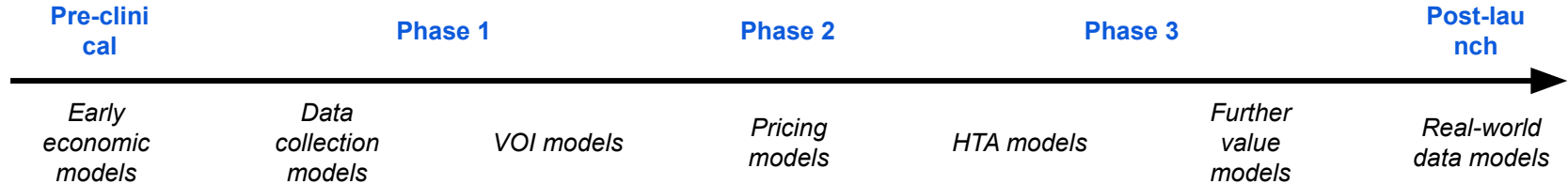


## assertHE: an R package to improve quality assurance of health economic models

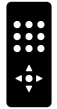
**Smith et al.** assertHE: an R package to improve quality assurance of health economic models. 2024. (<https://github.com/dark-peak-analytics/assertHE>)



# Why change?



**Usability:** Through intuitive app-style interfaces (e.g., R Shiny), enables confident interaction with little technical experience



**Communication:** Enables interactive and customisable output designed for communication and interpretability across multiple audiences

**Efficiency:** Significant improvement in computation time and ability



**Flexibility & Adaptability:** An improved ability to cater to different technical and conceptual requirements, ease of adaptation, and intuitive interaction with a host of other tools, including LLMs

# Background & Motivation

# Poll

Who is currently building health economic models in R?

Who is building models as a set of functions?

Who is building models as a package?

Who is writing unit tests for functions?

Who is assessing coverage of the unit tests?

Sure, I'll  
review your  
model

Good  
Luck!

```
def PRINT_HEAD  
printf(" (%c%c%c)", c, ccharU(...func...));  
*ends;  
// D:\D:\Scene(C, scene)V骨序pare_.clear();  
// (MoMoV骨序pareG.empty())  
#ifdef PC(C, o); // PTMoV骨序Pg(MoMoM+pare)(V+pareG[o]); // return;  
#endif  
// G= " " G=0;  
if(o->type == OB_ARMATURE)  
// V骨序V= " " LIB.resize(20);  
bArmature* arm骨=(bArmature*)o->data; int i=0;  
// Object*o_ = o->c("o_"); C); oG=o_> Object*oV=o->c("oV"); C); Object*o_ = o->c("o_"); C);  
// o_ = o->c("o_"); C);  
bPoseChannel* pcA=CTX_data_active_pose_bone(C), *pcX=NULL, *pcY=NULL;  
if(pcA&&pcA->parent&&pcA->parent->parent)  
Object*oTarget=o->c("oTarget"); C); 正Vector丁目标=loc+pcA(oTarget->ubmat);  
// 三("TypeOfIK", "PoseBone", pcA)!=1)return;  
// 骨序pare_ = MoMoV骨序pareG[o];
```







# The software



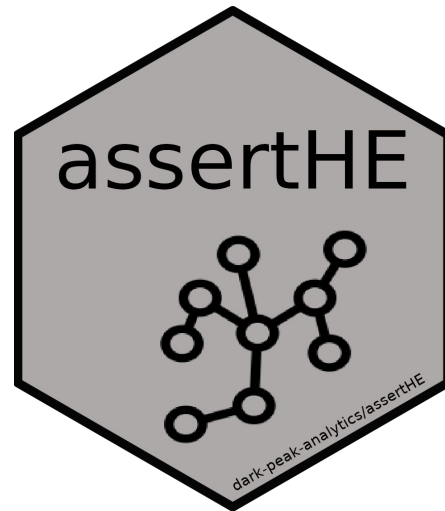
<https://github.com/dark-peak-analytics/assertHE>

# assertHE R package

*Aim: to help modellers build and review health economic models in R.*

Functionality:

- 1. Check that the objects created in models conform to standard rules (e.g. probabilities between 0 and 1).
- 2. Summarise & visualise the structure of a model
  - Plot function network color coded by test coverage.
  - Click on the nodes to see function and test source code and test coverage.
  - Display a LLM generated summary of any function.



<https://github.com/dark-peak-analytics/assertHE>

# Using the *assertHE* R package

```
# install.packages("devtools")
devtools::install_github("dark-peak-analytics/assertHE")

library(assertHE)
```

A: visualise network of functions

```
visualise_project(
  project_path = "path_to_project_directory",
  foo_path = "R",
  test_path = "tests/testthat",
  run_coverage = T)
```

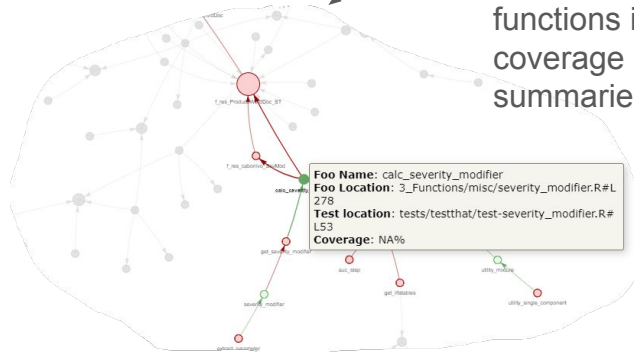
B: insert checks for common errors into the code

```
check_trans_prob_array(a_P = a_P,
  stop_if_not = T)
```

Flags if there are errors or potential problems.

```
# Warning message:
# In check_array_rows_balanced(a_P, stop_if_not = stop_if_not) :
# Not valid transition probabilities
# Transition probabilities not valid from Health States:
# 1 H; at cycle 1
# 2 H; at cycle 2
# 3 H; at cycle 3
# 4 H; at cycle 4
# 5 H; at cycle 5
# 6 H; at cycle 6
# 7 H; at cycle 7
# 8 H; at cycle 8
# 9 H; at cycle 9
# 10 H; at cycle 10
```

Inspect the network to understand how the model functions interact, their test coverage and get AI function summaries.



## *assertHE* checks

**check\_trans\_prob\_array()** Checks transition probability array for common errors ensuring the same number of rows and columns, only numerical values between 0 and 1, with rows summing to 1. The function provides confirmation or warnings/error messages as appropriate.

**check\_markov\_trace()** Validates Markov trace for feasibility, confirming numerical values, equal row sums, and optionally monotonic increase in dead state proportions, generating confirmation or warnings/error messages.

**check\_init()** Checks initial health state proportions vector for validity, ensuring values within valid probability range, no missing values, sum equals 1, and distinct, non-duplicated names, generating messages for inconsistencies.

**plot\_PSA\_stability()** Generates informative plots to inspect stability of results across model iterations, calculating metrics like INMB, ICER, incremental costs, or effects, allowing customization for specific needs, enhancing visual clarity.



# *assertHE* checks

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I'm

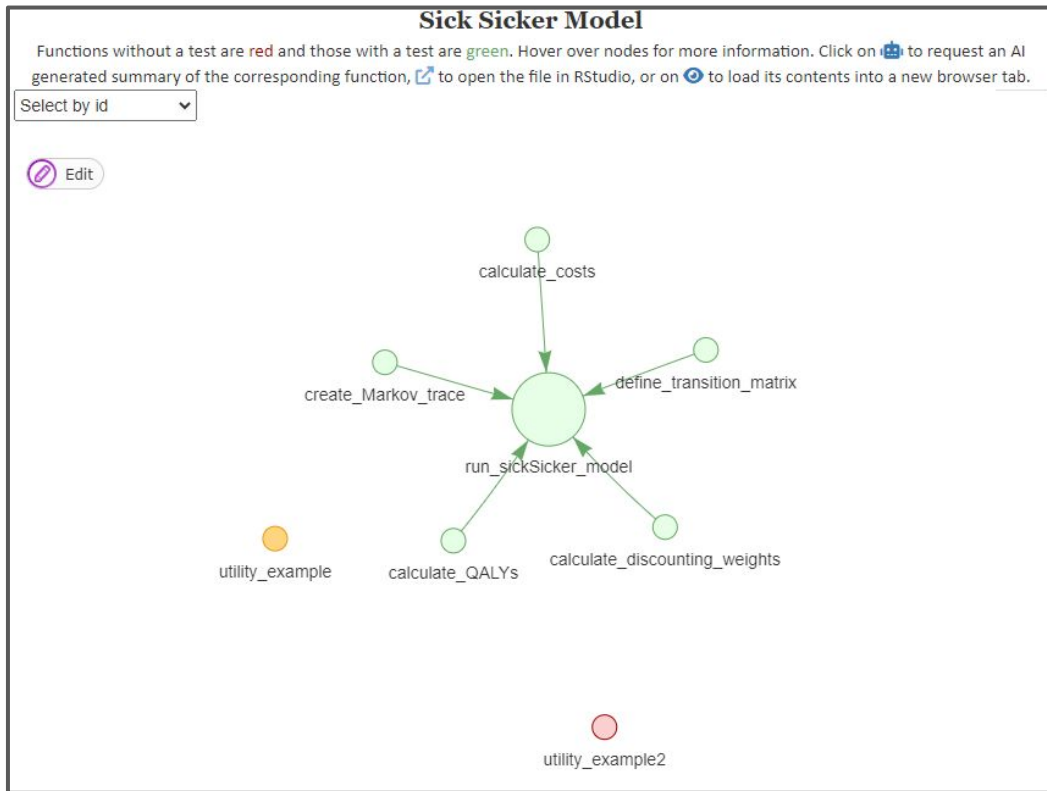
so

BORED!








# assertHE model reviewer



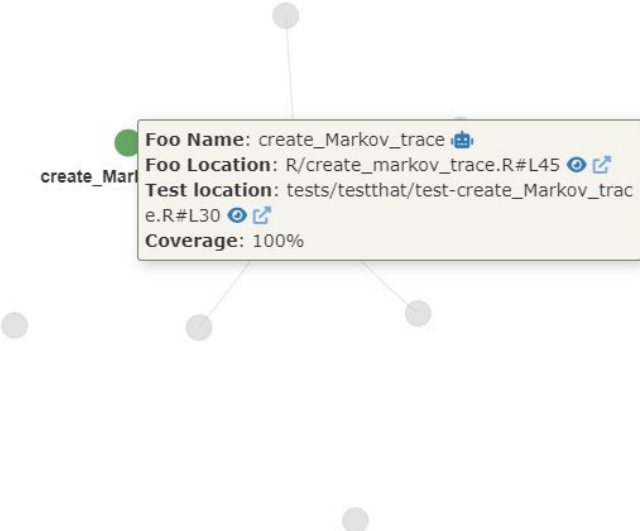
# assertHE model reviewer


## Sick Sicker Model



Functions without a test are **red** and those with a test are **green**. Hover over nodes for more information. Click on  to request an AI generated summary of the corresponding function,  to open the file in RStudio, or on  to load its contents into a new browser tab.



create\_Markov\_traci

Edit



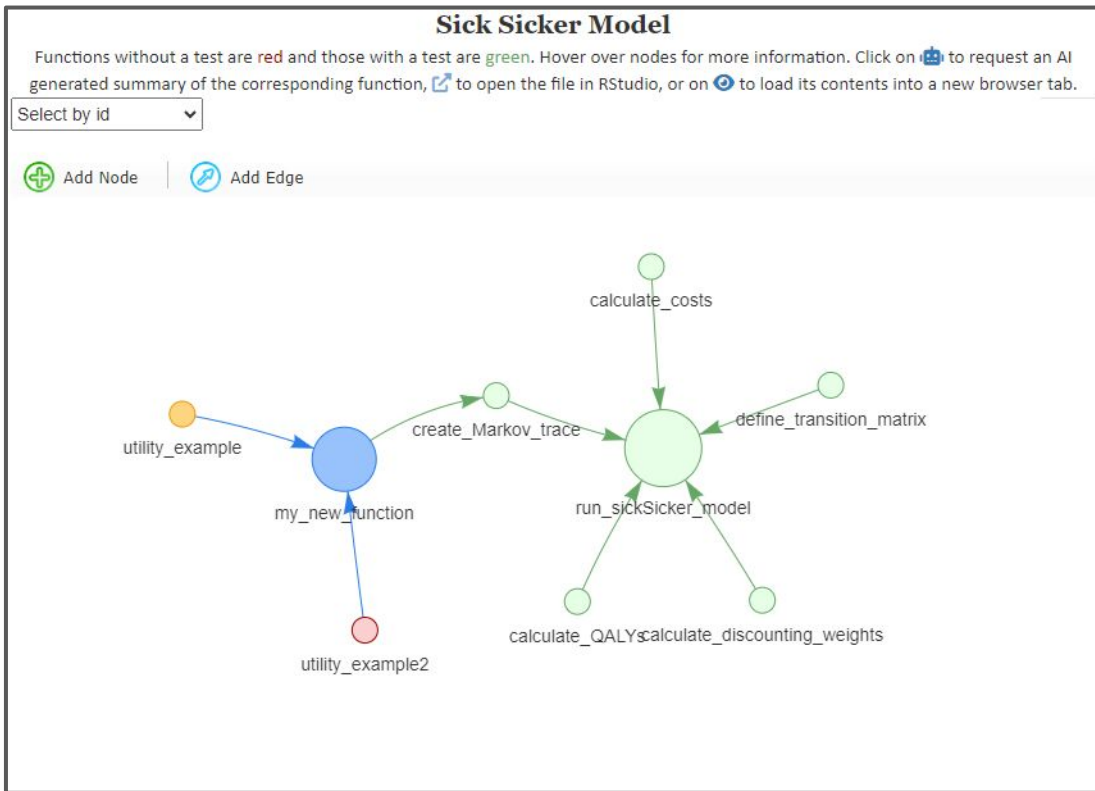
**Foo Name:** create\_Markov\_trace 

**Foo Location:** R/create\_markov\_trace.R#L45  

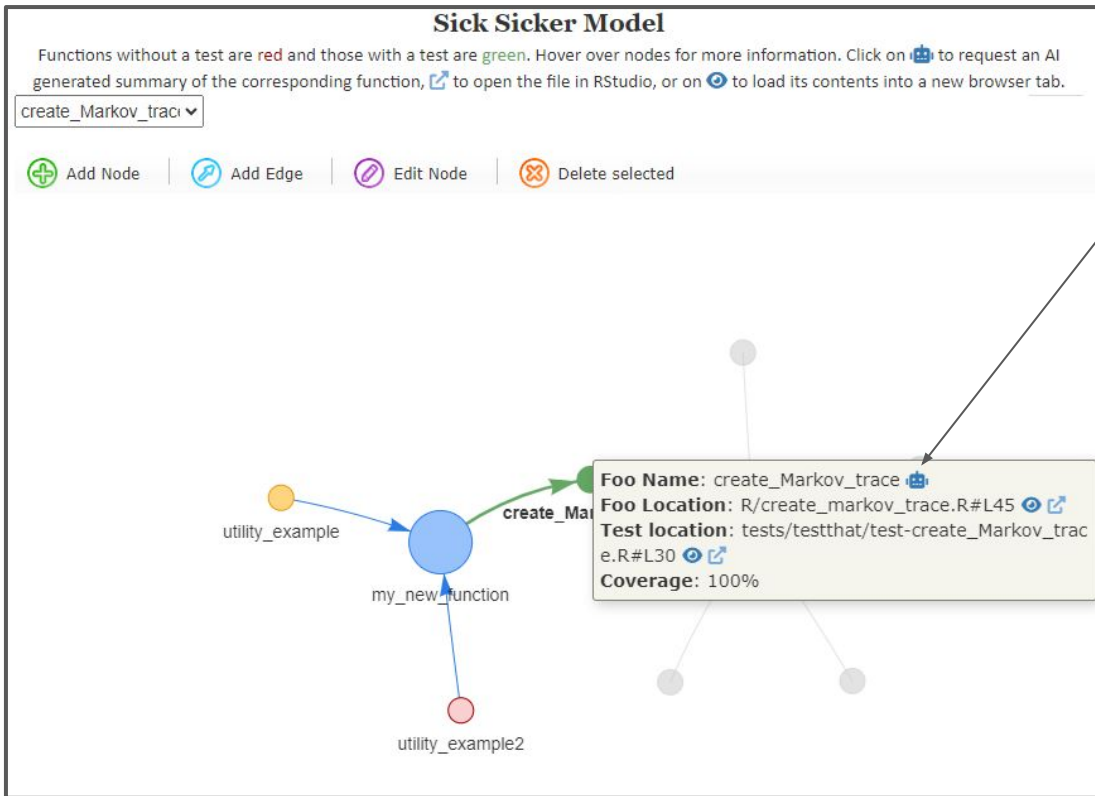
**Test location:** tests/testthat/test-create\_Markov\_trace.R#L30  

**Coverage:** 100%

# assertHE model reviewer

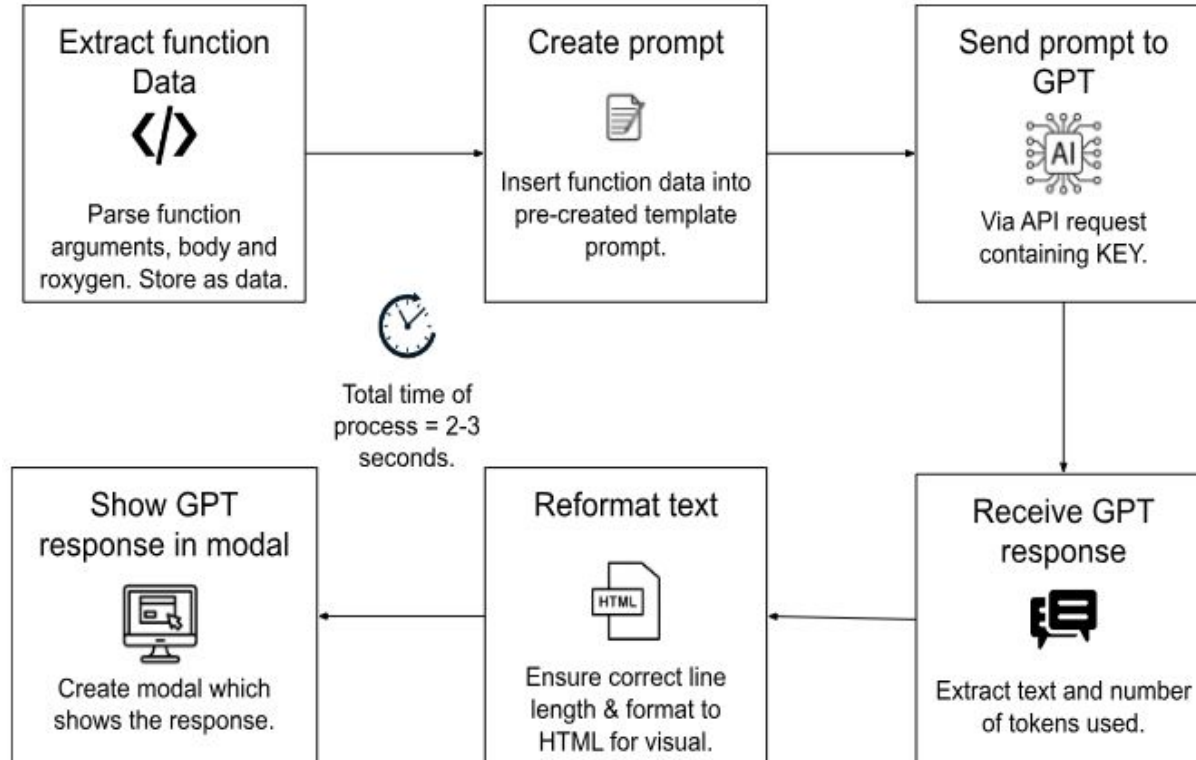


# assertHE model reviewer

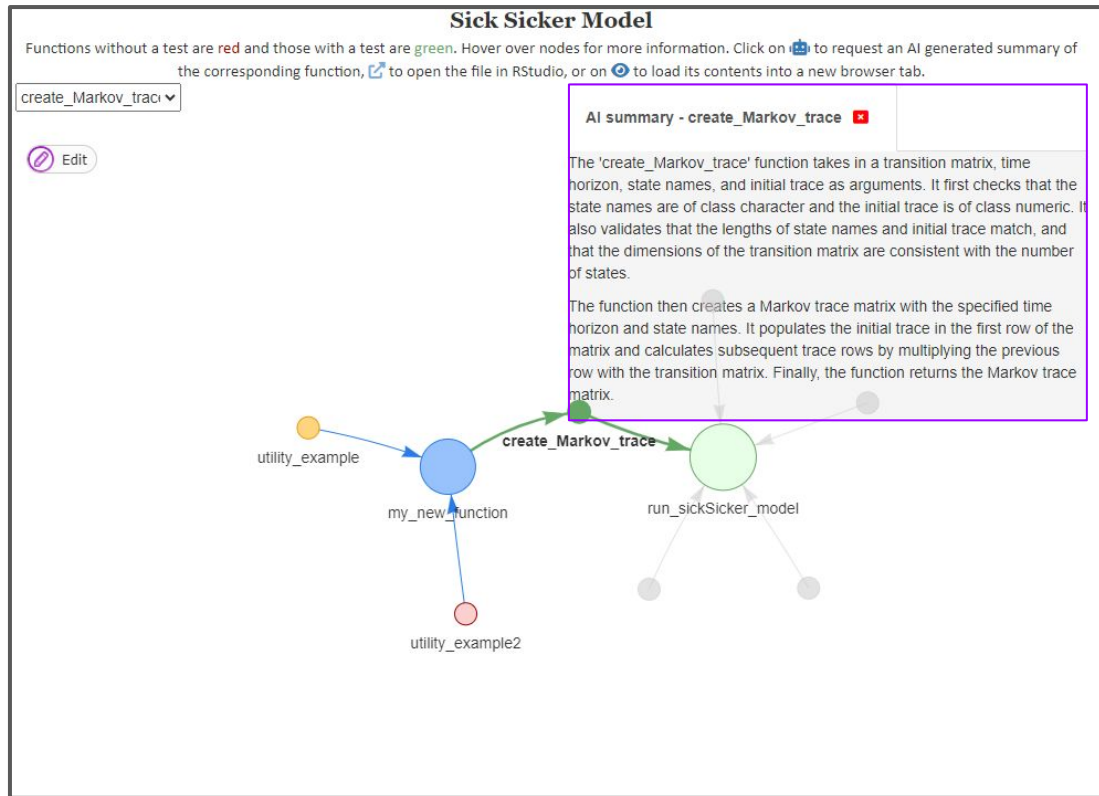


Generate LLM  
summary of  
function.

# *assertHE* model reviewer



# assertHE model reviewer





# Case Studies

# Case Studies

We have used the assertHE package on several models as test cases:




- NICE RCC Model
- sicksickerPack teaching model contained in a package.
- cdx2cea as described in Alarid-Escudero et al. 2022
- DOACs-AF-Economic-model developed by Bristol University
- The CGD AMR Cost model - in press.
- Embedding Economics Analysis Diabetes Microsimulation model described in (in press).

Others have used assertHE on their own models that are not in the public domain. We welcome this. Please get in contact if you have any issues or suggestions for improvements.



# Case Study

## Function Network

Functions without a test are **red** and those with a test are **green**. Hover over nodes for more information. Click on  to request an AI generated summary of the corresponding function,  to open the file in RStudio, or on  to load its contents into a new browser tab.

run\_probsa

### AI summary - run\_probsa

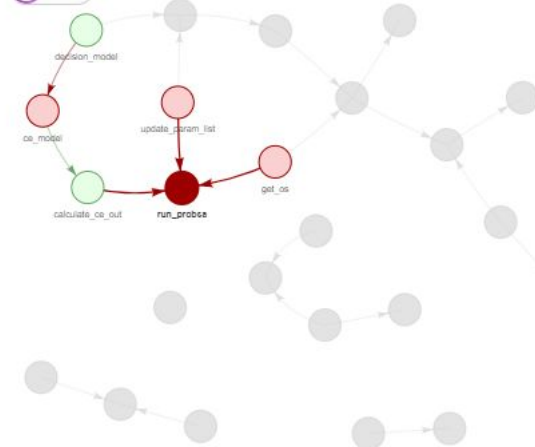
```
'''html
```

The 'run\_probsa' function runs probabilistic sensitivity analysis (PSA) on a given input dataset. If the 'parallel' argument is set to TRUE, the function parallelizes the PSA process using multiple cores based on the operating system. It then calculates costs and effects for each simulation, aggregates the results, and returns them in separate data frames.

If the 'parallel' argument is set to FALSE, the function runs the PSA simulations in series. It iterates through each simulation, updates parameters, calculates costs and effects, and prints the progress. Finally, it aggregates the results and returns them in separate data frames. The function returns a list containing the costs and effects data frames.

```
'''
```

Edit



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Contents lists available at sciencedirect.com  
journal homepage: www.elsevier.com/locate/jco

### Economic Evaluation

### CDX2 Biomarker Testing and Adjuvant Therapy for Stage II Colon Cancer: An Exploratory Cost-Effectiveness Analysis

Fernando Alarid-Escudero, PhD, Deborah Schrag, MD, MPH, Karen M. Kuntz, ScD

### ABSTRACT

**Objectives:** Adjuvant chemotherapy is not recommended for patients with average-risk stage II (T2N0) colon cancer. Nevertheless, a subgroup of these patients who are CDX2-negative might benefit from adjuvant chemotherapy. We evaluated the cost-effectiveness of testing for the absence of CDX2 expression followed by adjuvant chemotherapy (fluorouracil combined with oxaliplatin [FOLFOX]) for patients with stage II colon cancer.

**Methods:** We developed a decision model to simulate a hypothetical cohort of 65-year-old patients with average-risk stage II colon cancer with 7.2% of these patients being CDX2-negative under 2 different interventions: (1) test for the absence of CDX2 expression followed by adjuvant chemotherapy for CDX2-negative patients and (2) no CDX2 testing and no adjuvant chemotherapy for any patient. We derived disease progression parameters, adjuvant chemotherapy effectiveness and utilities from published analyses, and cancer care costs from the Surveillance, Epidemiology, and End Results (SEER)-Medicare data. Sensitivity analyses were conducted.

**Results:** Testing for CDX2 followed by FOLFOX for CDX2-negative patients had an incremental cost-effectiveness ratio of \$550/quality-adjusted life-year (QALY) compared with no CDX2 testing and no FOLFOX (\$478 vs \$438 discounted QALY and \$80,901 vs \$80,797 discounted US dollar lifetime costs). In sensitivity analyses, considering a cost-effectiveness threshold of \$100,000/QALY, testing for CDX2 followed by FOLFOX in CDX2-negative patients remains cost-effective for hazard ratios of <0.975 of the effectiveness of FOLFOX in CDX2-negative patients in reducing the rate of developing a recurrent recurrence.

**Conclusions:** Testing tumors of patients with stage II colon cancer for CDX2 and administration of adjuvant treatment to the subgroup found CDX2-negative is a cost-effective and high-value management strategy across a broad range of plausible assumptions.

**Keywords:** CDX2, cost-effectiveness analysis, decision-analytic model, immunohistochemistry testing, stage II colon cancer.

VALUE HEALTH 2022; 25(3):409-418

### Introduction

Adjuvant chemotherapy is not recommended for patients with average-risk stage II (T2N0) colon cancer.<sup>1</sup> And thus, these patients are usually treated with surgery alone.<sup>2</sup> Nevertheless, a recent study by Talerbit et al<sup>3</sup> described a small subgroup of patients with average-risk stage II colon cancer who lack expression of the CDX2 transcription factor that associated with clinical benefit from adjuvant chemotherapy. CDX2 is a master transcription factor involved in intestinal development<sup>4</sup> and serves as a candidate biomarker of mature colonic epithelial tissue. In this study, the authors used Boolean implication networks<sup>5</sup> to conduct a systematic search for a biomarker to identify undifferentiated tumors in a collection of human colon gene expression array experiments from the National Center for Biotechnology Information Gene Expression Omnibus repository<sup>6</sup> (<https://www.ncbi.nlm.nih.gov/geo/>) used as a discovery data set. As a validation data set, the authors used tissue microarrays from the Cancer Therapy Program of the

National Cancer Institute, which were analyzed for CDX2 expression by immunohistochemical (IHC) analysis. Among all tumors analyzed in the validation data set, 48 of 669 (7.2%) were CDX2-negative, defined as completely lacking CDX2 expression or showing expression in a minority of malignant epithelial cells.<sup>3</sup> The study also showed that CDX2-negative patients had poorer 5-year disease-free survival (DFS) than CDX2-positive patients (those with biomarker expression). More importantly, the 5-year DFS was greater for the CDX2-negative patients who received adjuvant chemotherapy than similar patients who did not receive adjuvant chemotherapy. The ability to test average-risk patients with stage II colon cancer for CDX2 biomarker expression to target adjuvant chemotherapy to a subgroup most likely to benefit could reduce colon cancer mortality and minimize adjuvant chemotherapy harms.<sup>3</sup>

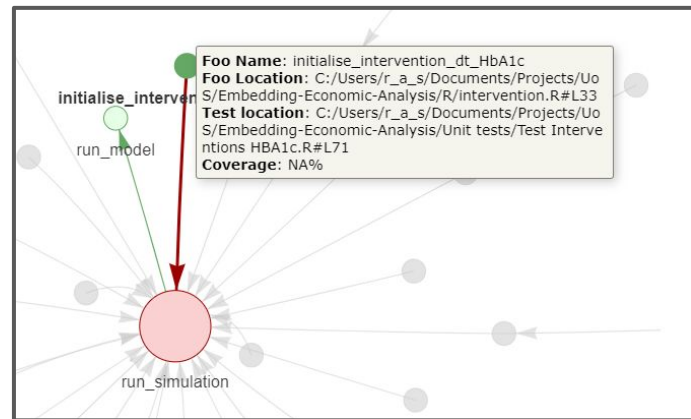
This study aims to quantify the long-term benefits, costs, and cost-effectiveness of testing average-risk patients with stage II colon cancer for the absence of CDX2 biomarker expression followed

# Case Study: Embedding Economic Analysis

## Embedding-Economic-Analysis Repository

Functions without a test are red and those with a test are green. Hover over nodes for more information.

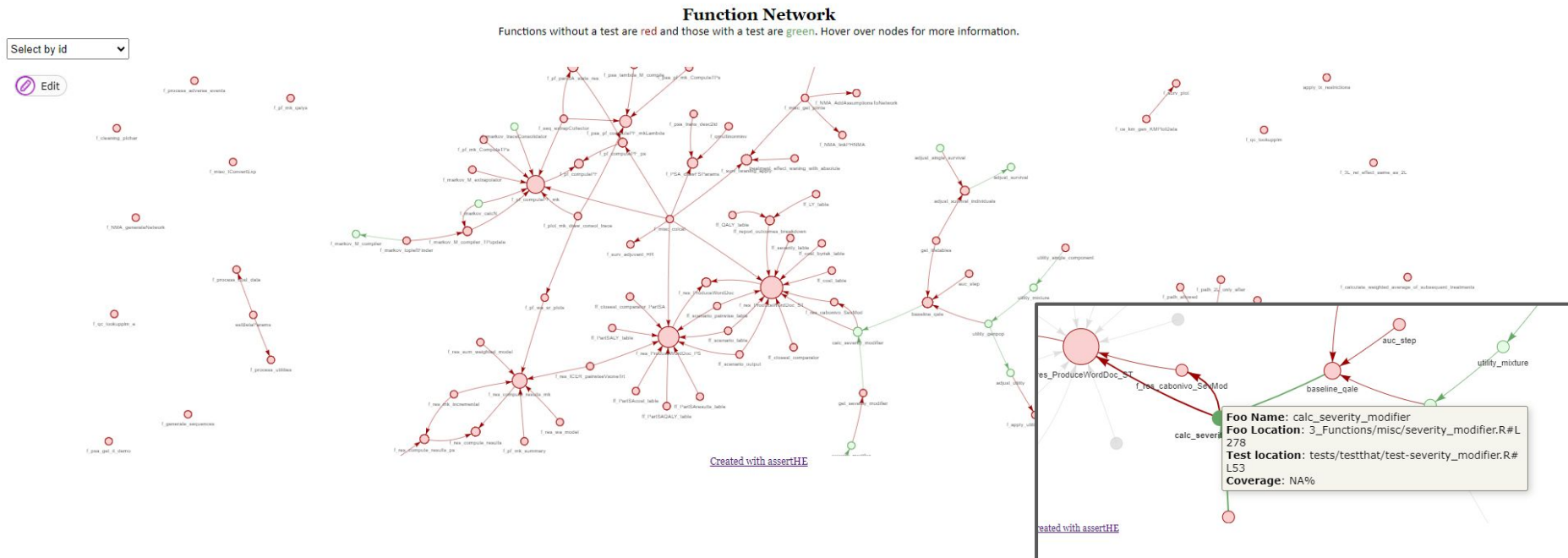
Select by id ▼



Created with assertHE

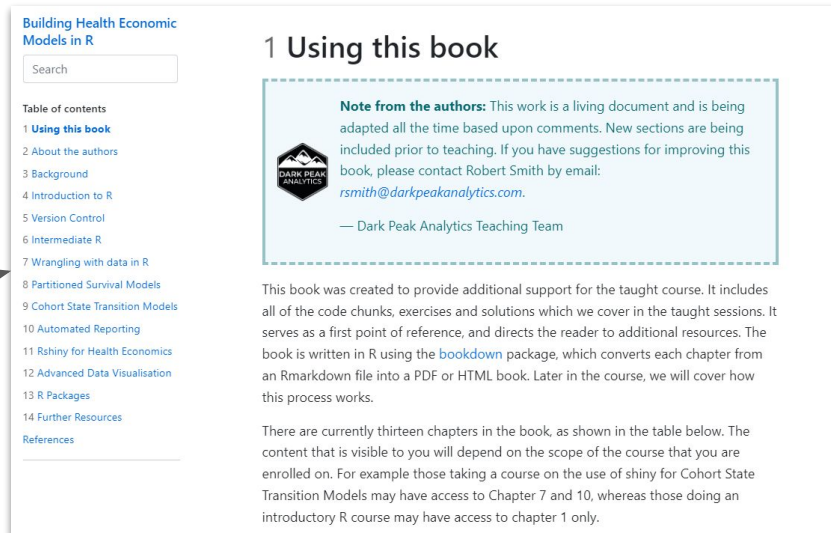
<https://github.com/DanPollardSheff/Embedding-Economic-Analysis>

# Case Study: NICE RCC Pilot



# Next steps

- Welcome contributions
  - Testing the software on your models
  - Suggesting improvements (see contribution page on GitHub)
  - Expansion of testing functionality
- Future development:
  - LLM Chatbot integration (using DPA teaching material to fine-tune).
  - Language selection (in progress)
- Open access publication imminent
- CRAN submission (Autumn '24)
- **Continued open-access development to maintain a collaborative tool**



The screenshot shows the book's interface. On the left is a 'Table of contents' sidebar with a search bar and a list of chapters. Chapter 1, 'Using this book', is highlighted. An arrow points from the 'LLM Chatbot integration' bullet point in the 'Next steps' list to this chapter. The main content area shows the title '1 Using this book' and a 'Note from the authors' box. The note states that the work is a living document and provides contact information for Robert Smith. Below the note, a paragraph explains the book's purpose and its creation using the bookdown package. At the bottom, another paragraph details the chapter access for different course cohorts.

Building Health Economic Models in R

Search

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- 1 Using this book
- 2 About the authors
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- 8 Partitioned Survival Models
- 9 Cohort State Transition Models
- 10 Automated Reporting
- 11 Rahiny for Health Economics
- 12 Advanced Data Visualisation
- 13 R Packages
- 14 Further Resources

References

## 1 Using this book

**Note from the authors:** This work is a living document and is being adapted all the time based upon comments. New sections are being included prior to teaching. If you have suggestions for improving this book, please contact Robert Smith by email: [rsmith@darkpeakanalytics.com](mailto:rsmith@darkpeakanalytics.com).

— Dark Peak Analytics Teaching Team

This book was created to provide additional support for the taught course. It includes all of the code chunks, exercises and solutions which we cover in the taught sessions. It serves as a first point of reference, and directs the reader to additional resources. The book is written in R using the [bookdown](#) package, which converts each chapter from an Rmarkdown file into a PDF or HTML book. Later in the course, we will cover how this process works.

There are currently thirteen chapters in the book, as shown in the table below. The content that is visible to you will depend on the scope of the course that you are enrolled on. For example those taking a course on the use of shiny for Cohort State Transition Models may have access to Chapter 7 and 10, whereas those doing an introductory R course may have access to chapter 1 only.

# Open Access Publication

1  
2  
3 **asserTHE**: an R package to improve quality assurance of health  
4 economic models  
5  
6 Wellcome Open Research  
7  
8 **Authors**  
9 Robert A Smith (Dark Peak Analytics, University of Sheffield)  
10 Yevgeniy Samyshkin (GSK),  
11 Wael Mohammed (Dark Peak Analytics, University of Sheffield)  
12 Tom Ward (GSK)  
13 Alan Martin (GSK)  
14 Sarah-Jane Anderson (GSK)  
15 Paul Schneider (Dark Peak Analytics, University of Sheffield)  
16 Baris Deniz (GSK)  
17 Dawn Lee (University of Exeter)  
18 Prof. Gianluca Baio (University College London)  
19 Howard Thom (University of Bristol)  
20 Nathan Green (University College London)  
21 Felicity Lamrock (Queens University Belfast)  
22 Brett McQueen (University of Colorado at Denver)  
23 Marina Richardson (Institute for Clinical and Economic Review)  
24 Mohamed El Alili (Zorginstituut Nederland)  
25 Xavier Pouwels (University of Twente).  
26 March 2023  
27

28 **Abstract**  
29  
30 **Background:** Health economic evaluation models are increasingly used to inform decisions about the  
31 allocation of `health_care` resources. Ensuring the robustness, reliability, and reproducibility of these  
32 models is critical. Currently, quality assurance is conducted by experts assessing the different  
33 components of the model manually in isolation and in combination. However, this is resource  
34 intensive. Understanding how the different components of the model fit together is time consuming,  
35 and testing each part of the model is sometimes not feasible under the timescales provided to  
36 reviewers. To aid in this, we propose the *asserTHE* R package.  
37 **Methods:**  
38 The open source *asserTHE* package provides testing functionality for modellers and reviewers of  
39 health economic models. It provides a series of common checks, which can be integrated into the  
40 model development workflow to reduce the probability of common errors. It also provides a suite of  
41 functions which allow users to better understand the network of algorithms (functions) contained in the  
42 model, where they are defined, if (and where) they are tested, and the test coverage of those that  
43 have.  
44 **Results:** We applied the *asserTHE* package to two health economic models, showing how to include  
45 the check functions within the model code and showing how to visualise a network of functions, see  
46 the test coverage, and obtain a Generative Pretrained Transformer (GPT) Large Language Model  
47 (LLM) generated summary of any function in the codebase. We have worked with collaborators from  
48 industry, regulators and academia to develop the package to be applicable to the widest possible  
49 range of models, making adaptations to the source code based upon feedback.  
50 **Conclusions:** The *asserTHE* R software package offers a toolkit for health economists building and  
51 reviewing models, facilitating a more robust and efficient quality assurance process. We hope this will  
52 ultimately improve the quality, transparency and efficiency of the health economic evaluation process  
53 for models built in R.  
54  
55 **Key Words:**  
56 *R, Health Economics, Unit Testing, Model Validation*  
57  
58

<https://drive.google.com/file/d/1ZR0zMZjiEERdzoQM49Pm2LXtOSe4agMi/view?usp=sharing>

A large, diagonal photograph of a rugged mountain landscape. The foreground shows a grassy slope with a stone wall and a few sheep. In the background, a prominent, rocky mountain peak rises against a cloudy sky. The image is cut off by a diagonal line.

# assertHE: R model reviewer

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**R-HTA 24 | Robert Smith & Tom Ward | June 2024**



[rsmith@darkpeakanalytics.com](mailto:rsmith@darkpeakanalytics.com)



<https://github.com/dark-peak-analytics/assertHE>



<https://www.linkedin.com/company/dark-peak-analytics>



# Additional resources

# Book topics

We run courses on several topics relating to building health economic models in R.

- Introduction to R
- Version Control
- Intermediate R
- Wrangling with data in R
- Partitioned Survival Models
- State Transition Models
- Efficient Microsimulation in R
- Automated Reporting
- RShiny for Health Economics
- Advanced Data visualisation
- R packages
- Reviewing Health Economic Models in R

Building Health Economic Models in R

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References

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The logo for Dark Peak Analytics, featuring a stylized mountain range inside a hexagon with the text "DARK PEAK ANALYTICS" below it.

**Note from the authors:** This work is a living document and is being adapted all the time based upon comments. New sections are being included prior to teaching. If you have suggestions for improving this book, please contact Robert Smith by email: [rsmith@darkpeakanalytics.com](mailto:rsmith@darkpeakanalytics.com).

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[Bespoke training courses](#)



# Making Health Economic Models Shiny: Sept 24



## Dates

The online course sessions are held on four consecutive Thursdays in September and October 2024:

1. Thursday, 12 September 2024
2. Thursday, 19 September 2024
3. Thursday, 26 September 2024
4. Thursday, 03 October 2024

Each session runs from:

13:00 - 16:00 GMT (London time)  
08:00 - 11:00 EST (New York time)  
17:00 - 20:00 GST (Dubai time)

**PLUS:** optional drop-in code clinics are held on Tuesdays:

1. Tuesday, 17 September 2024
2. Tuesday, 24 September 2024
3. Tuesday, 01 October 2024
4. Tuesday, 08 October 2024

Each code clinic runs from:

13:00 - 14:30 GMT (London time)  
08:00 - 09:30 EST (New York time)  
17:00 - 18:30 GST (Dubai time)

<https://www.courses.darkpeakanalytics.com/>