assertHE:
R model reviewer

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

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

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

Acknowledgements

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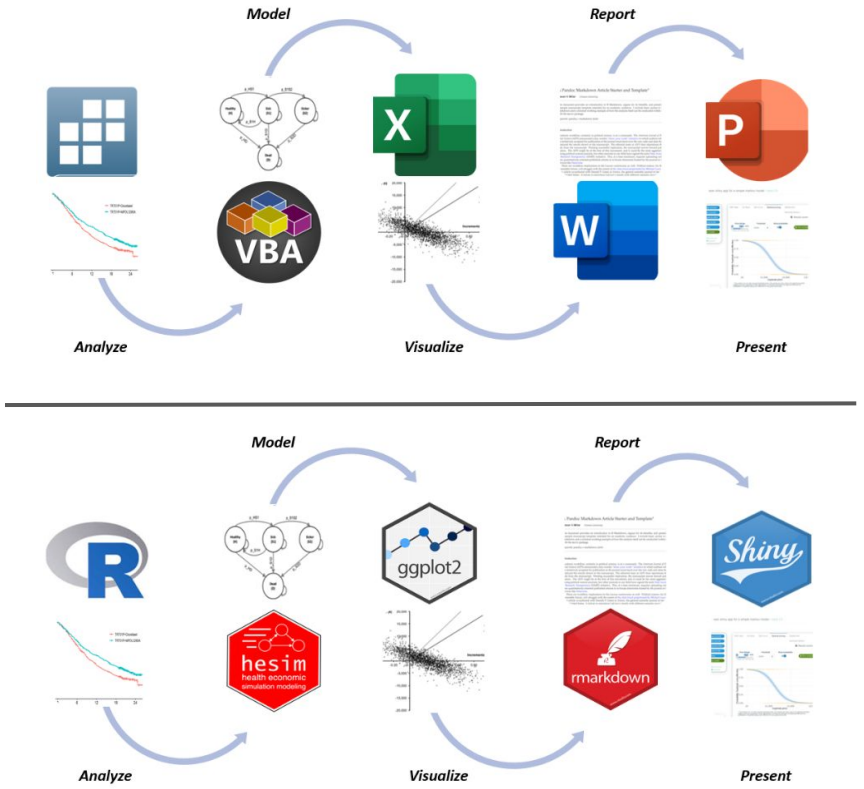
Overarching aim

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

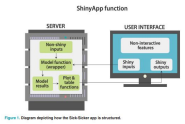


Related publications

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)



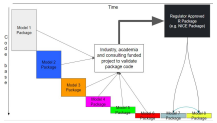
covid-19 work

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.

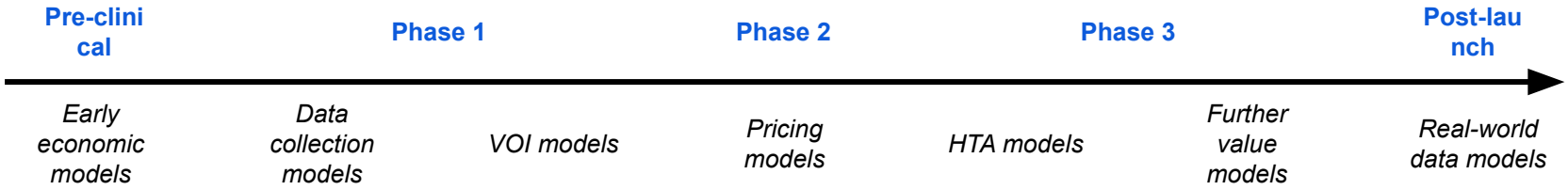
Smith RA, Mohammed W and **Schneider PP**. R Packaging cost-effectiveness models in R: A tutorial. 2023. (https://wellcomeopenresearch.org/articles/8-419)



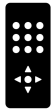
assertHE: an R package to improve quality assurance of health economic models

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

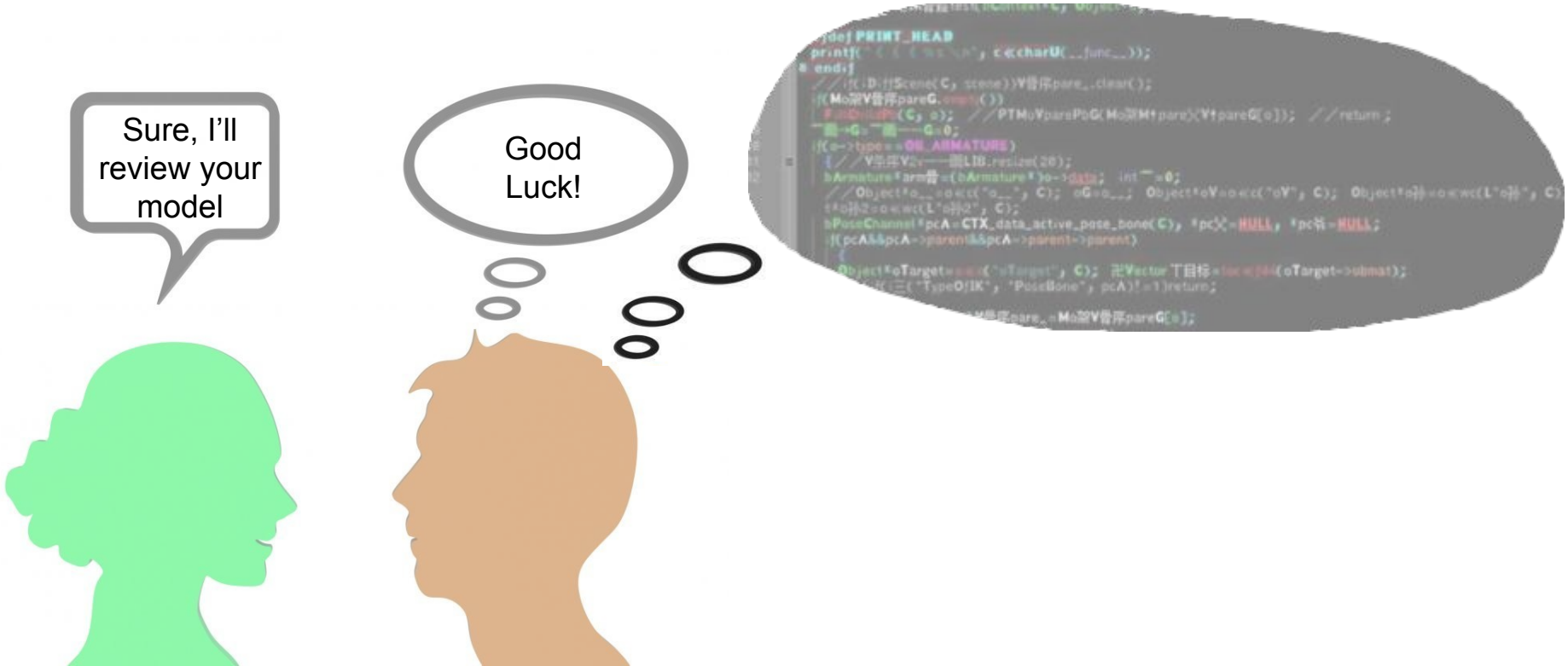
Efficiency: Significant improvement in computation time and ability

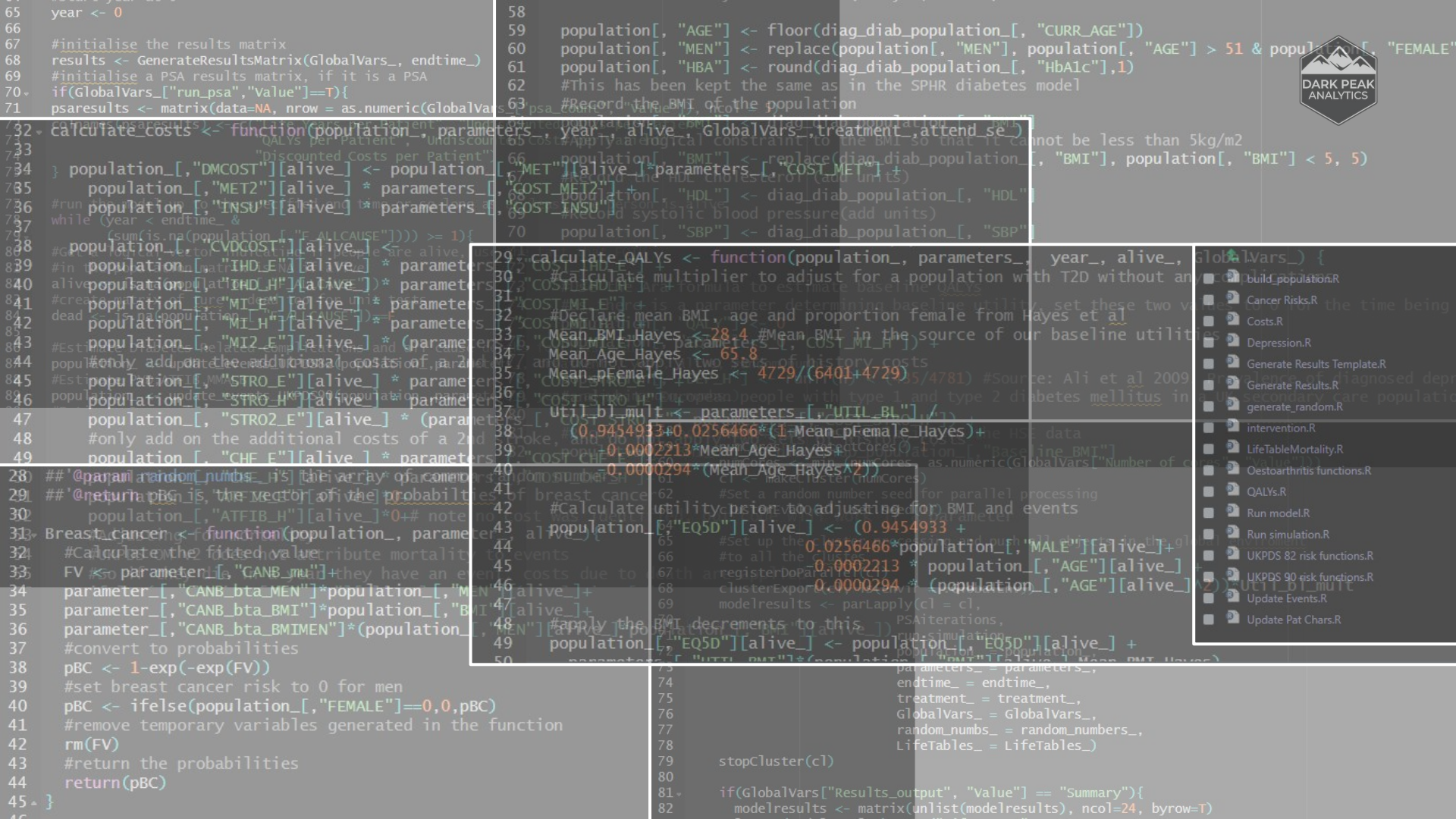
Flexibility & Adaptability: An improved ability to cater to different technical and conceptual requirements, ease of adaptation, and intuitive interaction with a host of other tools, including LLMs

Background & Motivation

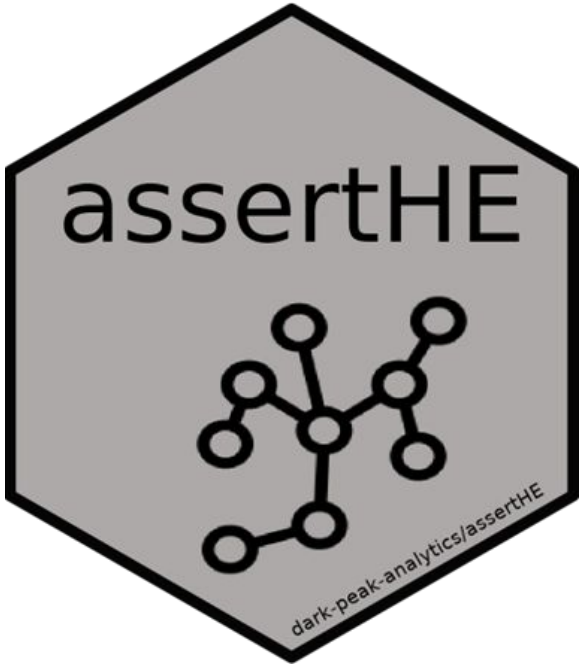
Poll

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!


DARK PEAK ANALYTICS
build_population.R
Cancer Risks.R
Costs.R
Depression.R
Generate Results Template.R
Generate Results.R
generate_random.R
intervention.R
LifeTableMortality.R
Oestoarthritis functions.R
QALYs.R
Run model.R
Run simulation.R
UKPDS 82 risk functions.R
UKPDS 90 risk functions.R
Update Events.R
Update Pat Chars.R

The software



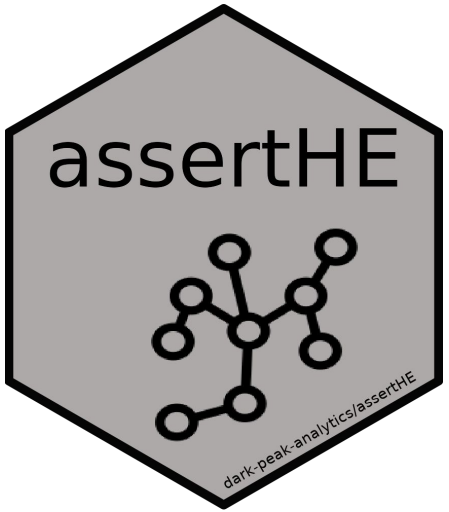
https://github.com/dark-peak-analytics/assertHE

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

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

library(assertHE)
```

A: visualise network of functions

B: insert checks for common errors into the code

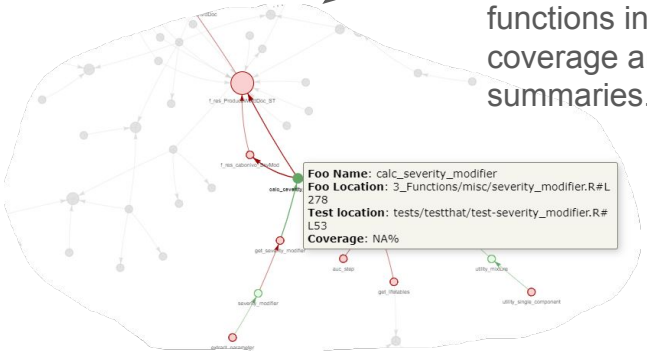
```r
check_trans_prob_array(a_P = a_P,
                       stop_if_not = T)
```

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
```

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

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.

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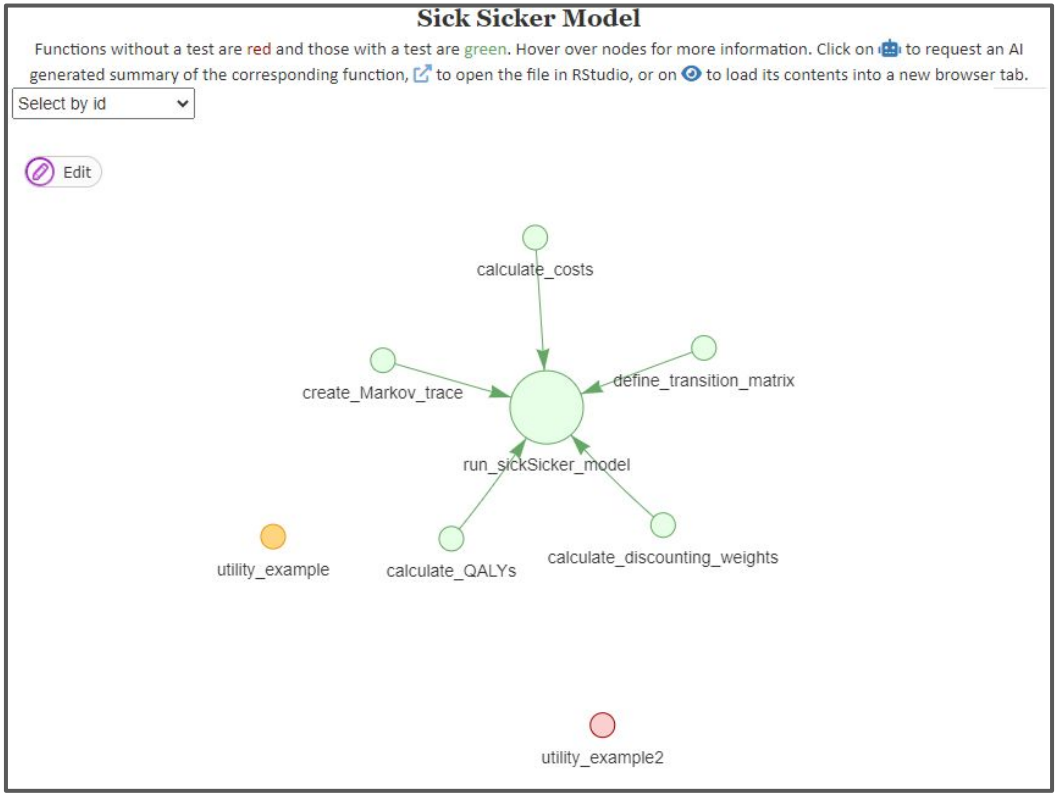
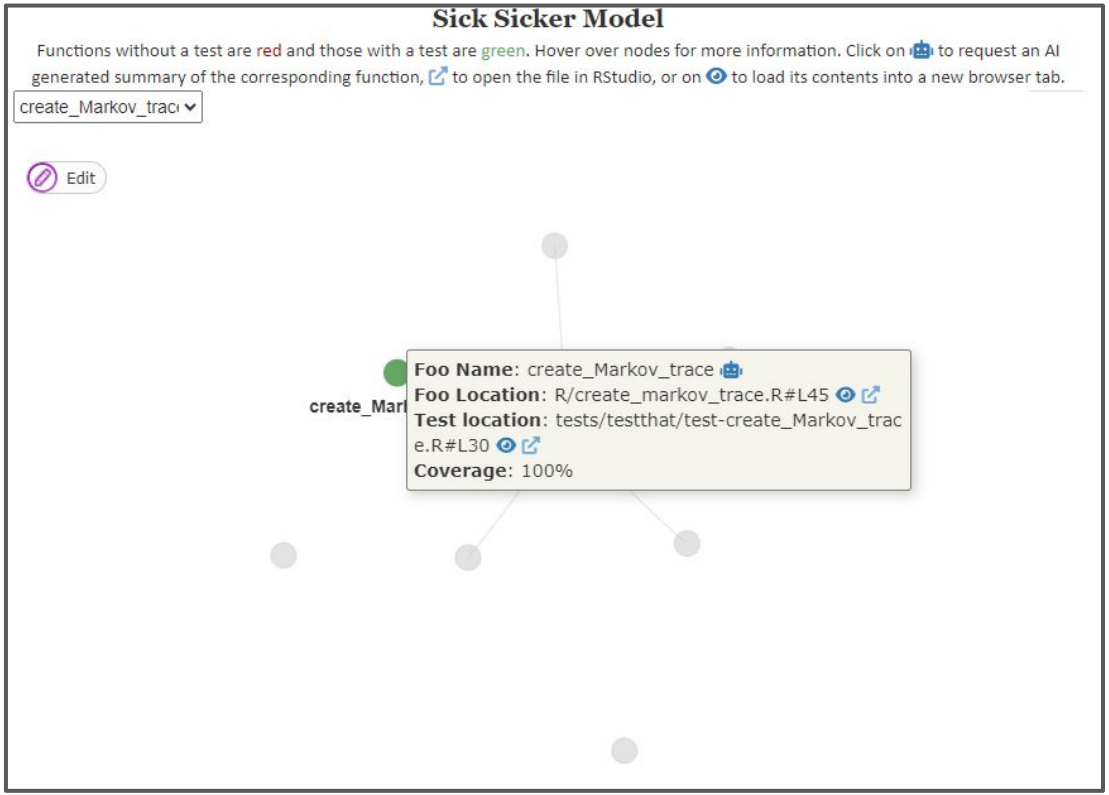
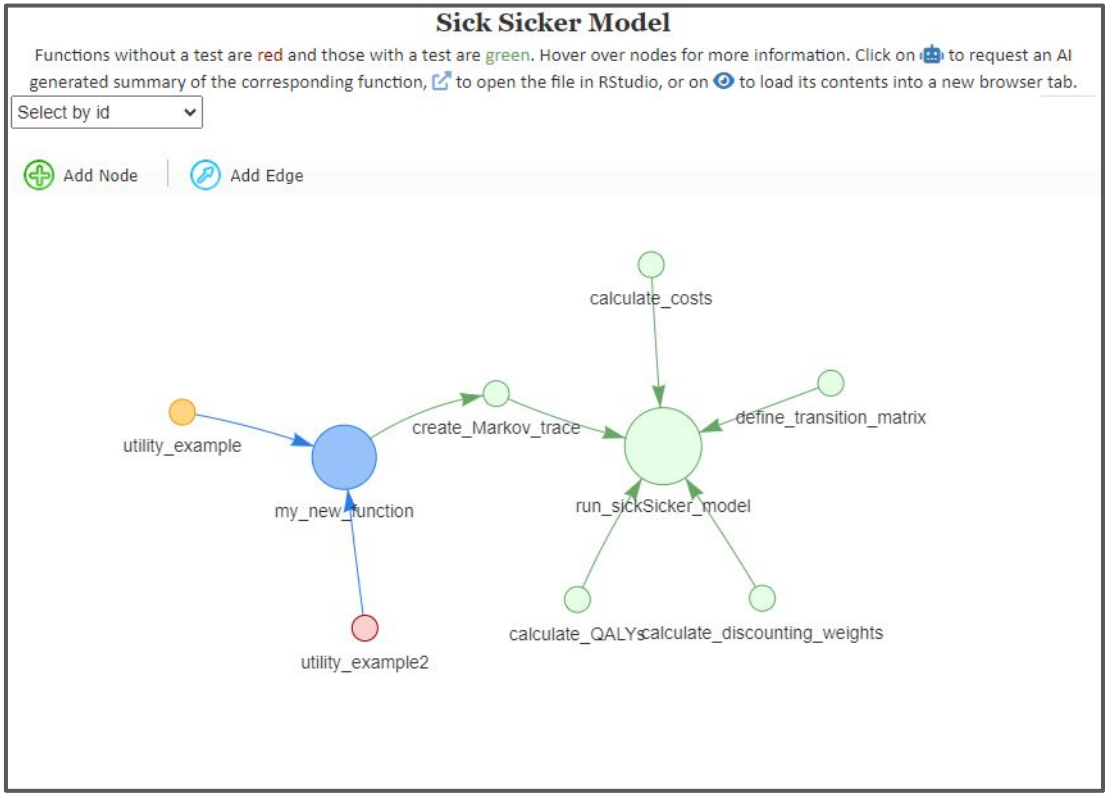
assertHE model reviewer



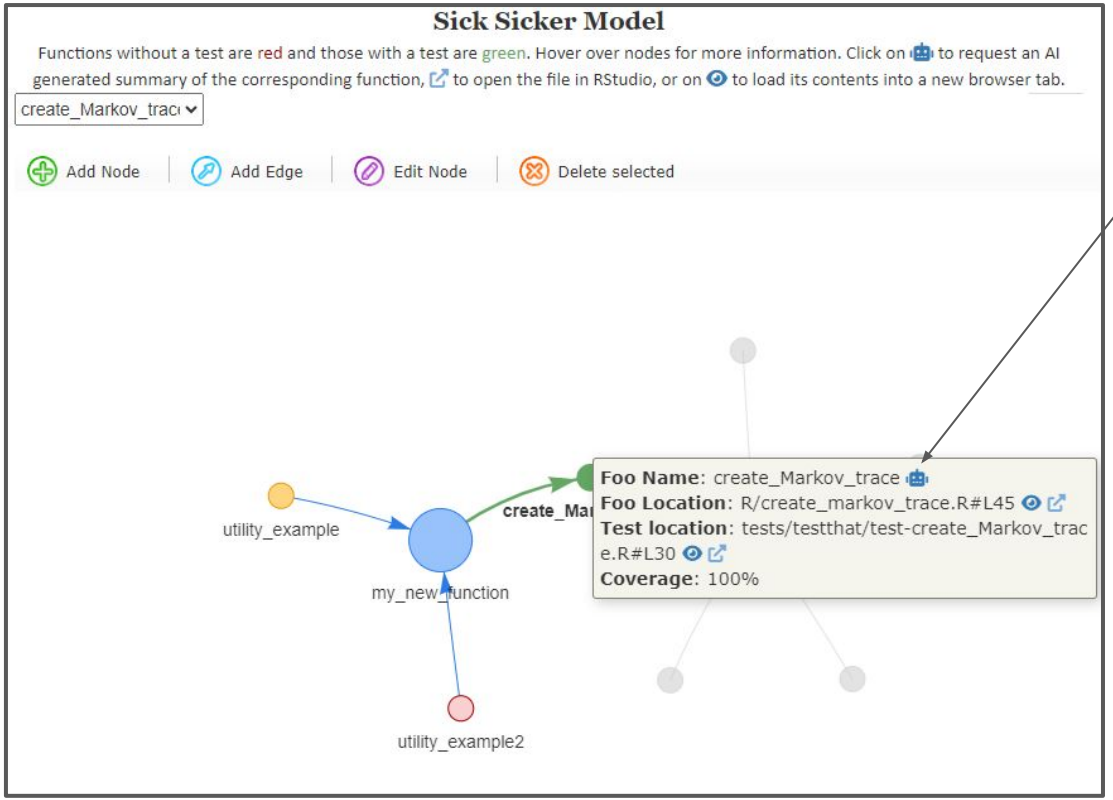
assertHE model reviewer



assertHE model reviewer

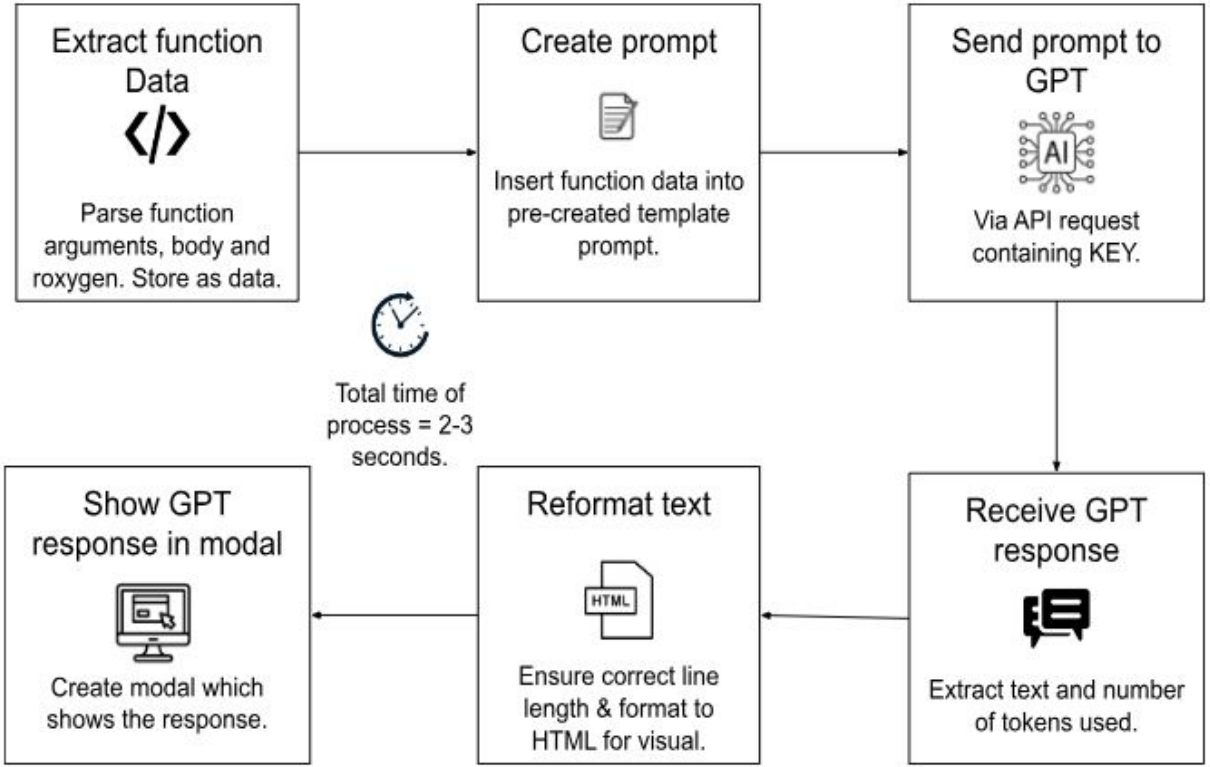


assertHE model reviewer

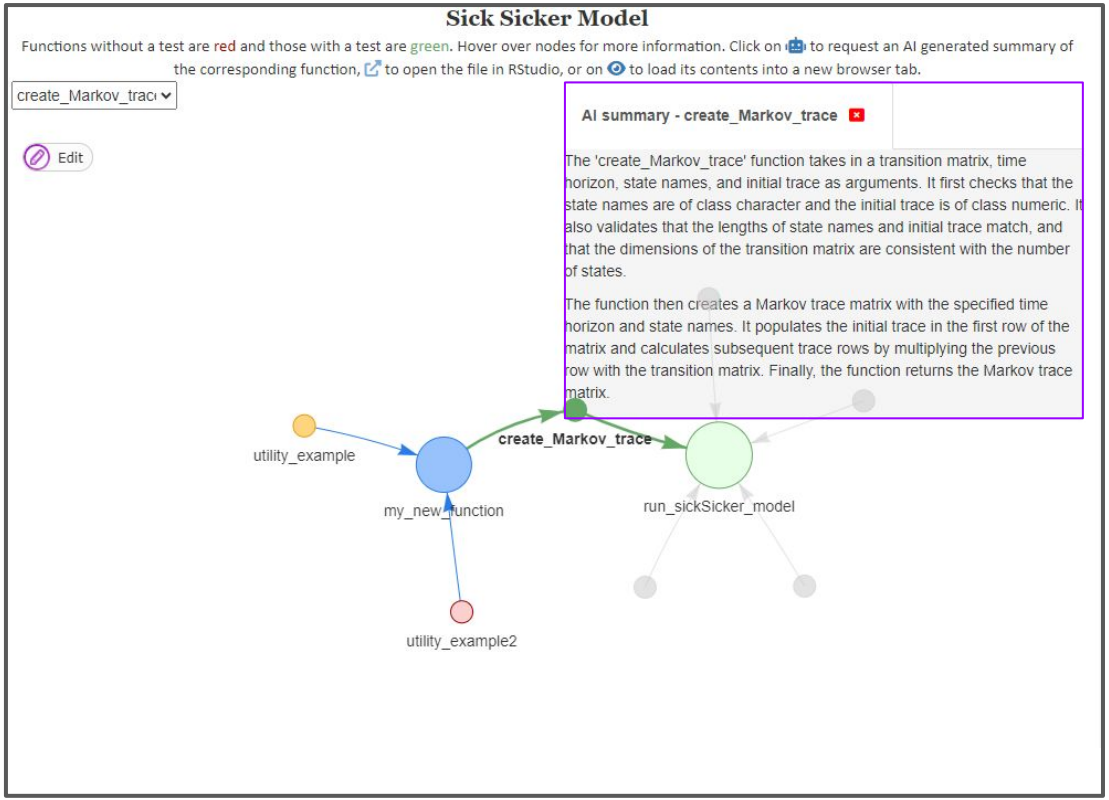


Generate LLM summary of function.

assertHE model reviewer



assertHE model reviewer



Case Studies

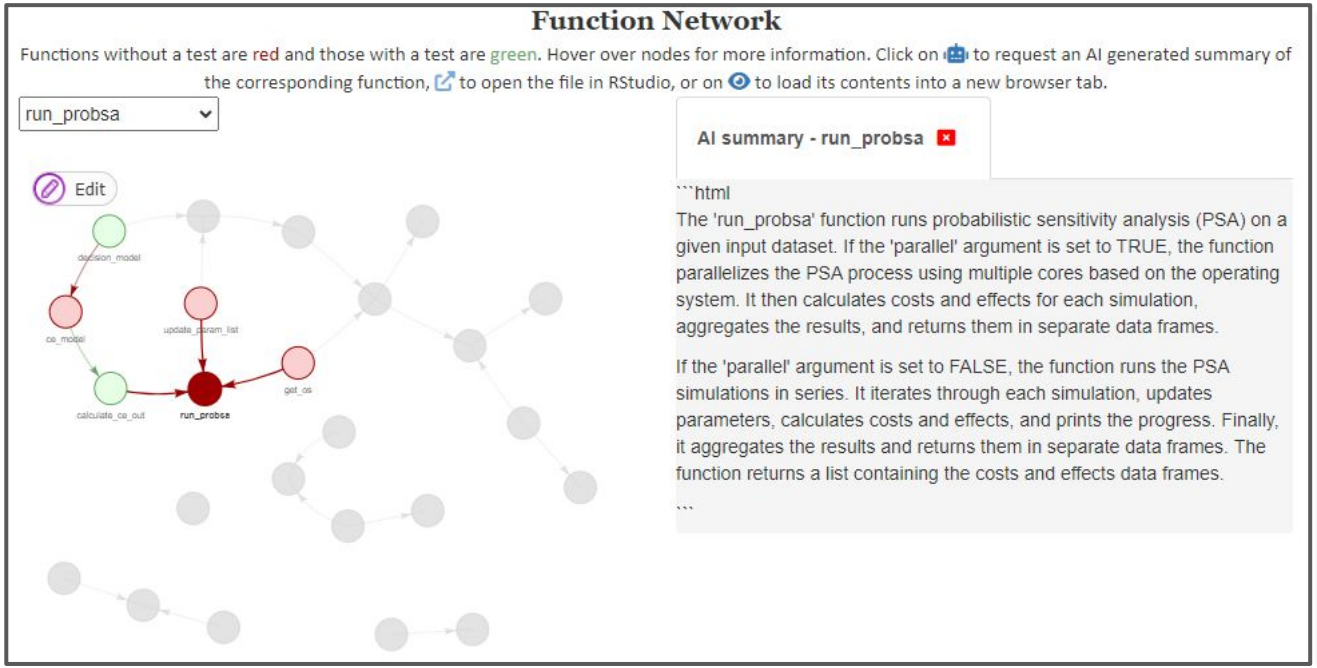
Case Studies

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



ScienceDirect

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 (T3N0) 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 $55500/quality-adjusted life-years (QALYs) compared with no CDX2 testing and no FOLFOX (8.874 vs 8.838 discounted QALYs and $89 991 vs $89 797 discounted US dollar lifetime costs). In sensitivity analyses, considering a cost-effectiveness threshold of $100 000/QALY, testing for CDX2 followed by FOLFOX on 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 metastatic 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 (T3N0) colon cancer,[1–4] and thus, these patients are usually treated with surgery alone.[5] Nevertheless, a recent study by Dalerba et al[6] 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[7] and serves as a candidate biomarker of mature colon epithelial tissues. In this study, the authors used Boolean implication networks[8] 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 (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 Diagnosis 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.[6,9] 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.[10]

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

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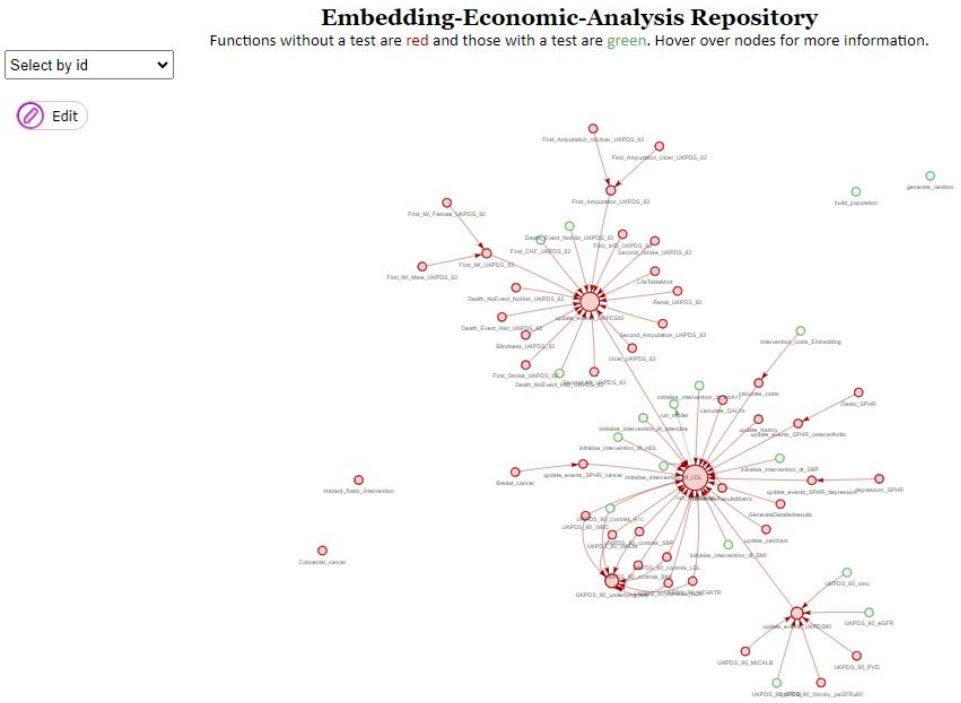
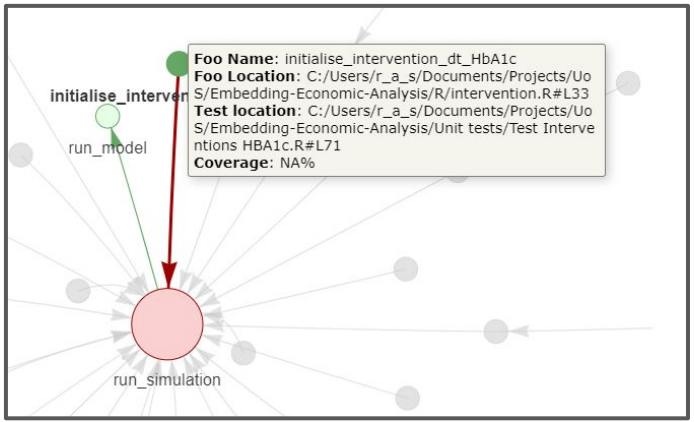
https://github.com/feralaes/cdx2cea

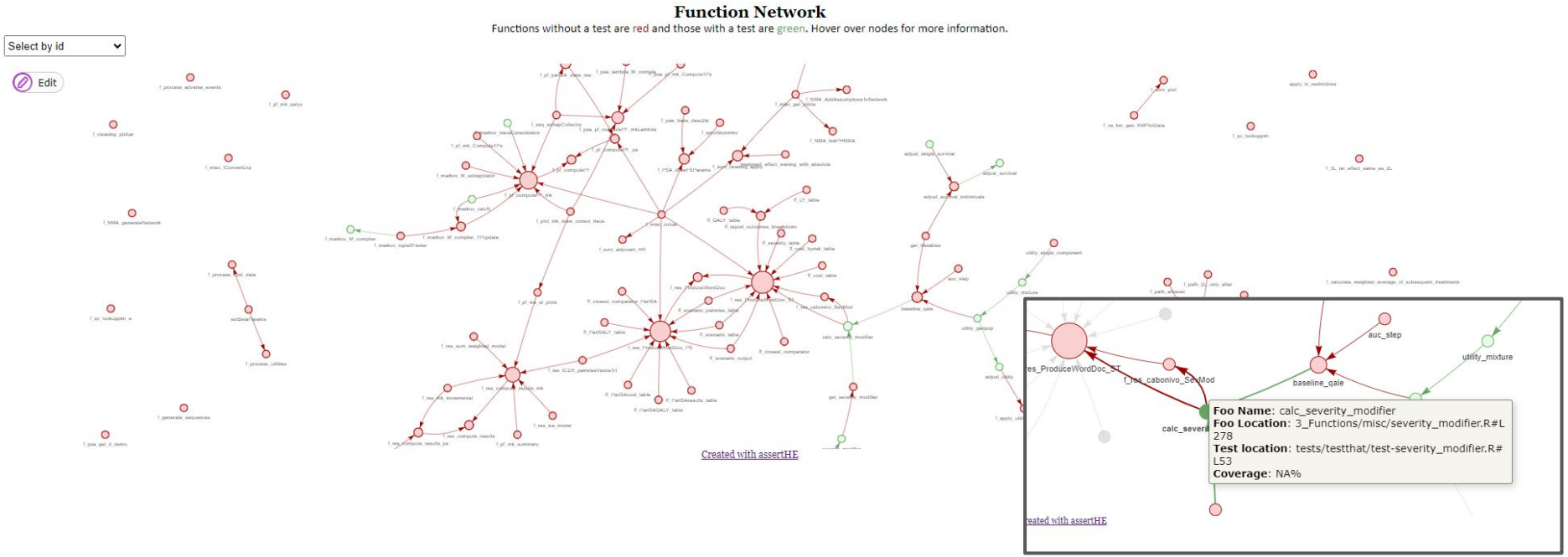
Case Study: Embedding Economic Analysis





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

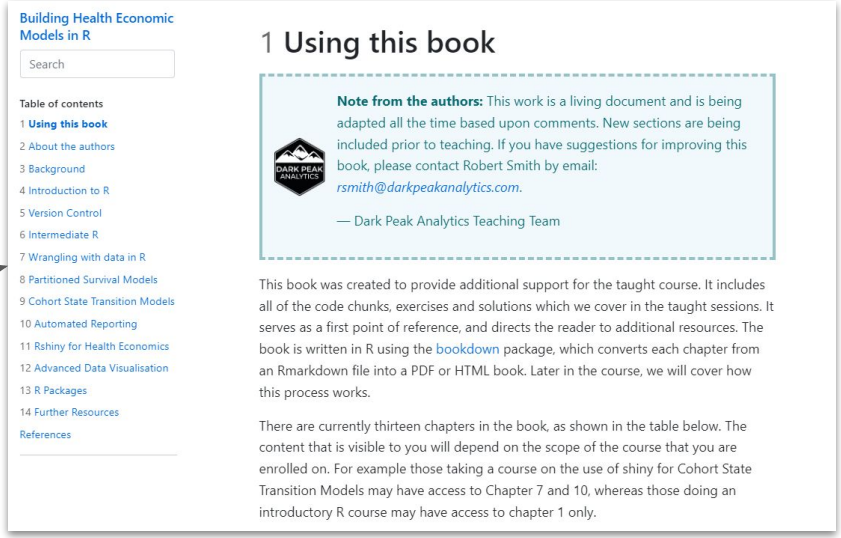
Case Study: NICE RCC Pilot



https://github.com/nice-digital/NICE-model-repo

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**



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

Open Access Publication

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

Wellcome Open Research

Authors

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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).

March 2023

Abstract

Background: Health economic evaluation models are increasingly used to inform decisions about the allocation of health care resources. Ensuring the robustness, reliability, and reproducibility of these models is critical. Currently, quality assurance is conducted by experts assessing the different components of the model manually in isolation and in combination. However, this is resource intensive. Understanding how the different components of the model fit together is time consuming, and testing each part of the model is sometimes not feasible under the timescales provided to reviewers. To aid in this, we propose the *assertHE* R package.

Methods:

The open source *assertHE* package provides testing functionality for modellers and reviewers of health economic models. It provides a series of common checks, which can be integrated into the model development workflow to reduce the probability of common errors. It also provides a suite of functions which allow users to better understand the network of algorithms (functions) contained in the model, where they are defined, if (and where) they are tested, and the test coverage of those that have.

Results: We applied the *assertHE* package to two health economic models, showing how to include the check functions within the model code and showing how to visualise a network of functions, see the test coverage, and obtain a Generative Pretrained Transformer (GPT) Large Language Model (LLM) generated summary of any function in the codebase. We have worked with collaborators from industry, regulators and academia to develop the package to be applicable to the widest possible range of models, making adaptations to the source code based upon feedback.

Conclusions: The assertHE R software package offers a toolkit for health economists building and reviewing models, facilitating a more robust and efficient quality assurance process. We hope this will ultimately improve the quality, transparency and efficiency of the health economic evaluation process for models built in R.

Key Words:

R, Health Economics, Unit Testing, Model Validation

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

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

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

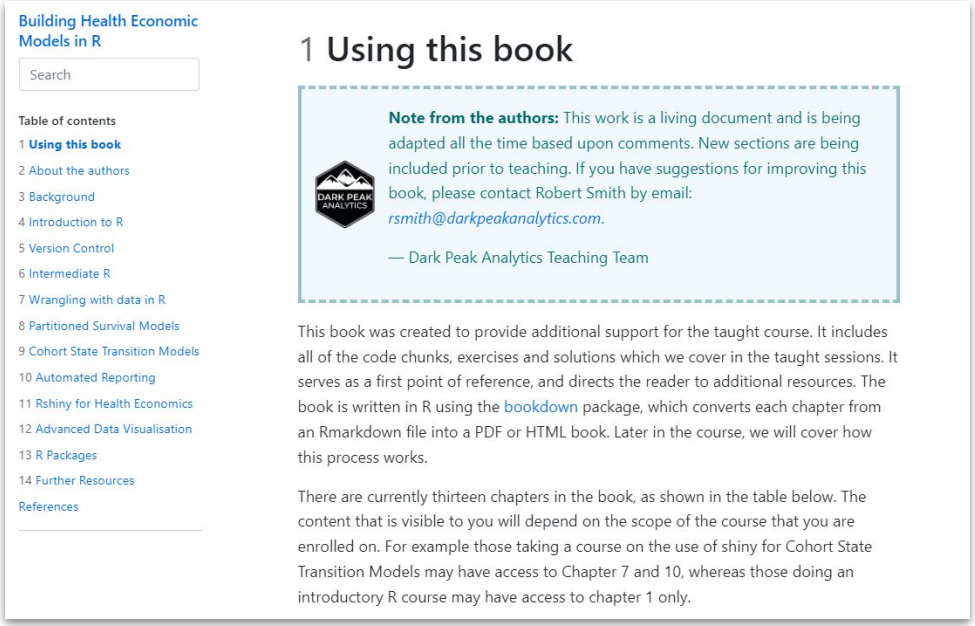
https://www.linkedin.com/company/dark-peak-analytics

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



[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/