

A large, diagonal photograph of a rugged, green mountain peak under a cloudy sky, with a stone wall and a sheep in the foreground.

# assertHE: HTA R model review

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



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

# Acknowledgements

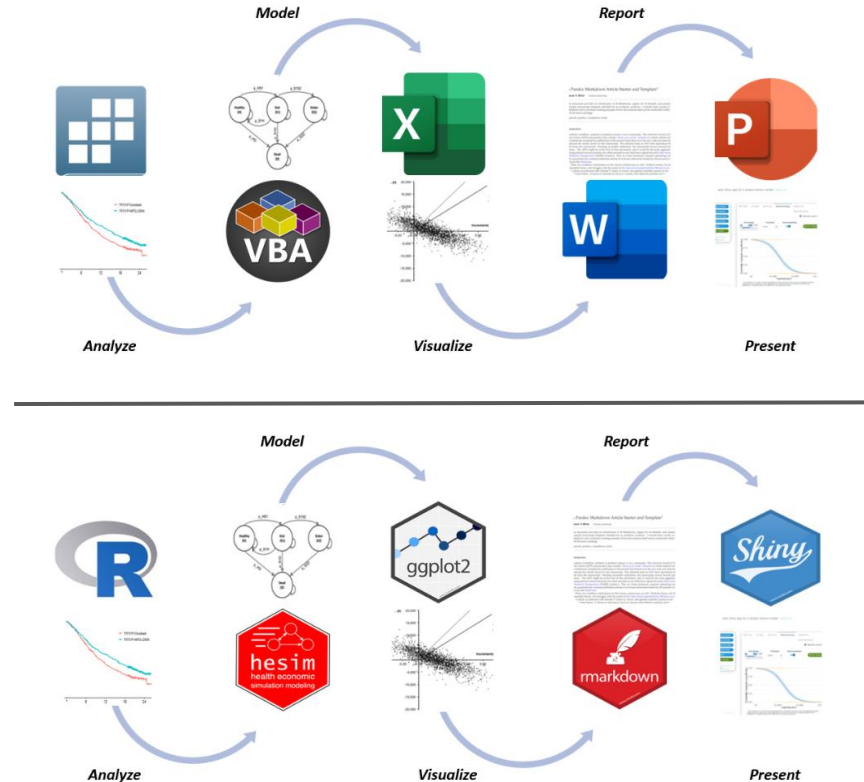
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# Overarching aim

*Shifting the HTA 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>)



# 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
print[" (%d %s %s)", C<<charW(__func__));
end;}
// (D)Scene C, scene)V暂停pare, clear();
// ModeV暂停pareG, mode();
// OnQueue(C, o); // PTM VparaPaG(ModeM+pare)(V+pareG(o)); // return;
// G=G-1;
if(a->type == ON_ARMATURE)
{ // 选择V2, 高LIB.resize(20);
Armature *arm = (Armature *)o->data; int i=0;
for(Object*o=o->c("o"), C; oG=o; Object*oV=o->c("v"), C; Object*oB=o->c("l-oB"), C)
{oB->c("l-oB"), C;
PassChannel *pcA=CTX_data_active_pose_bone(C), *pcC=NULL, *pcB=NULL;
if(pcAB&pcA->parent&pcA->parent->parent)
Object*oTarget=o->c("oTarget"), C; 无Vector T目标loc = loc(oTarget->obmat);
if(!("TypeOfIK", "PoseBone", pcA)!=1)return;
// 模式V暂停pare, ModeV暂停pareG[]];

```

```

65 year <- 0
66
67 #initialise the results matrix
68 results <- GenerateResultsMatrix(GlobalVars_, endtime_)
69 #initialise a PSA results matrix, if it is a PSA
70 if(GlobalVars_["run_psa"]=="T"){
71   psareresults <- matrix(data=NA, nrow = as.numeric(GlobalVars_["Number of cores"]), ncol = 1, byrow=T)
72 }
73
74 calculate_costs <- function(population_, parameters_, year_, alive_, GlobalVars_) {
75   #Discounted Costs per Patient
76   population_["DMCOST"][alive_] <- population_["MET1"][alive_] * parameters_["COST_MET1"] +
77     population_["MET2"][alive_] * parameters_["COST_MET2"] +
78     population_["INSU"][alive_] * parameters_["COST_INSU"]
79   while (year < endtime_ &
80         (sum(is.na(population_["F_ALLCAUSE"]))) >= 1){
81     #Cost of cardiovascular events
82     population_["IHD_E"][alive_] * parameters_["COST_IHD_E"] +
83     population_["IHD_H"][alive_] * parameters_["COST_IHD_H"] +
84     population_["MI_E"][alive_] * parameters_["COST_MI_E"] +
85     population_["MI_H"][alive_] * parameters_["COST_MI_H"] +
86     population_["MI2_E"][alive_] * parameters_["COST_MI2_E"] +
87     population_["MI2_H"][alive_] * parameters_["COST_MI2_H"]
88     #only add on the additional costs of a 2nd stroke
89     population_["STRO_E"][alive_] * parameters_["COST_STRO_E"] +
90     population_["STRO_H"][alive_] * parameters_["COST_STRO_H"]
91     population_["CHE_E"][alive_] * parameters_["COST_CHE_E"] +
92     population_["CHE_H"][alive_] * parameters_["COST_CHE_H"]
93   }
94   #Set a random number seed for parallel processing
95   #Calculate the fitted value
96   FV <- parameter_["CANB_mu"] + they have an event
97   parameter_["CANB_bta_MEN"] * population_["MEN"][alive_] +
98   parameter_["CANB_bta_BMI"] * population_["BMI"][alive_] +
99   parameter_["CANB_bta_BMIMEN"] * (population_["MEN"][alive_] + population_["BMI"][alive_])
100   #convert to probabilities
101   pBC <- 1-exp(-exp(FV))
102   #set breast cancer risk to 0 for men
103   pBC <- ifelse(population_["FEMALE"]==0,0,pBC)
104   #remove temporary variables generated in the function
105   rm(FV)
106   #return the probabilities
107   return(pBC)
108 }
109

```

```

58
59 population_["AGE"] <- floor(diag_diab_population_["CURR_AGE"])
60 population_["MEN"] <- replace(population_["MEN"], population_["AGE"] > 51 & population_["FEMALE"]==0, 1)
61 population_["HBA"] <- round(diag_diab_population_["HbA1c"],1)
62 #This has been kept the same as in the SPHR diabetes model
63 #Record the BMI of the population
64 #Set a random number seed for parallel processing
65 calculate_QALYs <- function(population_, parameters_, year_, alive_, GlobalVars_) {
66   #Calculate multiplier to adjust for a population with T2D without any history of diabetes
67   #Declare mean BMI, age and proportion female from Hayes et al
68   Mean_BMI_Hayes <- 28.4 #Mean BMI in the source of our baseline utilities
69   Mean_Age_Hayes <- 65.8
70   Mean_pFemale_Hayes <- 4729 / (6401+4729) #Source: Ali et al 2009
71   #Costs due to cardiovascular events
72   "COST_IHD_E" + is a parameter determining baseline utility, set these two variables to the time being
73   "COST_IHD_H" + is a parameter determining baseline utility, set these two variables to the time being
74   "COST_MI_E" + is a parameter determining baseline utility, set these two variables to the time being
75   "COST_MI_H" + is a parameter determining baseline utility, set these two variables to the time being
76   "COST_MI2_E" + is a parameter determining baseline utility, set these two variables to the time being
77   "COST_MI2_H" + is a parameter determining baseline utility, set these two variables to the time being
78   "COST_STRO_E" + is a parameter determining baseline utility, set these two variables to the time being
79   "COST_STRO_H" + is a parameter determining baseline utility, set these two variables to the time being
80   "COST_CHE_E" + is a parameter determining baseline utility, set these two variables to the time being
81   "COST_CHE_H" + is a parameter determining baseline utility, set these two variables to the time being
82   Util_b1_mult <- parameters_["UTIL_B1"]
83   (0.9454933+0.0256466*(1-Mean_pFemale_Hayes)+
84     0.00002213*Mean_Age_Hayes+
85     0.0000294*(Mean_Age_Hayes^2))
86   #Set a random number seed for parallel processing
87   #Calculate utility prior to adjusting for BMI and events
88   population_["EQ5D"][alive_] <- (0.9454933 +
89     0.0256466*population_["MALE"][alive_] +
90     0.00002213 * population_["AGE"][alive_] +
91     0.0000294 * (population_["AGE"][alive_]^2))
92   #apply the BMI decrements to this
93   population_["EQ5D"][alive_] <- population_["EQ5D"][alive_] +
94     parameters_["UTIL_B1"]*(population_["BMI"][alive_] - Mean_BMI_Hayes)
95   #Set up the cluster for parallel processing
96   #to all the events
97   registerDoParallel(cl)
98   clusterExport(cl, list("parameters_", "GlobalVars_", "random_nums_", "LifeTables_"))
99   modelresults <- parLapply(cl = cl,
100     X = parameters_,
101     Y = GlobalVars_,
102     Z = random_nums_,
103     LifeTables_ = LifeTables_)
104   stopCluster(cl)
105   if(GlobalVars_["Results_output", "Value"] == "Summary"){
106     modelresults <- matrix(unlist(modelresults), ncol=24, byrow=T)
107   }
108 }

```



- ☒ Build\_population.R
- ☒ Cancer\_Risks.R
- ☒ Costs.R
- ☒ Depression.R
- ☒ Generate\_Results\_Template.R
- ☒ Generate\_Results.R
- ☒ generate\_random.R
- ☒ intervention.R
- ☒ LifeTableMortality.R
- ☒ Oostoarthritis\_functions.R
- ☒ QALYs.R
- ☒ Run\_model.R
- ☒ Run\_simulation.R
- ☒ UKPDS\_82\_risk\_functions.R
- ☒ UKPDS\_90\_risk\_functions.R
- ☒ UTIL\_B1\_mult.R
- ☒ Update\_Events.R
- ☒ Update\_Pat\_Chars.R





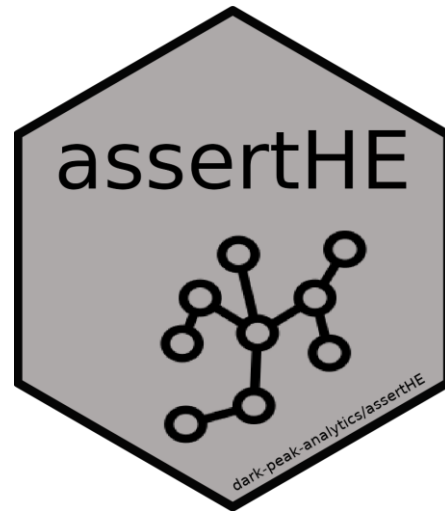
# The software

# assertHE R package

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

Functionality:

- *Check that the objects created in models conform to standard rules (e.g. probabilities between 0 and 1).*
- *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)
```

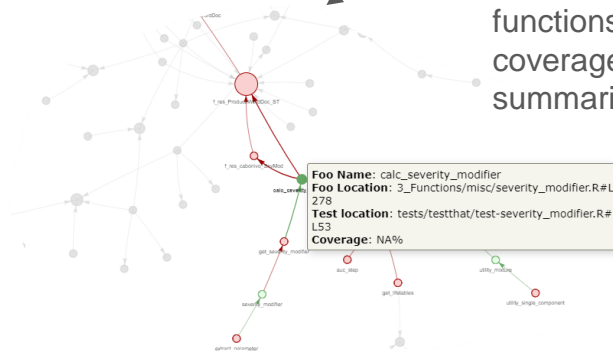
B: insert checks for common errors into the code

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

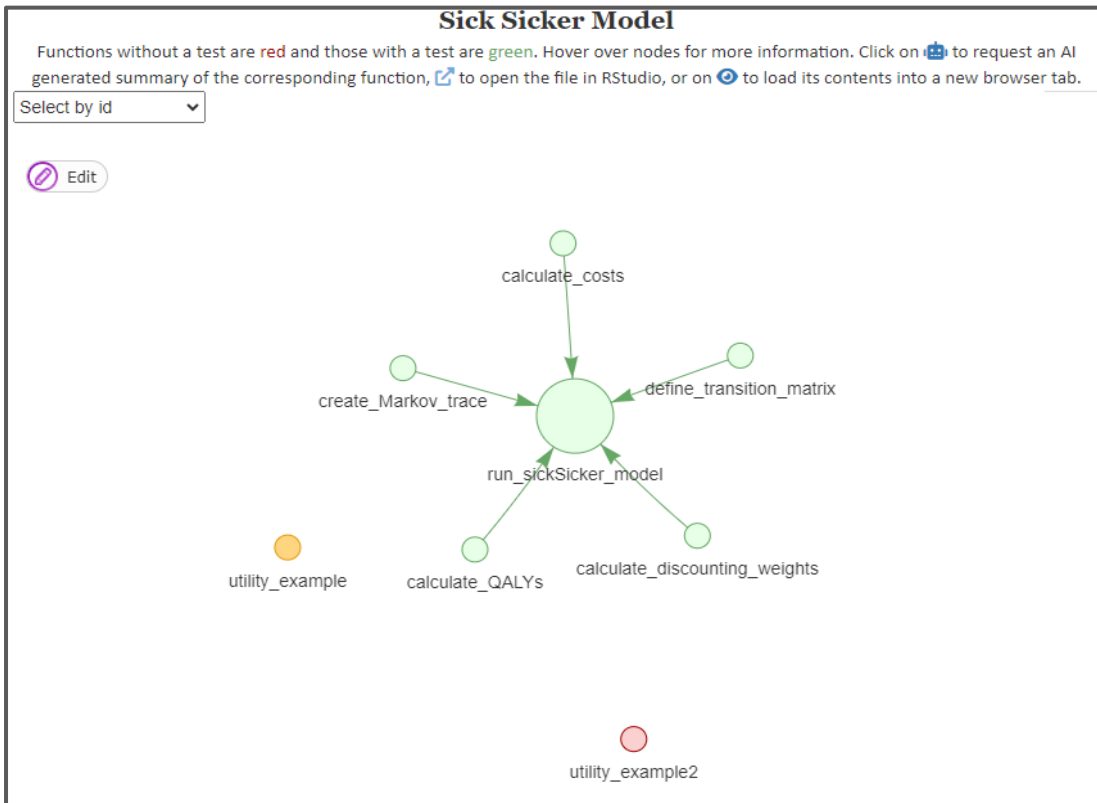
Flags if there are errors or potential problems.

```
# 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.






# Using the *assertHE* R package



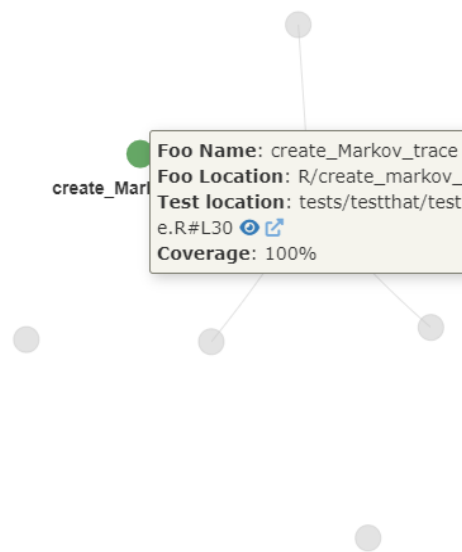
# Using the *assertHE* R package


## 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



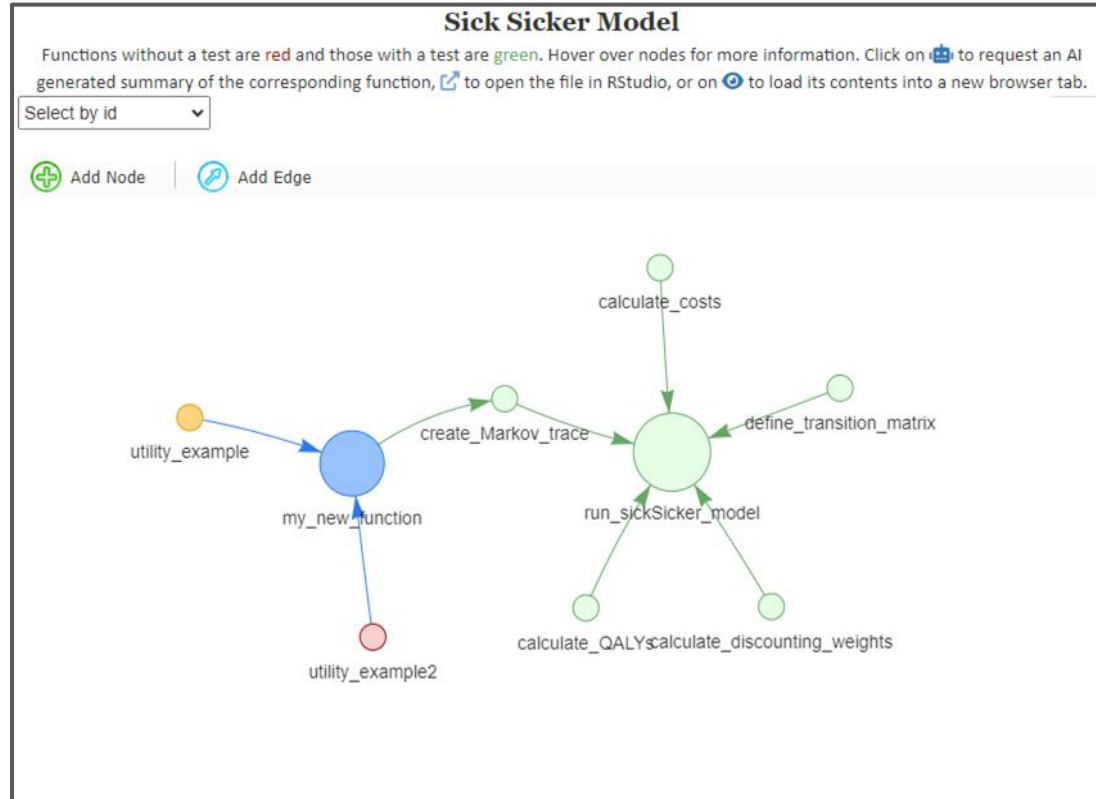
**Foo Name:** create\_Markov\_traci 

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

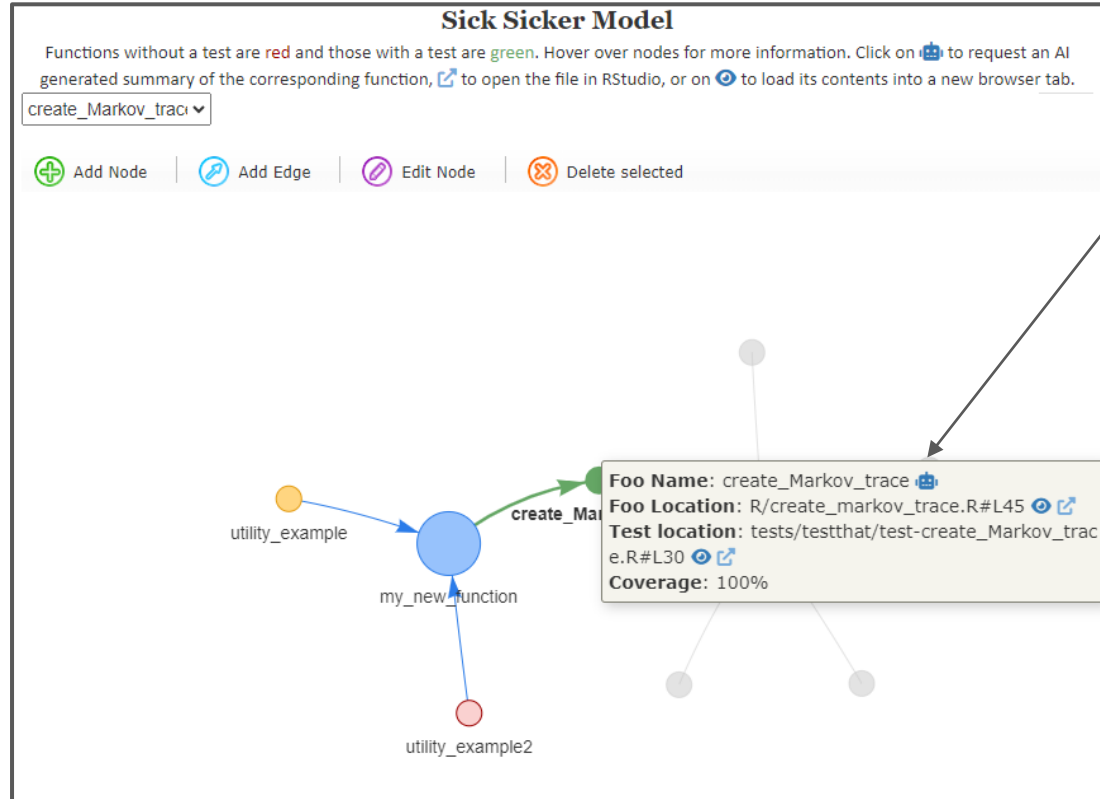
**Test location:** tests/testthat/test-create\_Markov\_trace.R#L30  

**Coverage:** 100%

# Using the *assertHE* R package



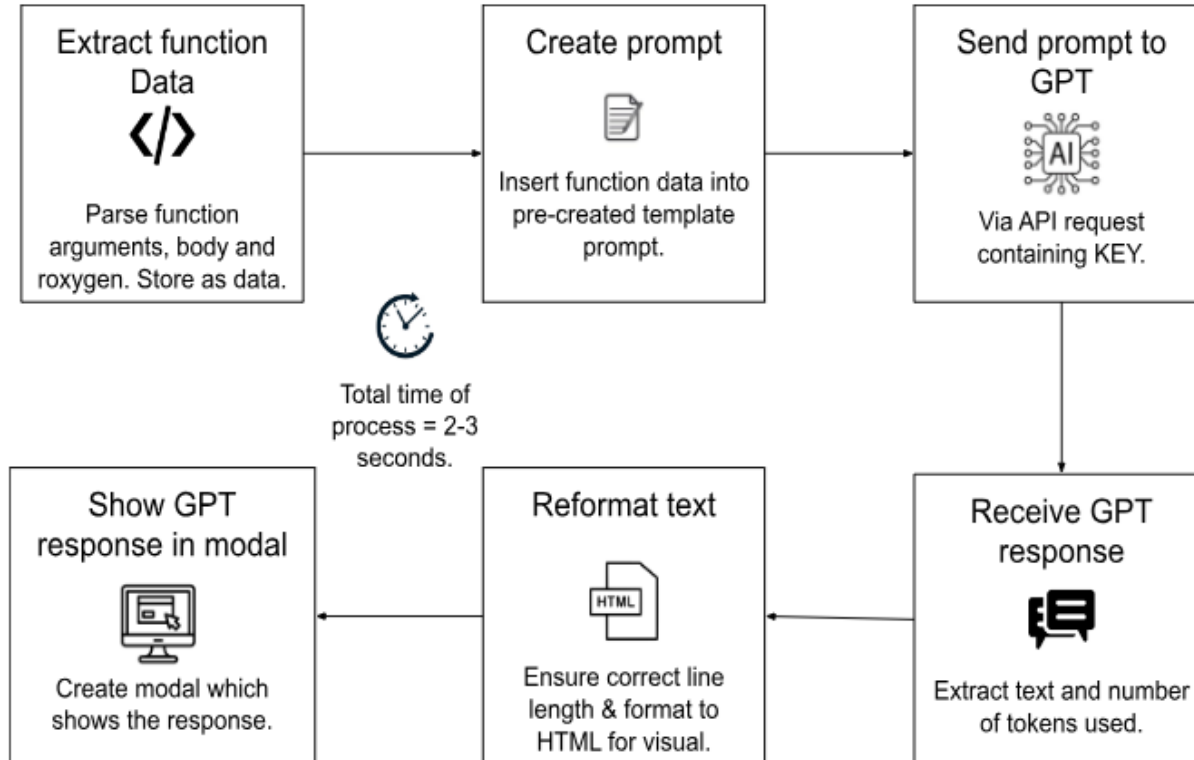
# Using the *assertHE* R package



Generate LLM  
summary of  
function.






# Using the *assertHE* R package




# Using the *assertHE* R package

## 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.

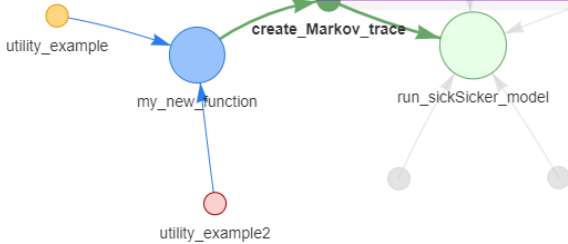
create\_Markov\_trace

 Edit

**AI summary - create\_Markov\_trace** ✖

The 'create\_Markov\_trace' function takes in a transition matrix, time horizon, state names, and initial trace as arguments. It first checks that the state names are of class character and the initial trace is of class numeric. It also validates that the lengths of state names and initial trace match, and that the dimensions of the transition matrix are consistent with the number of states.

The function then creates a Markov trace matrix with the specified time horizon and state names. It populates the initial trace in the first row of the matrix and calculates subsequent trace rows by multiplying the previous row with the transition matrix. Finally, the function returns the Markov trace matrix.



```

graph TD
    utility_example((utility_example)) --> my_new_function((my_new_function))
    utility_example2((utility_example2)) --> my_new_function
    my_new_function --> create_Markov_trace((create_Markov_trace))
    create_Markov_trace --> run_sickSicker_model((run_sickSicker_model))
    node1(( )) --> run_sickSicker_model
    node2(( )) --> run_sickSicker_model
    style utility_example fill:#f96
    style utility_example2 fill:#f99
    style my_new_function fill:#99f
    style create_Markov_trace fill:#9f9
    style run_sickSicker_model fill:#9f9
    style node1 fill:#ccc
    style node2 fill:#ccc
        
```



# 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.

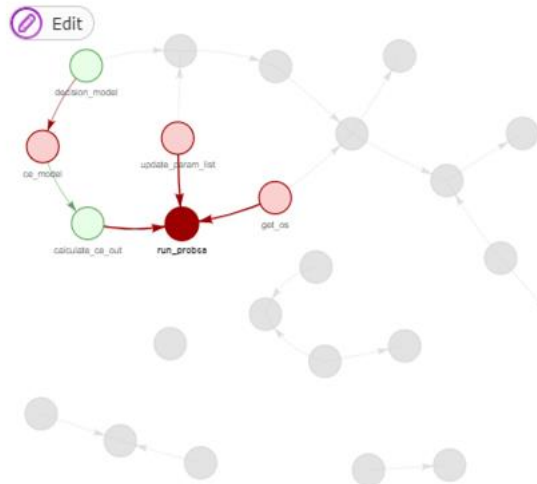
run\_probsa

### AI summary - run\_probsa

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, the function returns a list containing the costs and effects data frames.

...



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journal homepage: [www.elsevier.com/locate/jco](http://www.elsevier.com/locate/jco)

### Economic Evaluation

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

Fernando Alvarado-Figueroa, PhD, Deborah Schrag, MD, MPH, Karen M. Kuntz, ScD

### ABSTRACT

**Objective:** Adjuvant chemotherapy is not recommended for patients with average-risk stage II (T4N0) 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 60-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 \$80,991 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.

**Conclusion:** 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 (T4N0) colon cancer.<sup>1</sup> And thus, these patients are usually treated with surgery alone.<sup>2</sup> Nevertheless, a recent study by Dalerba 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 tissues. 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 (<https://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 660 (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>

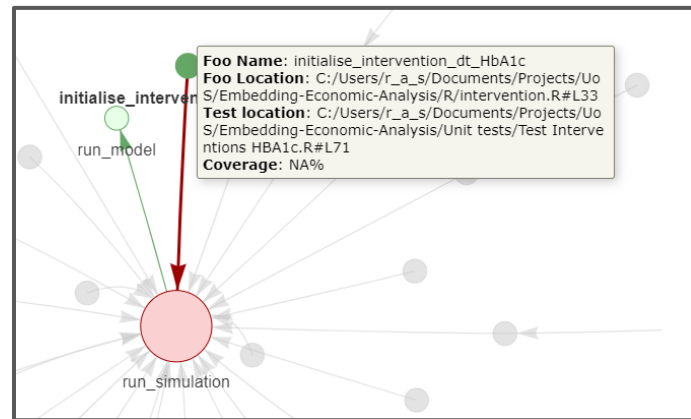
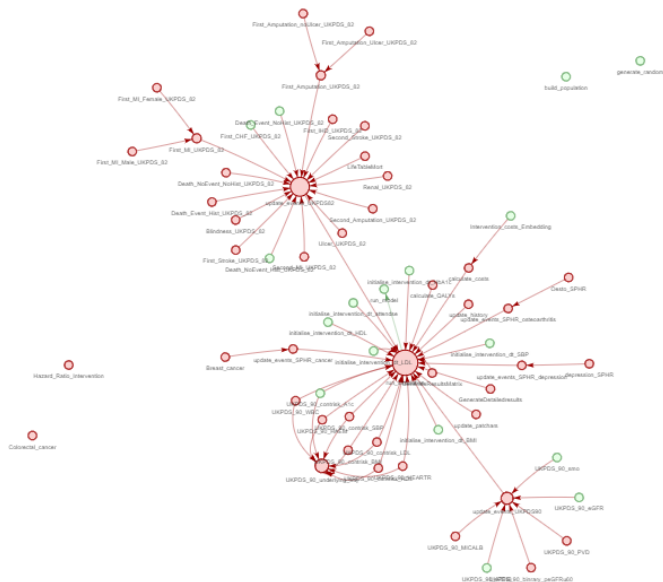
This study aims to quantify the long-term benefits, costs, and cost-effectiveness of testing average-risk patients with stage II colon cancer for the absence of CDX2 biomarker expression followed

# 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.

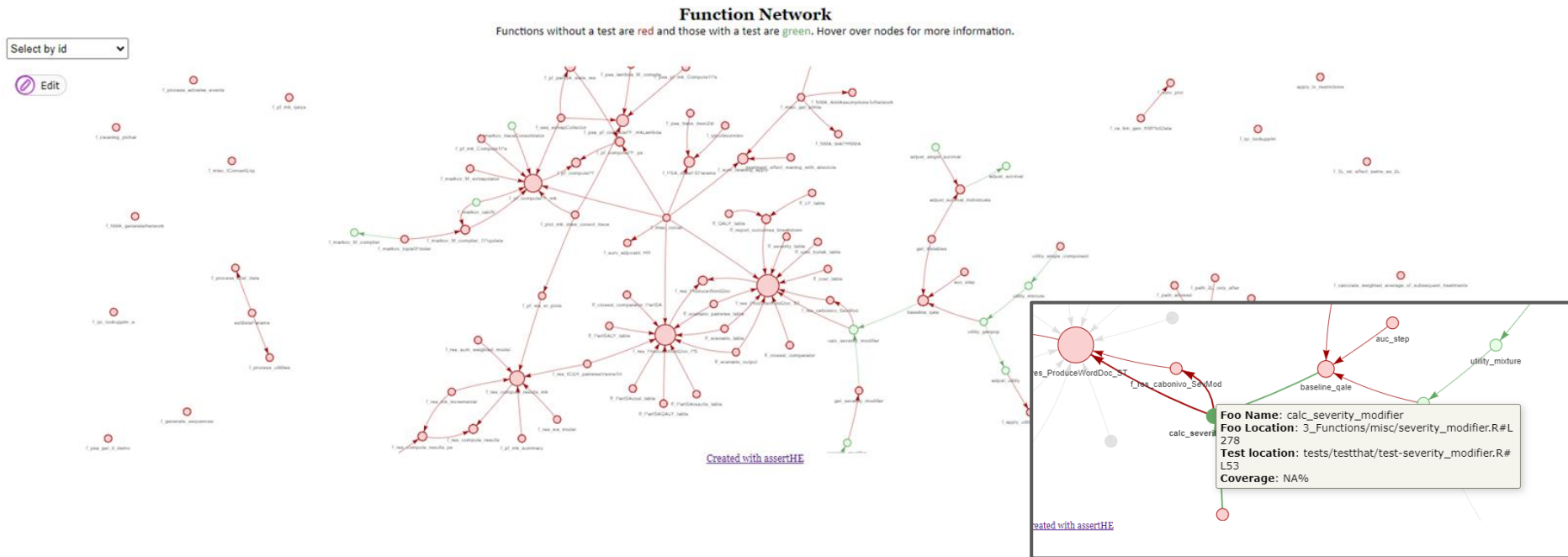
Select by id ▼



Created with assertHE

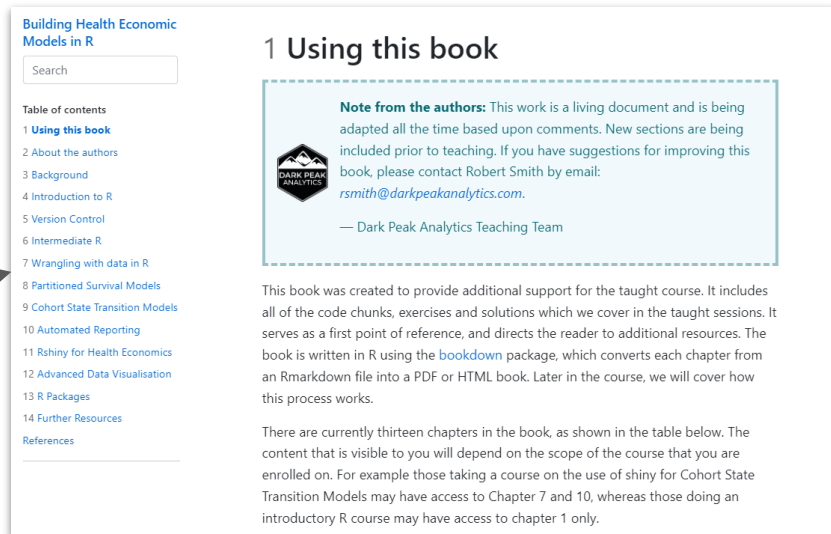
<https://github.com/DanPollardSheff/Embedding-Economic-Analysis>

# Case Study: NICE RCC Pilot



# Next steps

1. Welcome contributions
  - a. Testing the software on your models
  - b. Suggesting improvements (see contribution page on GitHub)
2. Future development:
  - a. LLM Chatbot integration (using DPA teaching material to fine-tune).
  - b. Language selection (in progress)
3. Open access publication + CRAN submission (Summer 24)

A screenshot of a web browser showing the first chapter of a book. The page title is "Building Health Economic Models in R". On the left is a "Table of contents" with 14 items, where "1 Using this book" is highlighted in blue. An arrow points from item 2a in the list on the left to the "Using this book" chapter. The main content area shows the start of "1 Using this book", including a "Note from the authors" in a light blue box with a dashed border, a small "DARK PEAK ANALYTICS" logo, and contact information for Robert Smith. Below this is a paragraph about the book's purpose and a paragraph about access to different chapters based on the course.



# Open Access Publication

1  
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**asserTHE**: an R package to improve quality assurance of health economic models

Wellcome Open Research

## Authors

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- Brett McQueen (University of Colorado at Denver)
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- 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

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

# assertHE: HTA R model review

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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

## Building Health Economic Models in R

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## 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.

[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/>