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| **A Pathway Pilot Appraisal**  **Instructions for using the Exeter Oncology Model: RCC edition** | | |
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List of Abbreviations

|  |  |
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| Acronym | Definition |
| ACIC | Academic and commercial in confidence |
| CIC | Commercial in confidence |
| cPAS | Confidential patient access scheme |
| FAD | Final appraisal document |
| HTA | Health technology assessment |
| IPD | Individual participant data |
| NICE | National Institute for Health and Care Excellence |
| NMA | Network meta-analysis |
| PartSA | Partitioned-survival analysis |
| PenTAG | Peninsula Technology Assessment Group |
| PFS | Progression free survival |
| RCC | Renal cell carcinoma |
| RWE | Real world evidence |
| TTD | Time to treatment discontinuation |
| TTP | Time to progression |
| UK | United Kingdom |
| URL | Uniform Resource Locator |

# Using the R decision model

The Exeter Oncology Model: RCC edition which was produced by PenTAG as part of the NICE pathways pilot (ID6186 and ID6184) has been built in R with an Excel front end. R was ideal for this model due to its ability to handle the extensive computations required. With 744 potential treatment sequences across various populations, the model efficiently executed block-diagonal sparse matrix multiplications for sequencing calculations. This would be infeasible to implement efficiently in Excel. Unfortunately, we were not able to add a graphical user-interface in the timeframes available for the model build; instead, we built the front-end in Excel allowing the stakeholders a familiar and flexible means to interact with it.

The model extracts all inputs directly from Excel, separating all sensitive data and inputs from the code. Consequently, no confidential information is contained in the code.

## Input files

There are a number of files which contain raw or intermediate inputs:

1. The Excel user interface - contains user input sheets with different model inputs which feeds into R tables (named in excel as R\_table…) and subsequently being read by the R program. The version available to the public does not contain confidential company data, confidential price discounts or company individual patient data and treatment sequence data. The model does now contain UK real-world evidence (RWE) data which was redacted at the time of the appraisal at the request of the UK real-world evidence (RWE) data holders.

2. The proportional hazards NMA CODA RDS file; note the version of this using time to next treatment as a surrogate for nivolumab plus ipilimumab is not available to the public as this data was marked as confidential by the data holders.

3. The fractional polynomials NMA RDS file; note the version of this using time to next treatment as a surrogate for nivolumab plus ipilimumab is not available to the public as this data was marked as confidential by the data holders.

4. The raw data file containing the pseudo-IPD for all trials for survival analysis (in the publicly available version data has been simulated to replaced data considered confidential by either the UK RWE dataholders or involved companies); or

5. The RDS output from the survival analysis using company data (in the publicly available version TTD and TTP are set equal to PFS in order to protect data considered confidential by the involved companies) and PPS is set equal to the UK RWE.

These files are contained within the data folder in the github repository.

## Software required to run the code

Before using the code make sure you have installed:

* R (Version 4.3 or higher)
* RStudio
* Rtools
* Git

## Running the model

### Amending inputs

If you would like to amend inputs you should do this in the Excel front end file. Use the cells and drop-down menus provided. The way the model works is that inputs / tables which are named with “R\_” are extracted by the R code and used to populate the R model. We would recommend the user avoid adding columns or rows to the Excel file as this may change the format of the tables being pulled into R in ways that break the code. Instead, please use the input cells provided.

R will always use the version of the front end named “ID6184\_RCC\_model inputs FAD version [ACIC redacted, cPAS redacted and CIC redacted]” saved in folder 1.Data on your local computer. If there is no version with that name saved in there it will instead ask you to select the file to use for inputs.

### Accessing the R code

To access the code simply click the [link](https://github.com/nice-digital/NICE-model-repo) and go to the ID6184 model branch:

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There are 2 methods available to interact with the model and make any comments on the code: using Git or by downloading the model to your local machine. If you wish to use Git instructions are provided in the section on accessing the code via Git.

The main code to run the model is contained in folder 2\_Scripts in the Model\_Structure.R file.

### Installing packages

First you will need to make sure you have installed all the relevant packages on lines 6 to 28 of the code. Use ctrl+shift+C to uncomment and uncomment lines and ctrl+enter to run a line or a group of highlighted lines. You only need to do this once and then should recommend the lines.

### How to run the model

Once you have done this you can run the entire model using the Source button in R studio or by pressing ctrl+shift+S or you can run parts of the model by highlighting and using ctrl+enter.

When run, the model will:

* Extract cost, resource use, utility, relative effectiveness and treatment sequence settings inputs from Excel front-end
* Compute possible treatment sequences for each population
* Either load patient level data and conduct survival analyses or load the pre-run survival analysis
* Load network meta-analyses
* Populate and propagate relative efficacy network for all treatments at all lines
* Compute patient flow for all possible sequences at all possible lines and apply cost and utility weights
* If you have set the model up to look at the cabo+nivo decision problem: compute weighted average patient flow by first-line treatment and calculate the impact of patient access schemes (confidential discounts on the published list price) in increments of 1 from 1 to 100% for all treatments
* Output results as files to store and as a fully automated Word document following formatting requirements for NICE

### Model structure

Previous appraisals in RCC highlighted issues with subsequent treatments in trials not being available in UK practice and difficulties in matching cost and effectiveness data when trying to compensate. Consequently, we built a state transition model with tunnel states to incorporate time-dependency at later lines. This approach simplified incorporation of the sequencing features which arose within the scope of the pilot. For prudence, we incorporated a partitioned-survival (PartSA) modelling approach in parallel. This allowed comparison with models following implementation precedent in advanced RCC evaluations.

You can change which model structure is run using the drop down menu on the Controls sheet in the Excel front end.

### Model run time

The runtime for the full state transition model is around 90 processor-minutes. This simulates hundreds of treatment pathways for tens of thousands of health states for thousands of time cycles for each pathway. By contrast, the PartSA version of the model takes less than 5 minutes, though without addressing any of the issues of that approach.

### Future versions

The publicly accessible version of the model aligns with the final appraisal determination produced for NICE appraisal ID6184: Cabozantinib with nivolumab for untreated advanced renal cell carcinoma.

Additional changes were originally planned following use for the initial decision problem including:

* Addition of Shiny user interface
* Genericisation of the code to allow wider use as the Exeter Oncology Model is not fundamentally specific to RCC and could be adapted to any oncology indication
* Programming and analysis of model outputs related specifically to sequencing, this may include value of information analyses

Unfortunately funding for this has not been confirmed currently. If you are interested in discussing further development, please contact the PenTAG team at [pentag@exeter.ac.uk](mailto:pentag@exeter.ac.uk).

## Accessing the code via Git (version control)

To access the model using Git the easiest method is to create a new project in RStudio which links to the NICE github website.

Simply click New Project in the right hand of your RStudio screen:



Then Version Control

A screenshot of a software project

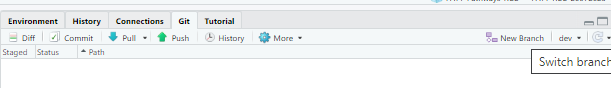
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Then Git

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Paste in the URL of the NICE repository: <https://github.com/nice-digital/NICE-model-repo> in the repository URL and decide where you want the project to be saved on your computer using the Browse functionality. All of your team can access the code then in the same way. If there is more than one branch of code available as the model is updated you can select what branch of the code to look at on the top right of your screen.



## Accessing the code by downloading the model

If you do not wish to access the model via Git you can instead download the code and run the model on your local machine either using RStudio or R.

To do this click the Code button and then Download ZIP:

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Extract the zip file to wherever on your machine you want to store the model. We would suggest saving it somewhere other than the Downloads folder.

Open Rstudio and press File then New Project:

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Click Existing Directory

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Click on the folder where you have saved the model. Make sure you click fully through until you can see the sub folders.

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Then press Open and then Create Project.

## License

The model is provided under an MIT License as follows:

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