

Health policy model with R

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Motivation:

what is a health policy model?

A health policy model is a tool to inform policy decisions by projecting people's life courses. Predictions include

- disease events
- life expectancy
- quality of life
- healthcare costs
- effects of treatments
 - positive (disease risk reduction) and negative (adverse effects)

Projections made over long time periods (eg lifetime)



Motivation:

why are health policy models needed?

Healthcare budgets are limited and not all treatments can be recommended even if effective

- Models show whether treatments are good value for money
- Health policy models are increasingly used by policy makers and clinicians
- In UK, cost-effectiveness analyses are required by NICE
 - Good-value-for-money: £20-30K per additional quality-adjusted life-year (QALY)
- Flexible models can help answer many policy questions
- Aim for transparency, reliability, reproducibility and usability



Case study: SHARP CKD-CVD model

Background

- Chronic kidney disease (CKD) increases cardiovascular (CV) risk
- Want to project long-term outcomes in CKD
 - cardiovascular events, CKD progression, life expectancy, quality of life, healthcare costs;
 - enable implementation of treatments to reduce cardiovascular risk
 - assess long-term effects and cost-effectiveness.
- Patient-level data from a trial
 - baseline characteristics, within-trial events
- Risk equations derived from the data
- Combined into a Markov model to do lifelong projections
 - validated internally and externally



SHARP CKD-CVD model:

Computational challenges and solutions

- Due to complex structure (68 states), initial run on 10,000 patients took **>24 hours** even without uncertainty.
- Ways to optimise the algorithm:
 - Parallel programming across patients
 - Reducing size of transitional matrices
 - Remove rows corresponding to disallowed transitions / starting states (as opposed to setting them to 0)
- Only basic R functionality was used
 - 9 packages: data manipulation (reshape2, plyr, data.table); parallel programming (foreach, snowfall, doSNOW); plotting and saving (xtable, scales, ggplot2)
 - No specific CEA packages (hence fine-tuning possible)
- Simple tinkering reduced the time to **50 minutes**



SHARP CKD-CVD model: need for a user-friendly interface

- The model to be useful for NICE, other analysts, clinicians...
- User-friendly interface accessible from anywhere
- No need for knowledge / installation of R
- Adaptation to other scenarios/countries
 - national mortality rates
 - national healthcare costs
- Customising parameters in the current setting
 - treatment to be assessed
 - population characteristics
 - duration of treatment / time horizon
 - discount rate



SHARP CKD-CVD model: Shiny interface

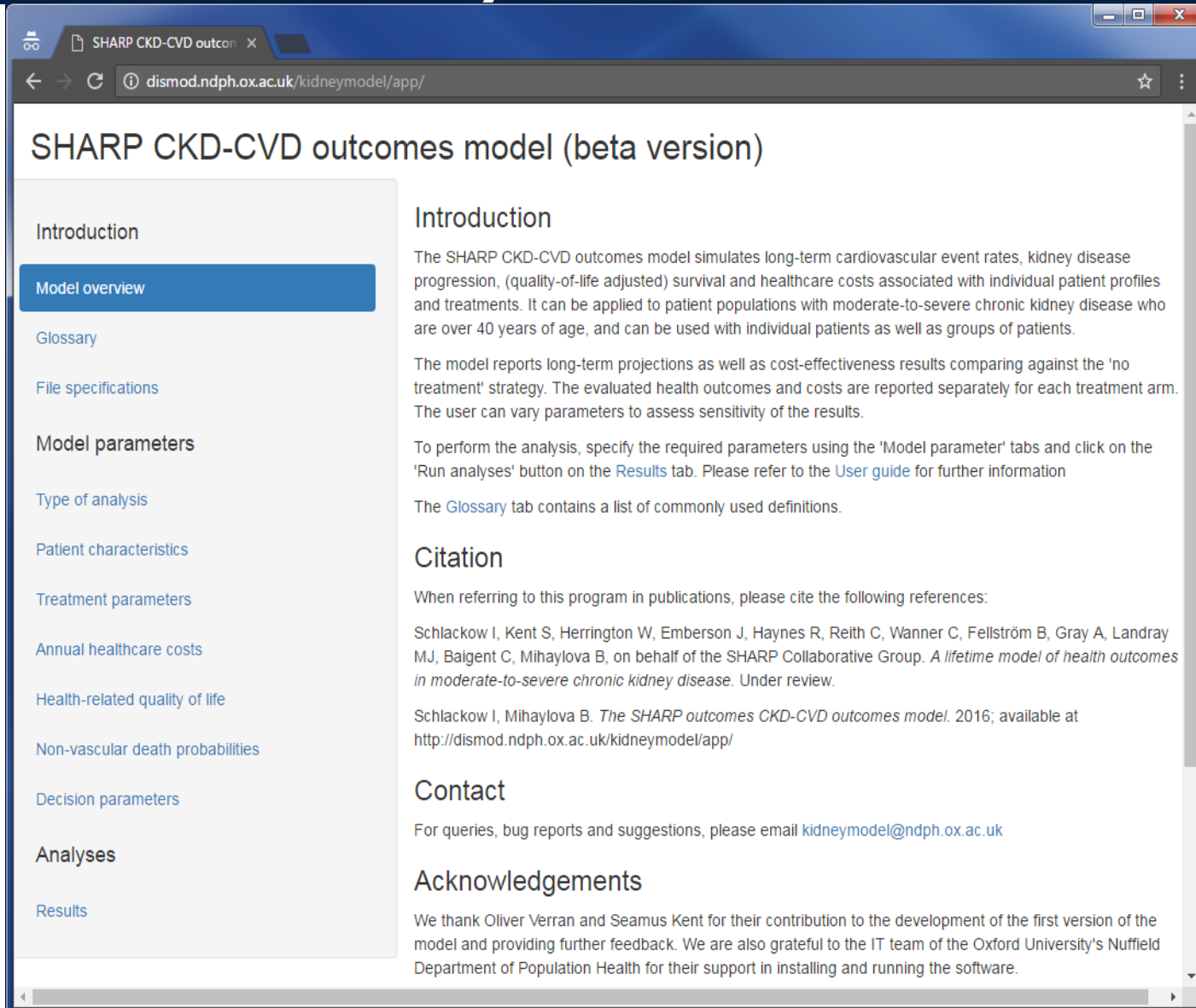


<http://one-elevenbooks.com/shiny-or-the-truth/>

- Application accessed via a link
- The user only sees the front end
- All programs/data stored externally
- The front end can be modified using CSS themes, htmlwidgets, and JavaScript actions
 - fancy fonts, links, email addresses etc
 - error checking on data entry

<http://dismod.ndph.ox.ac.uk/kidneymodel/app/>

SHARP CKD-CVD model: Shiny interface



The screenshot shows a web browser window with the address bar displaying `dismod.ndph.ox.ac.uk/kidneymodel/app/`. The page title is "SHARP CKD-CVD outcomes model (beta version)". On the left, a sidebar contains a list of navigation links: "Introduction", "Model overview" (highlighted in blue), "Glossary", "File specifications", "Model parameters", "Type of analysis", "Patient characteristics", "Treatment parameters", "Annual healthcare costs", "Health-related quality of life", "Non-vascular death probabilities", "Decision parameters", "Analyses", and "Results". The main content area is titled "Introduction" and contains the following text:

The SHARP CKD-CVD outcomes model simulates long-term cardiovascular event rates, kidney disease progression, (quality-of-life adjusted) survival and healthcare costs associated with individual patient profiles and treatments. It can be applied to patient populations with moderate-to-severe chronic kidney disease who are over 40 years of age, and can be used with individual patients as well as groups of patients.

The model reports long-term projections as well as cost-effectiveness results comparing against the 'no treatment' strategy. The evaluated health outcomes and costs are reported separately for each treatment arm. The user can vary parameters to assess sensitivity of the results.

To perform the analysis, specify the required parameters using the 'Model parameter' tabs and click on the 'Run analyses' button on the [Results](#) tab. Please refer to the [User guide](#) for further information

The [Glossary](#) tab contains a list of commonly used definitions.

Citation

When referring to this program in publications, please cite the following references:

Schlackow I, Kent S, Herrington W, Emberson J, Haynes R, Reith C, Wanner C, Fellström B, Gray A, Landray MJ, Baigent C, Mihaylova B, on behalf of the SHARP Collaborative Group. *A lifetime model of health outcomes in moderate-to-severe chronic kidney disease*. Under review.

Schlackow I, Mihaylova B. *The SHARP outcomes CKD-CVD outcomes model*. 2016; available at <http://dismod.ndph.ox.ac.uk/kidneymodel/app/>

Contact

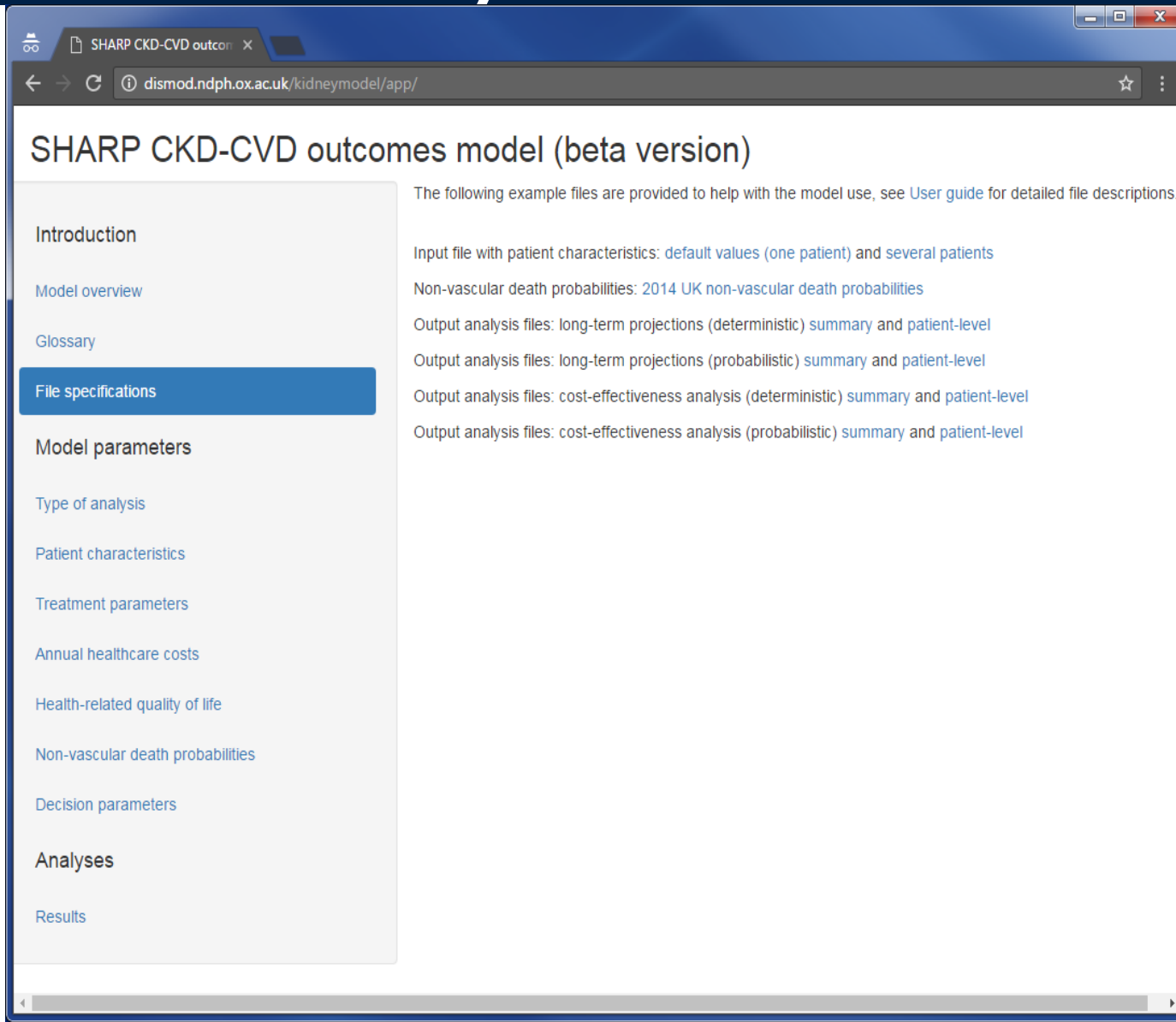
For queries, bug reports and suggestions, please email kidneymodel@ndph.ox.ac.uk

Acknowledgements

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SHARP CKD-CVD model: Shiny interface



The screenshot shows a web browser window with the address bar displaying `dismod.ndph.ox.ac.uk/kidneymodel/app/`. The page title is "SHARP CKD-CVD outcomes model (beta version)". On the left, a sidebar menu lists various sections: Introduction, Model overview, Glossary, File specifications (highlighted in blue), Model parameters, Type of analysis, Patient characteristics, Treatment parameters, Annual healthcare costs, Health-related quality of life, Non-vascular death probabilities, Decision parameters, Analyses, and Results. The main content area, under the "File specifications" section, provides a list of example files for model use, with a reference to the "User guide" for detailed descriptions. The files listed are: "Input file with patient characteristics: default values (one patient) and several patients", "Non-vascular death probabilities: 2014 UK non-vascular death probabilities", "Output analysis files: long-term projections (deterministic) summary and patient-level", "Output analysis files: long-term projections (probabilistic) summary and patient-level", "Output analysis files: cost-effectiveness analysis (deterministic) summary and patient-level", and "Output analysis files: cost-effectiveness analysis (probabilistic) summary and patient-level".

SHARP CKD-CVD outcomes model (beta version)

The following example files are provided to help with the model use, see [User guide](#) for detailed file descriptions.

Input file with patient characteristics: [default values \(one patient\)](#) and [several patients](#)

Non-vascular death probabilities: [2014 UK non-vascular death probabilities](#)

Output analysis files: long-term projections (deterministic) [summary](#) and [patient-level](#)

Output analysis files: long-term projections (probabilistic) [summary](#) and [patient-level](#)

Output analysis files: cost-effectiveness analysis (deterministic) [summary](#) and [patient-level](#)

Output analysis files: cost-effectiveness analysis (probabilistic) [summary](#) and [patient-level](#)

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SHARP CKD-CVD outcomes model (beta version)

Introduction

Model overview

Glossary

File specifications

Model parameters

Type of analysis

Patient characteristics

Treatment parameters

Annual healthcare costs

Health-related quality of life

Non-vascular death probabilities

Decision parameters

Analyses

Results

Type of analysis

Long-term projections

Long-term projections

Cost-effectiveness analysis

Include uncertainty?

No (deterministic analysis)

SHARP CKD-CVD model:

Shiny interface

SHARP CKD-CVD outcomes model (beta version)

Select characteristics for a single patient or import a text file with these characteristics for one or more patients.

☐ Import a file with patient characteristics


Reset inputs

Demographic and socio-economic characteristics

Age (years) 65	Gender Female	Ethnicity White
Highest educational attainment Any post-secondary education	Adult dependants No	Smoking status Never smoked
Alcohol drinker No	Body mass index 25-29 kg/m ²	

Clinical factors

Diastolic blood pressure 75-84 mmHg	Systolic blood pressure 130-149 mmHg	HDL cholesterol 0.9-1.1 mmol/L
Albumin 3.9-4.1 g/dL	Haemoglobin 11.6-12.9 g/dL	Phosphate 1.2-1.4 mmol/L
Urinary albumin:creatinine ratio 30-300 mg/g		



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The main content area has the heading "Select characteristics for a single patient or import a text file with these characteristics for one or more patients." Below this is a checkbox labeled "Import a file with patient characteristics" which is checked. There are two buttons: "Browse..." and "example_input_data_error.csv". Below these is a blue button labeled "Upload complete".

Below the buttons, a red error message is displayed:

The model cannot be executed. Please check the following conditions:
The following columns are missing: ethnicity
The following columns are in the wrong format: smoker (needs to be numeric)
The following columns contain disallowed values: age (age column can only take values between 40 and 90); sex (sex column can only take values 0, 1); DM (DM column can only take values 0, 1. Participants with diabetic nephropathy should be marked as having diabetes); CKDDuration (CKDDuration column values should be between 0 and the participant's age)

SHARP CKD-CVD model: Shiny interface

SHARP CKD-CVD outcomes model (beta version)

Hazard ratios should correspond to full compliance with treatment for each of the outcomes below. The rates should be on the exponential scale.

[Reset inputs](#)

Treatment effects

Treatment effects for the probabilistic sensitivity analyses are sampled from log-normal distributions using the correlation matrix from the SHARP study. Enter the estimates for the hazard ratios together with the 95% confidence interval (CI) on the exponential scale.

Cardiovascular death

Hazard ratio	Lower 95% CI	Upper 95% CI
<input type="text" value="0.9"/>	<input type="text" value="0.8"/>	<input type="text" value="1"/>

Cardiovascular death or non-fatal major atherosclerotic event

Hazard ratio	Lower 95% CI	Upper 95% CI
<input type="text" value="0.9"/>	<input type="text" value="0.8"/>	<input type="text" value="1"/>

Cardiovascular death or non-fatal major vascular event

Hazard ratio	Lower 95% CI	Upper 95% CI
<input type="text" value="0.9"/>	<input type="text" value="0.8"/>	<input type="text" value="1"/>

Compliance (%)

Daily treatment cost (full use)

Introduction

Model overview

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Health-related quality of life

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SHARP CKD-CVD model: Shiny interface

SHARP CKD-CVD outcomes model (beta version)


The default values are based on SHARP data and UK 2014 prices.

[Reset inputs](#)

The default costs for the probabilistic sensitivity analyses are derived from the SHARP data using the bootstrap method. To provide alternative costs, enter the means and the standard errors below, and the costs will be sampled from gamma distributions. The displayed values are based on SHARP data and UK 2014 prices [1].

Annual cost of CKD

CKD stage	mean estimate	standard error
CKD stage 3B	<input type="text" value="427"/>	<input type="text" value="32"/>
CKD stage 4	<input type="text" value="417"/>	<input type="text" value="27"/>
CKD stage 5	<input type="text" value="556"/>	<input type="text" value="41"/>
On dialysis, for year of dialysis initiation	<input type="text" value="20112"/>	<input type="text" value="198"/>
On dialysis, not for year of dialysis initiation	<input type="text" value="24709"/>	<input type="text" value="51"/>



SHARP CKD-CVD model: Shiny interface

SHARP CKD-CVD outcomes model (beta version)

The default values are UK quality of life (QoL) utilities estimates derived from the SHARP data.

Baseline QoL is the quality of life utility of a 60 year old female, non-smoker, with above secondary education, with BMI 25-30 kg/m², pre-RRT CKD and without diabetic nephropathy or vascular disease.

Reset inputs

Baseline QoL

0.86

Additional effects

Demographic and socio-economic characteristics

Age (per 10 years)	Male
-0.048	0.059
Completed secondary education	Below secondary education
-0.017	-0.036
Ex-smoker	Current smoker
-0.009	-0.037
BMI <25 kg/m²	BMI ≥30 kg/m²
0.011	-0.043

Disease history



Discount cost-effectiveness results

Long-term projections in the control group (cumulative probabilities per 1,000 participants)

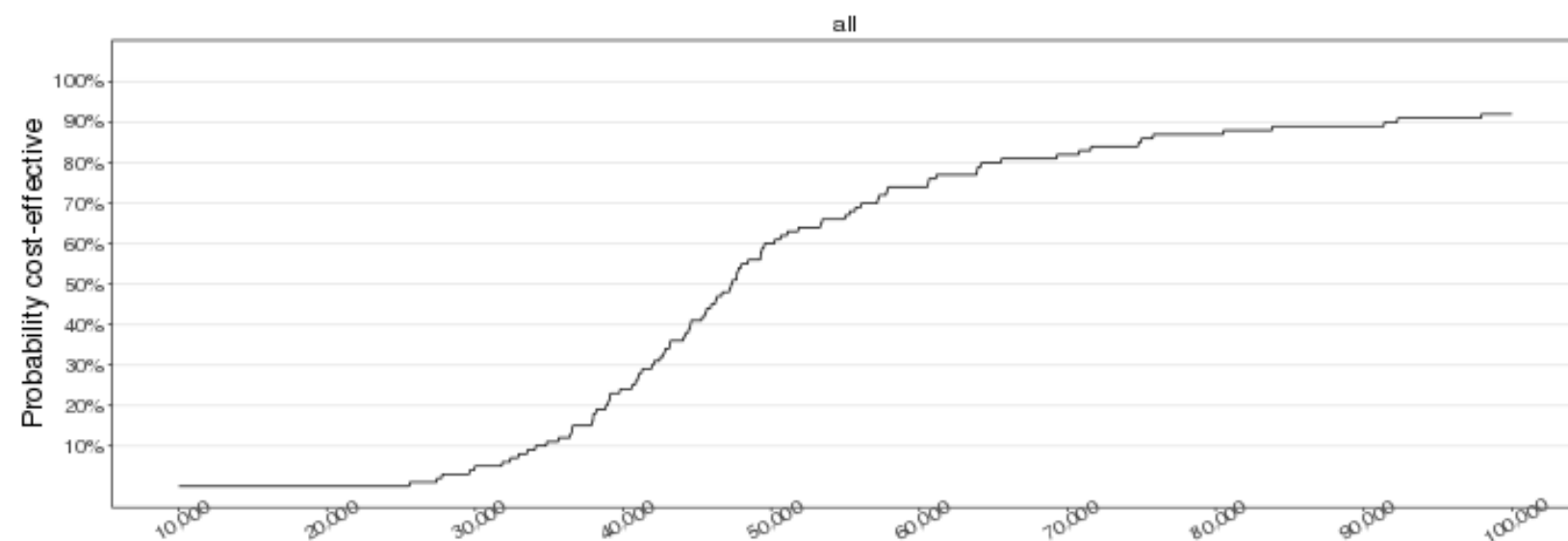
	MVE or VD	RRT	Vascular deaths	All deaths
At 5 years	184 (159, 213)	409 (357, 444)	57 (44, 76)	205 (194, 222)
At 10 years	281 (244, 319)	643 (594, 683)	118 (92, 155)	415 (398, 438)
Over simulation duration	419 (358, 501)	884 (826, 935)	292 (225, 379)	907 (897, 918)

Long-term projections in the treatment group (cumulative probabilities per 1,000 participants)

	MVE or VD	RRT	Vascular deaths	All deaths
At 5 years	169 (138, 193)	407 (355, 439)	51 (37, 70)	200 (189, 216)
At 10 years	263 (214, 299)	638 (593, 675)	106 (81, 140)	407 (389, 429)
Over simulation duration	397 (328, 477)	877 (813, 927)	271 (207, 371)	905 (896, 915)

Incremental cost-effectiveness over the simulation duration (results per 1,000 participants)

LYs gained	QALYs gained	Incremental hospital costs	Treatment costs	Cost per LY gained	Cost per QALY gained
135 (-4, 279)	107 (22, 227)	698,152 (-416,384, 1,308,000)	5,074,512 (4,904,776, 5,201,336)	42,646 (20,617, 304,068)	54,085 (27,412, 179,555)



User-friendly interface: help with debugging and transparency

- Face validity debugging
 - Easier to do on a user-friendly interface (even for the developers!)
- Feedback from external users
- Running several models against a reference simulation
 - Mount Hood diabetes challenge: models predicting long-term outcomes in diabetes patients
 - everyone gets the same tasks (eg change in life expectancy after statin initiation)
 - core assumptions same for everyone
 - additional assumptions must be documented in a pre-defined template
 - the results are presented, compared and (usually) published
 - user-friendly interface enables replication



SHARP CKD-CVD model: conclusions

- SHARP CKD-CVD model is a novel resource for evaluating health outcomes and cost-effectiveness of interventions in CKD
- Efficient coding is important and much can be achieved using basic functionality only
- User-friendly web-based freely available interface aids model use
- Together with the published equations / methods helps ensure reliability of the underlying code and methods transparency
- Using R was paramount in model development process
 - Wrapping code chunks in functions
 - Straightforward debugging
 - Parallel programming
 - Shiny interface



SHARP CKD-CVD model:

Remaining challenges and discussion points

- Day-to-day support
 - Replying to queries, fixing bugs
 - R/package updates may break everything!
 - Not updating is not an option (according to our IT team)
- Is R the best option for such an interface?
 - Might another language(s) be faster and/or have better visualisation capabilities?
- Do the benefits of releasing the code outweigh the risks?

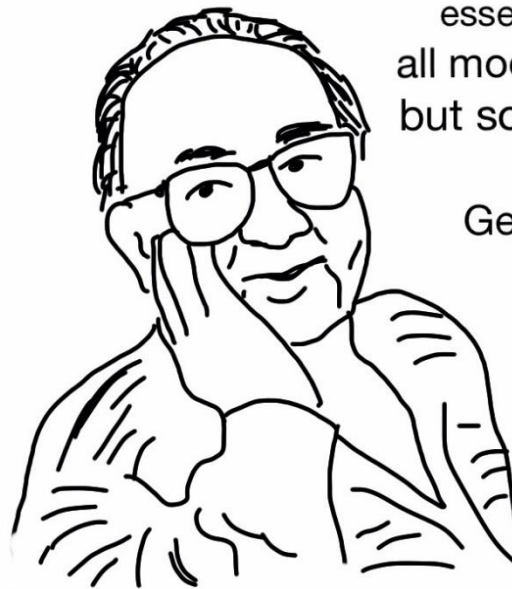


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SHARP CKD-CVD model



essentially,
all models are wrong,
but some are useful

George E. P. Box

freshspectrum.com

<http://dismod.ndph.ox.ac.uk/kidneymodel/app/>

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