Health Economics Research Centre

HERC news

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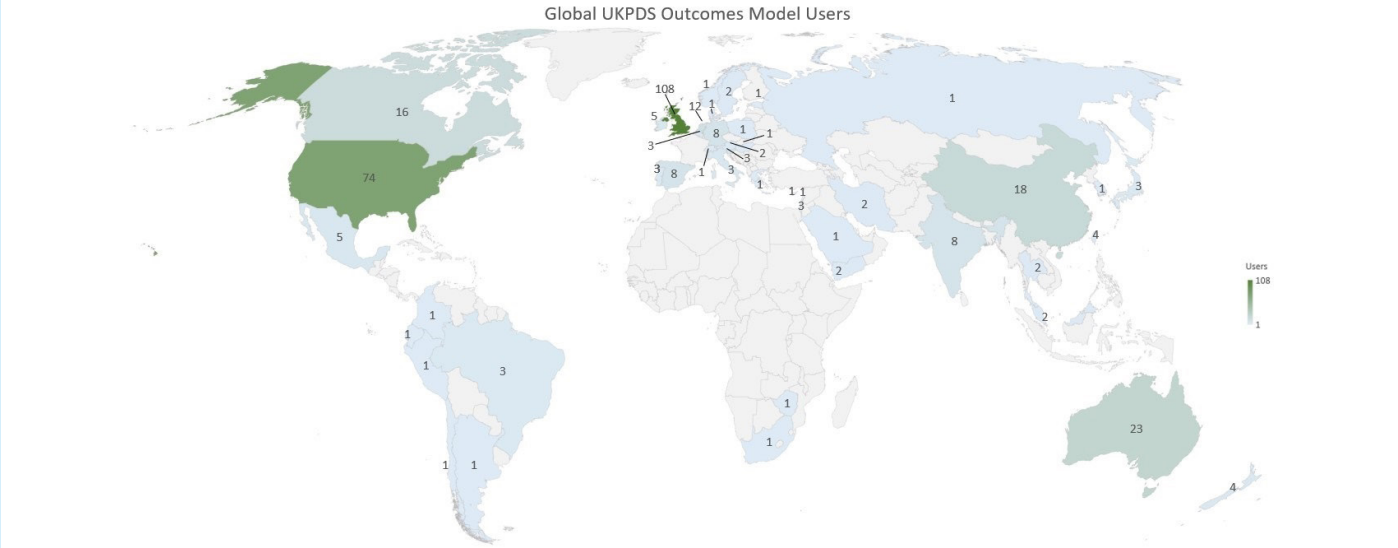

Virtual launch of the UK Prospective Diabetes Study (UKPDS) Outcomes Model Version 2.1

HERC project team: Helen Dakin, Philip Clarke, José Leal, Teresa Day, Barbara Kitchener

On 6th July, the latest version of the UK Prospective Diabetes Study (UKPDS) Outcomes Model was officially launched in an interactive webinar attended by 71 researchers from academic, government and commercial organisations around the world.

The UKPDS Outcomes Model is a computer simulation model developed by researchers at HERC and the Diabetes Trials Unit that predicts clinical events, life expectancy, costs and QALYs over a lifetime for populations with type 2 diabetes. The model is available through Oxford University Innovation, with no charge to non-commercial users and has been used by hundreds of people around the world.

The latest version (2.1) provides greater speed and additional features and outputs. Users can now compare up to 25 treatment groups, enabling comparisons against multiple comparators in health technology assessment. Users can define up to five composite endpoints to match trial endpoints and/or the outcomes of interest to decision-makers. Outputs can also be customised to minimise processing time and match the user's requirements. New output options facilitate subgroup analyses and handling uncertainty.

As part of the webinar, Philip Clarke, Rury Holman and Amanda Adler provided an introduction to the model and how it can be used in clinical trials and health technology assessment. Helen Dakin provided an overview of how to use the model and demonstrated the latest version, while James Groves demonstrated how to licence a copy of the model. Attendees were from Australia, USA, India and Europe, reflecting the international use of the model. Around a third of 29% of attendees currently use the model. A recording of the event is now available at https://youtu.be/4G2i-UMbNJQ.

For more information:
https://process.innovation.ox.ac.uk/software/p/9965/ukpds-outcomes-model-non-commercial/1

> "Version 2.1 provides greater speed and additional features and outputs"

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R for HTA Consortium

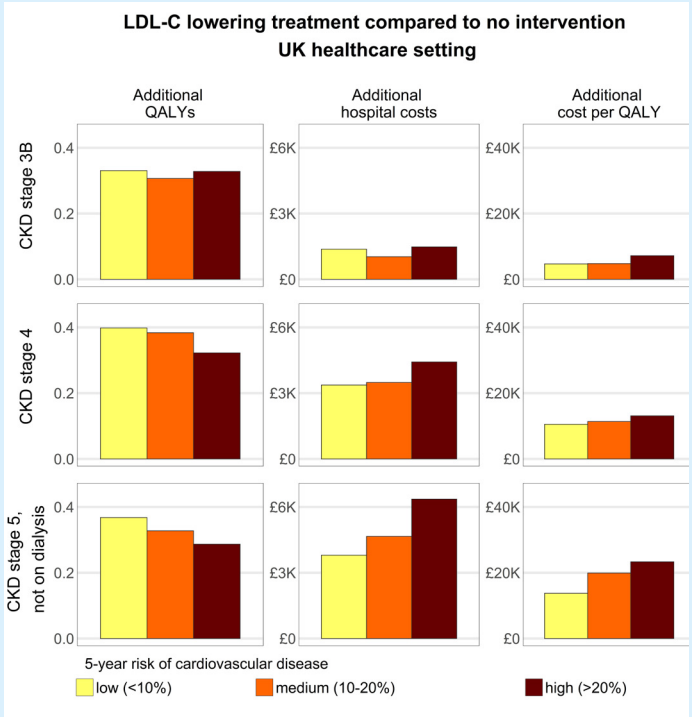
HERC project team: Iryna Schlackow, Claire Williams, Boby Mihaylova, on behalf of the R for HTA Scientific Committee

R is a freely available programming language used for statistical analyses. It has been growing in popularity in health sciences due to its efficiency, flexibility and superb graphical capabilities. Resources have been developed for health economists and HTA analysts, e.g. packages on Bayesian cost-effectiveness analysis, Markov modelling and value of information. Detailed documentation, open source software, friendly R community, numerous training resources – these ensure that people at all levels can make use of the most recent developments and produce efficient and reproducible research.

In 2018, the R for Health Technology Assessment (R for HTA) academic consortium was established to explore how R, and statistical software in general, could be integrated into the process of developing health economic evaluations. Our scientific committee is led by Gianluca Baio (University College London) and Howard Thom (University of Bristol) and consists of 11 members based in the UK and Ireland, including Iryna Schlackow, Claire Williams and Boby Mihaylova. Our members have extensive experience with academia, industry, NICE and governments worldwide, regularly present at conferences, publish methodological and tutorial papers and facilitate discussions across a range of technical aspects.

We also run regular events for health economists including short courses and summer schools, workshops and hackathons. Many of these are informal, with everyone from complete novices to advanced users welcome. In particular, we will hold our next annual R for HTA Showcase virtually on October 9 and October 12. We have an excellent string of speakers, including several current and former HERC members (Mi Jun Keng, Iryna Schlackow, Claire Simons and Seamus Kent), and a panel discussion involving representatives from academia, consultancy, NICE and industry. Please visit our website to find out more about our activities, and follow us on Twitter (@rhta16).

For more information: **https://r-hta.org/**



Reducing requests for antibiotics in primary care

HERC project team: Laurence Roope, Koen Pouwels, Sarah Wordsworth

Taking antibiotics when they are not required is a major public health concern, because it enables bacteria to resist antibiotic treatment. This means that, increasingly, we may not be able to find antibiotics that can cure serious infections.

About 50% of all antibiotic prescribing in primary care is for respiratory-tract infections, such as influenza-like illnesses. Much of this prescribing is not necessary, and previous studies have found that doctors sometimes make such prescriptions because they perceive that their patients want them.

To reduce patient requests for unnecessary antibiotics, public health campaigns often provide fear-based information about antibiotic resistance. However, research has shown that fear-based campaigns in other contexts, such as smoking and alcohol abuse, are likely to be ineffective, and can even backfire, unless people feel confident they can carry out the recommended behaviour. We hypothesised that this principle also applies to the effectiveness of fear-based information aimed at discouraging people from requesting antibiotics.

To test our hypothesis, we surveyed two waves of 4,000 members of the UK public, who were randomised to receive different messages about antibiotic-use and resistance. Working closely with behavioural scientists, we designed messages both with and without 'empowering information' on how to effectively self-manage influenza-like symptoms without antibiotics.

The results – recently published in *BMC Medicine* – confirmed our hypothesis. We found that messages warning of the dangers of antibiotic resistance could help to reduce requests for antibiotics, but they were much more effective when combined with messages empowering patients to self-manage symptoms effectively without antibiotics. Including the empowerment message was found to be particularly important for encouraging people with low awareness of antibiotic resistance not to ask for antibiotics.

We believe that this finding has important implications for the design of future public campaigns intended to reduce antibiotic use, and possibly for campaigns in other areas of public health where information is provided to the general public.

For more information:
https://doi.org/10.1186/s12916-020-01553-6

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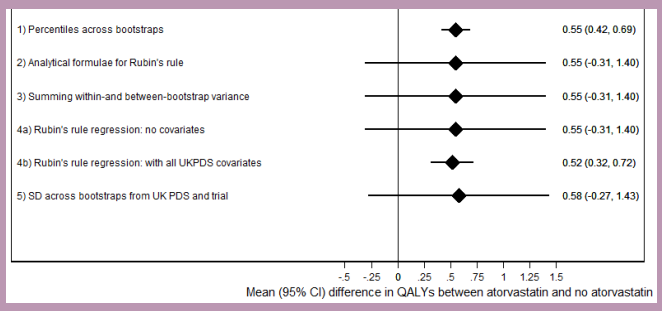
Accurately reflecting uncertainty in patient-level simulation models

HERC project team: Helen Dakin, José Leal, Philip Clarke, Alastair Gray

Patient-level simulation models are increasingly used to extrapolate data from clinical trials since they allow for heterogeneity, patients' history and non-linear relationships between patient characteristics and model outputs. However, there has been little research on how to estimate 95% confidence intervals that combine sampling uncertainty around the trial sample within the trial period and during the extrapolation, with parameter uncertainty around the model parameters used in the extrapolation.

HERC researchers have developed and tested new methods for combining different types of uncertainty and accurately reflecting precision within patient-level simulation models extrapolating data for trial participants, and the results of this work were recently published in *Medical Decision Making*.

We developed methods for combining parameter and sampling uncertainty: analytical formulae based on Rubin's rule; summing variances; Rubin's rule regression with/without covariates, and bootstrapping from the trial sample. We compared these methods using a simulation study based on an economic evaluation extrapolating the AFORRD randomised trial using the UK Prospective Diabetes Study Outcomes Model (UKPDS-OM). This demonstrated that ignoring sampling uncertainty gave confidence intervals that were too narrow, while all four methods that combined parameter and sampling uncertainty gave similar results with 96% coverage (see figure).



We also demonstrated the importance of adjusting for pre-randomisation variables that may be imbalanced between randomised groups: particularly in small trials extrapolated using patient-level simulation models. In our study, adjusting for baseline characteristics increased precision and had a small effect on point estimates. Baseline imbalance in variables such as age, gender, morbidity and pre-randomisation costs could also introduce bias for within-trial outcomes that are correlated with baseline characteristics, such as costs and QALYs.

For more information:
https://doi.org/10.1177/0272989X20916442

HERC Short Courses

HERC is running two short online courses in health economics this autumn.

★ **NEW COURSE** ★ **Integrating economic evaluation into clinical trials**, 8th-9th December. This course, for those working in clinical trials, will give participants an understanding of what is required to design and conduct an economic evaluation alongside a clinical trial.

Applied Methods of Cost-Effectiveness Analysis: Registration is now open for the next course, taking place between 16th - 20th November.

For further information on both courses, please click **here**.

Inaugural lecture: Philip Clarke

The inaugural lecture of Professor Philip Clarke, Director of HERC, is now available to watch on the NDPH Youtube channel **here**.

This lecture, titled "Tackling diabetes in the 21st century — an economic road map", is a wide ranging talk that touches on the economics of diabetes and of maps.

Spotlight on John Buckell

I joined HERC in May 2019 to work mainly on projects related to genomics and obesity. On the obesity side, HERC collaborates with the Health Behaviours team in the Nuffield Department of Primary Health Care Sciences. Here, we are studying the relationship between individuals' BMI and their Health-Related Quality of Life. This is an important topic, as valuations of this relationship feed into clinical commissioning decisions, which potentially affect many people with overweight or obesity. We are using data from large-scale randomised controlled trials, which we combine in joint analyses (an individual patient data meta-analysis). I am also working on projects where we are investigating behaviour related to shopping choices, price promotions and food labels.

On the genomics side, HERC is collaborating with researchers in Canada to value genomics-based healthcare for children with rare diseases. We are trying to understand if it makes economic sense to roll out genomic testing programs to help diagnose these conditions earlier along patients' clinical pathways. We are using data from the 100,000 Genomes Project, together with hospital data, to look at costs for our population of interest. We are also conducting discrete choice experiments to study parents' preferences for the genomic testing of their children, which will feed into economic evaluations.

Away from genomics and obesity, I am involved with researchers at HERC in promoting open science practices in health economics. For example, we are petitioning for the use of Registered Reports as a mechanism for peer review. I am also part of exciting special interest research groups across the university, covering topics such as discrete choice experiments/choice modelling, reproducible science, obesity, health psychology and tobacco.

Prior to joining HERC, I was at the Yale School of Public Health where I used experimental and quasi-experimental approaches to study tobacco behaviours. I gained my PhD at the University of Leeds in 2015 where I studied hospital efficiency using "frontier techniques".

Staff News

Welcome to:

Kushal Kadakia, who joined HERC in May. Kushal is studying on the NDPH MSc programme in Global Health Science and Epidemiology and is undertaking a summer placement at HERC. During his placement he will also write a dissertation under the supervision of Philip Clarke and Laurence Roope.

Samantha Field, who is writing her dissertation in HERC on 'Estimating the proportion of bystander exposure to antibiotics among potentially pathogenic bacterial microbiota in the UK' under the supervision of Liz Morrell and Koen Pouwels as part of her MSc in Global Health Science and Epidemiology undertaken at the Nuffield Department of Population Health.

Bastian Bohrmann, who joined HERC in June as a visiting student. Bastian is studying for an MSc in International Health Policy (Health Economics) at the London School of Economics and Political Science. As part of his course, he is undertaking a summer placement at HERC, during which time he will write a dissertation under the supervision of Philip Clarke and Laurence Roope.

Sijie Han (Dora), who is visiting HERC virtually this summer as part of her MSc at University of York. Dora is working with Helen Dakin and Paolo Candio to undertake a project reviewing how often NICE technology appraisals consider interactions between treatments, and how often interactions could change the conclusions about which treatments are cost-effective.

Lynn Yaolin Zheng and **David Stoye,** who are Public Health Registrars undertaking a 2-month placement at HERC. They will be working alongside José Leal, Filipa Landeiro, Ramón Luengo-Fernández and Koen Pouwels estimating the healthcare costs and lost earnings associated with the COVID-19 outbreak in Europe.

Congratulations to:

Five of HERCs senior staff who have been awarded academic titles: **José Leal**, **Ramón Luengo-Fernández**, **Apostolos Tsiachristas** and **Mara Violato** have become Associate Professors and **Helen Dakin** has become a University Research Lecturer. We are very pleased with this recognition of their longstanding contributions to research, teaching and to the discipline of health economics. More information can be found **here**.

Funding

UK Research and Innovation, Cancer Research UK and industry have recently invested more than £11 million in an Oxford-led artificial intelligence (AI) research programme to improve the diagnosis of lung cancer and other thoracic diseases. As part of this work, **Sarah Wordsworth** will co-lead a work package on Primary care, Population Health and Health Economics modelling, along with Professor Julia Hippisley-Cox (Nuffield Department of Primary Care Health Services). This work will estimate the cost-effectiveness of the current approach to lung cancer screening versus the use of cancer risk assessment tools. Please click **here** for more information.

Mara Violato has been awarded funding by the NIHR Applied Research Collaboration for Oxford and the Thames Valley to investigate the impact of COVID-19 on the quality of life of children and adolescents, as well as educational (for children) and productivity (for parents) losses throughout the COVID-19 pandemic in the UK.

Presentations

Richard Doll Seminar, Nuffield Department of Population Health, University of Oxford
June 2020
Philip Clarke and Laurence Roope
The Economics of COVID-19

XVIII Milan European Economy Workshop
June 2020
Philip Clarke
COVID 19 and the option value of research infrastructure funding

CMC Online Seminar Series, University of Leeds
August 2020
John Buckell
Smokers' choices and addiction: a hybrid choice model approach in the US (**Link to presentation**)

HERC involved in national COVID-19 survey

Koen Pouwels has co-designed the national Coronavirus (COVID-19) Infection Survey and performed the majority of the statistical analyses for the weekly bulletins on this survey published by the Office for National Statistics, available **here**.

Recent Publications

1. Bhatnagar R, **Luengo-Fernández R**, et al. *Thoracoscopy and talc poudrage compared with intercostal drainage and talc slurry infusion to manage malignant pleural effusion: the TAPPS RCT.* Health Technol Assess. 2020. doi:10.3310/hta24260

2. Beard DJ, Davies LJ, et al. [includes **Leal J**]. *Total versus partial knee replacement in patients with medial compartment knee osteoarthritis: the TOPKAT RCT.* Health Technol Assess. 2020. doi:10.3310/hta24200

3. Coleman RL, **Gray AM**, et al. *Can the cardiovascular risk reductions observed with Empagliflozin in the EMPA-REG OUTCOME trial be explained by the concomitant changes seen in conventional cardiovascular risk factor levels?* Diabetes Obes Metab. 2020. 22(7):1151-1156. doi:10.1111/dom.14017

4. **Dakin H**, **Eibich P**, et al. [includes **Gray A**]. *The use of patient-reported outcome measures to guide referral for hip and knee replacement: Part 2 – a cost-effectiveness analysis.* Bone Joint J. 2020. 102-B(7):950–958. doi:10.1302/0301-620X.102B7.BJJ-2019-0105.R2

5. **Dakin H**, **Eibich P**, **Gray AM**, et al. *Who gets referred for knee or hip replacement? A theoretical model of the potential impact of evidence-based referral thresholds using data from a retrospective review of clinic records from an English musculoskeletal referral hub.* BMJ Open. 2020. doi:10.1136/bmjopen-2019-028915

6. Davies L, Cook J, **Leal J**, et al. *Comparison of the clinical and cost effectiveness of two management strategies (rehabilitation versus surgical reconstruction) for non-acute anterior cruciate ligament (ACL) injury: study protocol for the ACL SNNAP randomised controlled trial.* Trials. 2020. doi:10.1186/s13063-020-04298-y

7. Ganesh A, **Luengo-Fernández R**, Rothwell PM. *Late functional improvement and 5-year poststroke outcomes: a population-based cohort study.* J Neurol Neurosurg Psychiatry. 2020. doi:10.1136/jnnp-2019-322365

8. Ganesh A, **Luengo-Fernández R**, et al. *Weights for ordinal analyses of the modified Rankin Scale in stroke trials: A population-based cohort study.* EClinicalMedicine. 2020. 23:100415. doi:10.1016/j.eclinm.2020.100415

9. Javanbakht M, Moloney E, et al. [includes **Becker F**]. *Economic evaluation of surgical treatments for women with stress urinary incontinence: a cost-utility and value of information analysis.* BMJ Open. 2020. doi:10.1136/bmjopen-2019-035555

10. Meijer E, van Eeden AE, et al. [includes **Tsiachristas A**]. *Exploring characteristics of COPD patients with clinical improvement after integrated disease management or usual care: post-hoc analysis of the RECODE study.* BMC Pulmonary Med. 2020. doi:10.1186/s12890-020-01213-8

11. Ooms A, Png ME, et al. [includes **Dakin H**]. *Statistical and Health Economic Analysis Plan for a Randomized Controlled trial of Surgical Fixation with K-Wires versus Plaster Casting in the Treatment of Dorsally Displaced Distal Radius Fractures: DRAFFT2.* Bone Joint Open. 2020. doi:10.1302/2046-3758.16.BJO-2020-0044.R1

12. Price A, Kang S, et al. [includes **Dakin H**]. *The use of patient-reported outcome measures to guide referral for hip and knee replacement: Part 1 – the development of an evidence based model linking pre-operative score to the probability of gaining benefit from surgery.* Bone Joint J. 2020. 102-B(7):941–949. doi:10.1302/0301-620X.102B7.BJJ-2019-0102.R2

13. **Rocks S**, Berntson D, et al. [includes **Tsiachristas A**]. *Cost and effects of integrated care: a systematic literature review and meta-analysis.* Eur J Health Econ. 2020. doi:10.1007/s10198-020-01217-5

14. **Rocks S**, Glogowska M, et al. [includes **Tsiachristas A**]. *Introducing a Single Point of Access (SPA) to child and adolescent mental health services in England: a mixed-methods observational study.* BMC Health Serv Res. 2020. doi:10.1186/s12913-020-05463-4

15. **Roope LSJ**, **Buchanan J**, et al. [includes **Morrell L**, **Pouwels KB**, **Wordsworth S**]. *Why do hospital prescribers continue antibiotics when it is safe to stop? Results of a choice experiment survey.* BMC Medicine. 2020. doi:10.1186/s12916-020-0166

16. Tew M, Dalziel K, **Clarke PM**, et al. *Patient-reported outcome measures (PROMs): can they be used to guide patient-centered care and optimize outcomes in total knee replacement?* Qual Life Res. 2020. doi: 10.1007/s11136-020-02577-4

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