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## Addressing Economic Questions in Mega-Trials



**Project team:** Bobby Mihaylova, Iryna Schlackow, Claire Simons, Seamus Kent and Rachael Morton

**'Big data' is an increasingly popular term used to refer to the collection and analysis of large, complex datasets, often in subject areas that are relevant to health economists, such as population health or genomics. There is a perception that big data is a recent development, but in fact researchers have been working on big data projects for many years.**

Since 2001, HERC researchers have been collaborating with trialists, epidemiologists and statisticians at the Clinical Trials Service Unit (CTSU), University of Oxford on economic analyses in a number of large cardiovascular trials. The good quality data available from large streamlined randomised studies (or mega-trials) enables health economists to address research questions such as "Do intervention effects on a range of outcomes differ in categories of participants?", "What are the likely long-term effects of interventions?" and "For whom are interventions effective and cost-effective?". Mega-trials can also inform assessment of effects of socioeconomic, behavioural, disease risk factors and disease events on future health outcomes and healthcare resources, and guide implementation of healthcare interventions.

The economic studies in the 20,536-large Heart Protection Study (HPS), 9,270-large Study of Heart and Renal Protection (SHARP) and the 25,000-large Treatment of HDL to Reduce the Incidence of Vascular Events (HPS2-THRIVE) study have shown that large trials can reliably inform models of effects of serious disease events on quality of life and healthcare costs, as well as the development of long-term disease models. The lifetime disease models for people at high cardiovascular risk (HPS) and people with chronic kidney disease (SHARP), confirm that longitudinal health event data is important in estimating the interdependence between adverse events and over time to estimate long-term quality-adjusted survival and costs. Our cost-effectiveness analyses in the HPS and SHARP studies also underlined the importance of multivariate cardiovascular risk in determining absolute benefits and cost-effectiveness of cardiovascular preventive interventions. Further work using the 175,000-large Cholesterol Trialists' Collaboration meta-analysis of 27 large statin trials showed reliably that statins are beneficial also at low cardiovascular disease risk.

This programme of work is thriving at HERC. Future projects are planned alongside new mega-trials which will address a larger range of questions and make full use of the expertise accumulated while working with big data over the past decade.

For more information: **HERC**

# HERC expands portfolio of discrete choice experiment research

**Project team:** James Buchanan, Helen Campbell, Alastair Gray, Rachael Morton, Laurence Roope, Sarah Wordsworth

HERC has recently experienced a rapid expansion of our portfolio of research into the elicitation of patient and clinician preferences for healthcare interventions using discrete choice experiments (DCEs). DCEs provide information about what is important to patients and health care providers, which can enhance clinical decision-making and support policies to maximise benefit to society as a whole. DCEs also provide a mechanism for estimating the monetary willingness to pay for different alternatives, which can be used in cost-benefit analysis. However, DCEs do have limitations as a stated preference technique: they can be open to 'hypothetical bias' i.e. what is measured is what respondents say they will choose, not necessarily what they actually choose. Within our portfolio of DCE research we aim to tackle a number of these challenges. Topics of particular methodological interest are outlined below.

## Conducting DCEs in hard to reach populations

Obtaining the preferences of hard to reach populations is extremely important when designing interventions to improve health outcomes for these (sometimes marginalised) groups. One example of such a group is young women who do not attend cervical cancer screening services: in some parts of the UK, only 1 in 4 young women attend their first cervical screening test. Helen Campbell is leading a team at HERC which is currently conducting a DCE among young non-attending women to explore their preferences for interventions designed to increase screening uptake. This project (STRATEGIC: Strategies to Increase Cervical Screening Uptake at First Invitation) is being undertaken in collaboration with the Universities of Manchester, York and Aberdeen, and is funded by the NIHR Health Technology Assessment Programme.

## Exploration of attribute non-attendance

Some DCEs require numerous attributes to be included to preserve face validity; however, the inclusion of too many attributes may increase the complexity of the choice task. In addition, the inclusion of attributes that are consistently ignored leads to biased coefficients, due to non-compensatory behaviour. Rachael Morton is conducting a DCE among nephrologists where the proposed alternatives are patients, described using 10 different attributes. At the end of the choice sets, the respondents are asked whether they ignored any attributes, and if so which ones. The effect of attribute non-attendance on the overall results of the DCE will be explored using latent class models. This study is being undertaken in collaboration with the George Institute and The University of Sydney.

## Risk presentation methods

Although the number of published DCE studies has increased rapidly in recent years, a key challenge to maintaining this momentum is that DCE respondents are increasingly being asked to evaluate complex risk information (including probabilities, frequencies and percentages). It is well known that the general public struggle with concepts of probability and uncertainty, and if respondents misinterpret (or ignore) risk information then this may invalidate WTP values generated using their preferences. James Buchanan and Sarah Wordsworth are currently conducting a DCE in the area of genomic testing in which graphical risk presentation techniques are compared with frequency statements to assess the extent to which this impacts on preferences and WTP.

## DCE

## Use of DCE trade-offs to populate decision analytic models

A series of economic decision models are being designed to explore the costs and effects of alternative antibiotic prescribing patterns in relation to patterns of antimicrobial resistance, in the context of both hospitals and primary care. Laurence Roope and Sarah Wordsworth are leading DCEs among patients and clinicians that will identify trade-offs between current and future actions and outcomes. It is hoped that this analysis will ultimately inform the development of behavioural interventions designed to curb excessive antibiotic use. This study is funded by NIHR Health Protection Research Unit and Public Health England.

## Efficient DCE survey designs

Bayesian statistical approaches are now commonly used to create d-efficient DCE survey designs using a two-step process. The first step is to run a pilot study to evaluate the logistics of the whole study and obtain priors for the model coefficients. In the second step, these priors are used to inform the selection of choice sets for the main survey. Rachael Morton is using Bayesian approaches to determine sample sizes for DCEs that incorporate conditional statements (where certain attribute levels cannot appear together in the same alternative), and at the same time provide an acceptable d-error. James Buchanan, Helen Campbell and Alastair Gray are investigating the use of model averaging approaches to generate experimental designs.

For more information: **HERC**

## Mount Hood 2014 Challenge Meeting

The Mount Hood 2014 Challenge Meeting was held in June at the University of Stanford, USA. The meeting provided a forum for computer modellers of diabetes to discuss and compare models via three different challenges: 1) external validation of the Look AHEAD study results; 2) external validation of mortality data from the Swedish National Diabetes Register data and 3) cross-model variation in model outcomes as a result of ethnicity. José Leal and Alastair Gray were part of a team representing the UKPDS Outcomes Model group. This computer simulation model is based on patient data from the UK

Alastair Gray and José Leal

Prospective Diabetes Study and can be used to forecast the likely occurrence of major diabetes-related complications and death in patients with Type 2 Diabetes Mellitus. The validation results of versions 1 and 2 of the model were presented at the meeting. Alastair and José also chaired several sessions and participated actively in the ensuing discussions. A paper is now being written relating the results of the meeting. Finally, the meeting was preceded by a one-day workshop titled 'Diabetes Modelling Masterclass', where José delivered a presentation on 'Techniques for model validation'.

## HERC at the 2014 iHEA and ECHE Joint Congress

Dublin, Ireland, July 2014

**Organised Session - Rachael Morton and Boby Mihaylova**  
Economic Analyses in Chronic Kidney Disease: The Study of Heart and Renal Protection

**Seamus Kent** Estimation of hospital care costs and health-related quality of life in chronic kidney disease patients

**Iryna Schlackow** A lifetime model in Chronic Kidney Disease: the SHARP Chronic Kidney – Cardiovascular Disease model

**Rachael Morton** The impact of social disadvantage on cardiovascular outcomes and mortality in people with moderate-to-advanced chronic kidney disease: The Study of Heart and Renal Protection

**Organised Session - Rachael Morton** Economic analyses of cancer screening and genomics

**José Leal** Cost-effectiveness of prostate cancer screening across jurisdictions in the absence of direct evidence: the case studies of England and the Republic of Ireland

**Individual Sessions - Alastair Gray** Adverse medical events in the UK National Health Service: comparison of frequency and severity over time based on repeat population surveys

**Filipa Landeiro** The impact of social isolation on delayed hospital discharges of older hip fracture patients and associated costs

**Ramon Luengo-Fernandez** Economic burden of cancer: evidence from the European Union

**Maria Alva** Self-reported quality of life as an independent predictor of mortality in type-2 diabetes: relevance of unobserved heterogeneity

**Richéal Burns** A Cost-Effectiveness Analysis of PSA testing for the secondary prevention of Prostate Cancer in the Republic of Ireland

**Judit Simon** Measuring the capability sets of people with severe mental health disorders using a novel multi-dimensional instrument: the OxCAP-MH.



## HERC at the forefront of improving disease diagnosis in primary care in the NHS

Jane Wolstenholme

In September 2013, the NIHR funded Diagnostic Evidence Co-operatives (DECs) in four locations in England with the aim of improving the way that diseases are diagnosed by the NHS. The focus of the Oxford University based DEC is on identifying, evaluating and implementing in-vitro diagnostics (IVDs) in primary care settings. A strong multi-disciplinary team has been assembled, including primary care clinicians, diagnostic test researchers, industry, NHS laboratory services, commissioners and the NICE diagnostics programme. HERC senior researcher, Jane Wolstenholme, is leading the health economics component of this work.

One of the components of the DEC in Oxford is the Oxford Diagnostic Horizon Scan Programme. This aims to identify new and emerging diagnostic technologies relevant to primary care in the NHS that are likely to have a significant impact, summarise the current evidence base for these technologies (including health economic evidence) and assess their likely impact on health and health care. The main outputs from the Horizon Scan Programme are technology reports, systematic reviews and health economic assessments, but in some cases pilot studies of new technologies in primary care settings are also conducted.

To date, 32 reports have been published, on a wide variety of topics ranging from iPhone/iPad related medical devices to non-contact infrared thermometers to dermoscopy for the diagnosis of melanoma in primary care. These reports are freely accessible online and are disseminated to the NIHR Health Technology Assessment Programme (HTA), NICE and commissioners of health care services to facilitate adoption and identify further research requirements.

For more information: [www.oxford.dec.nihr.ac.uk/](http://www.oxford.dec.nihr.ac.uk/)



## Spotlight on JACQUI MURPHY

I joined HERC in November 2012 to work on trial-based economic evaluations. Prior to this I conducted health technology assessments in the private sector (primarily economic modelling), after completing an MMath degree at Durham University.

My recent project work at HERC has included evaluating the cost-effectiveness of surgical techniques for the management of rotator cuff tears alongside the UKUFF trial (funded by the NIHR HTA programme). I am also conducting a cost analysis alongside the Arterial Revascularisation Trial (ART) trial, comparing the costs of single and bilateral internal mammary coronary artery bypass grafting.

Future work will include economic modelling alongside studies conducted within the remit of national cancer

screening programmes (the NHS Cervical Screening Programme and the NHS Bowel Cancer Screening Programme). Previous project involvement (prior to joining HERC) in the area of liver cancer and related disease pathways prompted an interest in disease modelling in cancer, so I look forward to expanding my experience in this broad area through these projects.

Over the past two years I have enjoyed the welcoming atmosphere at HERC and the opportunity to gain insights into the research being conducted in the wider Nuffield Department of Population Health, such as in the fields of epidemiology and medical statistics. I am keen to continue increasing my skills and experience with a view to starting doctoral research in the near future.

## Staff News



### Luke Blount

Luke joined HERC as the Unit Administrator in June 2014. For the past 8 years Luke has worked in various University departments including Research Services, the National Perinatal Epidemiology Unit and the Department of Paediatrics, gaining extensive experience. Luke heads the HERC administrative team which provides a range of support and services to the Director, staff and students in the group.



### Sam Williamson

Sam, a Public Health registrar, visited HERC from March – August 2014 to complete his thesis for the MSc in Global Health Science. Sam spent his time at HERC collecting data for the Fracture Free Study, at the John Radcliffe Hospital, and then analysing this data to determine the predictors of cost of hip fracture.



### Benjamin Parker

Ben, an MSc Health Economics student from the University of York, joined HERC at the beginning of July 2014 for his Summer Placement. He is working with James Buchanan and Sarah Wordsworth, building a cost-effectiveness model to compare surgery with surveillance for colorectal cancer in patients with Ulcerative Colitis.



### Oliver Verran

Oliver is an Oxford mathematics undergraduate who began his NIHR Research Methods 12-week Internship with HERC on the 7 July. Oliver will be working with Claire Simons, Iryna Schlackow and Boby Mihaylova on work related to the cost-effectiveness of interventions aimed at preventing cardiovascular disease.

## HERC Seminars

Convenor: Jacqueline Murphy

In May 2014, **Wiji Arulampalam**, Professor of Economics at the Department of Economics, University of Warwick visited HERC to give a talk on *Maternal autonomy and child nutrition in India*. In June, we welcomed **Dr Manuel Gomes**, Lecturer in Health Economics, London School of Hygiene and Tropical Medicine who presented *Addressing missing data in PROMs: implications for the use of PROMs for comparing provider performance*; and in July **Kathryn A. Phillips**, Professor of Health Economics and Health Services, University of CA, San Francisco, Visiting Professor at the London School of Economics spoke on *Genomic Sequencing: Panacea or Pandora's Box?*

In August, **Terry Flynn**, Health Economist, University of Western Sydney closed the series with his talk on *The future of best-worst scaling – quantifying attitudes towards health care and giving insights into how and, more importantly, why patients make the choices they do*.

The Seminar Series will re-commence on the 25 September.

To be added to our mailing list for future seminars, email us at [herc@dph.ox.ac.uk](mailto:herc@dph.ox.ac.uk)

## Recently Funded

**Partial Prostate Ablation versus Radical Prostatectomy (PART)**. This is a feasibility study which will run until Feb 2015 and is funded by the HTA. Economic analysis is led by Jane Wolstenholme.

**Video assisted thoroscopic lobectomy versus conventional Open Lobectomy for lung cancer, a multi-centre randomised controlled trial with an internal pilot. The VIOLET Study**.

This is a 5 year study, funded by NIHR HTA, which will compare the effectiveness, cost-effectiveness and acceptability of video assisted thoroscopic surgery (VATS) lobectomy versus open surgery for treatment of lung cancer. Economic analysis led by Sarah Wordsworth.

**Airways 2: Emergency Respiratory Treatments**. Funded by NIHR HTA. Out of hospital cardiac arrest (OHCA) is common, but survival rates are low. This 5 year study will investigate interventions, which improve OHCA outcomes, and the substantial uncertainty regarding the best initial airway management. Economic analysis led by Sarah Wordsworth.

## Presentations by members of HERC

**Nuffield Department of Population Health, University of Oxford, Work in Progress Seminars**  
Oxford, May 2014

**Helen Dakin**

*Economic evaluation of factorial randomised controlled trials*

**NIMAST/UKSF Northern Ireland Stroke Conference 2014**,  
Belfast, May 2014

**Ramón Luengo-Fernandez**

*Population-based study of acute- and long-term care costs after stroke in patients with AF*

**Public Health Thames Valley Service Academic Partnership, inaugural network meeting**  
Oxford, May 2014

**Sarah Wordsworth** gave a presentation on the work carried out by HERC.

**London School of Economics**  
London, May 2014

**Ingrid Slade**

*The Philosophy of Personalised Medicine*

**National Cancer Intelligence Network Conference**  
Birmingham, June 2014

**Richéal Burns**

*A Cost-Effectiveness Analysis of PSA testing for the secondary prevention of Prostate Cancer in the Republic of Ireland*

**British Society of Gastroenterology Annual Meeting, Poster presentation**

Manchester, June 2014

**Liz Stokes**

*Healthcare costs and quality of life associated with acute upper gastrointestinal bleeding in the UK*

**Economics, Modelling and Diabetes: Mount Hood 2014 Challenge, Diabetes Modelling Masterclass**  
Stanford University California, USA, June 2014

**José Leal**

*Techniques for model validation*

**Health Economists' Study Group, Glasgow Caledonian University**  
Glasgow, June 2014

**James Buchanan**

*Presenting risk information in discrete choice experiments: do graphical techniques influence willingness-to-pay?*

**Oxfam UK**

July 2014

**Laurence Roope and Paul Anand**

*Rethinking Welfare Economics: A Direct Operationalisation of Sen's Capability Approach*

**Supportive care for the renal patient – Annual workshop, Hammersmith Hospital**

London, July 2014

**Rachael Morton**

*KDIGO consensus and spotlight on new evidence in the cost-effectiveness of conservative care*

**Medical Sciences DPhil Day, University of Oxford, Poster presentation**

Oxford, July 2014

**Liz Stokes**

*How important are time horizons in health economic evaluation? A case study of platelet testing in cardiac surgery.*

## Recent Publications

For a complete list of HERC-authored publications to date and in press, visit our website.

**Leal J**, Hamdy F, **Wolstenholme J** (2014).

*Estimating age and ethnic variation in the histological prevalence of prostate cancer to inform the impact of screening policies*, International Journal of Urology, Epub (doi: 10.1111/iju.12458).

Fortnum D, Ludlow M, **Morton R** (2014). *Renal unit characteristics and patient education practices that predict a high prevalence of*

*home-based dialysis in Australia*. Nephrology, Epub (doi: 10.1111/nep.12274).

Li S, Wang G, Xu Y, **Gray A**, Chen G (2014). *Utility Values among Myopic Patients in Mainland China*. Optometry and Vision Science 2014; 91(7):723-729.

**Abdul Pari AA**, Simon J, **Wolstenholme J**, Geddes JR, Goodwin GM (2014). *Economic*

*evaluations in bipolar disorder: a systematic review and critical appraisal*. Bipolar Disord, Epub (doi: 10.1111/bdi.12213.)

Bourke S, **Burns R**, Gaynor R (2014). *Challenges in Generating Costs and Utilisation Rates Associated with Castration Resistant Prostate Cancer*. Journal of Market Access and Health Policy, 2:24072

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Health Economics Research Centre  
Nuffield Department of Population Health, University of Oxford  
Old Road Campus, Headington, Oxford OX3 7LF UK  
tel: +44 (0) 1865 289272/3  
email: [herc@dph.ox.ac.uk](mailto:herc@dph.ox.ac.uk)

To receive this newsletter quarterly email [herc@dph.ox.ac.uk](mailto:herc@dph.ox.ac.uk)

