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Body mass index and the use and costs of primary care services

Project team: Seamus Kent, Boby Mihaylova, Alastair Gray

Following large increases in the prevalence of overweight and obesity in recent decades, more than 60% of adults in Western populations including the UK are overweight or obese. Excess weight is a leading cause of death and disability globally, and is also contributing to the increased pressures on healthcare services.

HERC researchers have recently collaborated with colleagues in the Cancer Epidemiology Unit and Nuffield Department of Primary Care Health Services to investigate the impact of excess weight on the use and costs of primary care services in England. We analysed the primary care records over six years of 70,000 women in England aged 55-79 years who participated in the Million Women Study, comparing the use and costs of primary healthcare services between women at different levels of body mass index (BMI), while controlling for other observed differences such as smoking behaviour and level of socioeconomic deprivation.

We found that each 5kg of extra weight above a BMI of $20kg/m^2$ was associated with 5% more consultation costs and 10% more medication costs. Diagnostic and monitoring costs were similar irrespective of weight. Extrapolating these results to all women aged 55-79 years in England, we estimated that 11% (£229 million) of primary care consultation costs and 20% (£384 million) of prescription medication costs were due to overweight or obesity. The excess medication costs were predominantly due to treatments for diabetes, cardiovascular disease and pain management.

Our results quantify the substantial impact of excess weight on the use and costs of primary healthcare services and underscore the need for greater investment in cost-effective interventions to reduce weight or prevent weight gain.

For more information: **HERC**

“ Each 5kg of extra weight above a BMI of $20kg/m^2$ was associated with 5% more consultation costs and 10% more medication costs ”

Economic modelling and financing of personalised medicine (HEcoPerMed)

Project team: Sarah Wordsworth, Apostolos Tsiachristas

With increasing pressure on health care budgets, personalised medicine may increase opportunities for improving access to expensive prevention, diagnostic, monitoring and treatment strategies. Personalised medicine aims to optimally match patients with interventions by assessing the characteristics of patients in which treatments yield (the most) benefits. This is expected to make health care more cost-effective through better targeting of treatments. However, while the development of personalised medicine treatments is often an academic endeavour, the commercialisation of these treatments is often realised through private channels. This leads to high prices, reducing the societal affordability of these innovations. Commercially marketed medical products, such as specific drugs, are often priced at the margin, following companies' analysis of 'what the market can bear', rather than the size of the benefits for patients. There is therefore a need for economic models that evaluate personalised medicine treatments and analyse payment models that support innovations, linking financial rewards to health outcomes.

HEcoPerMed is a recently funded EU - Horizon 2020 research project that responds to the demand for appropriate economic models to evaluate personalised medicine, and to the need for adequate financial incentives for the rapid development and uptake of such innovations. HEcoPerMed aims to go beyond current assessment and payment models by generating more comprehensive cost-effectiveness estimates that incorporate patient and societal perspectives and improve the affordability of personalised medicine innovations.

This three-year project began in January 2019 and is a collaboration between the Austrian Institute of Technology (coordinator), German Aerospace Centre, Institute for Medical Technology Assessment at Erasmus University Rotterdam, Syreon Research Institute in Budapest and HERC.

HEcoPerMed will provide an overview, guidance, and demonstration of state-of-the-art economic modelling for personalised medicine. It will also propose financial agreements to accelerate the diffusion of personalised medicine in Europe. This work will be undertaken in collaboration with stakeholders at the national, European and international level, such as the International Consortium for Personalised Medicine. We will update you on our progress in future editions of the HERC newsletter!

For more information: **HERC**

Increasing efficiency in the English diabetic retinopathy screening programme

Project team: Ramón Luengo-Fernández, José Leal

Diabetic retinopathy (DR) is an important cause of blindness in the working age population in the UK, with diabetic macular oedema (DMO) being one of its complications. Screening for DR and DMO using retinal photography has been shown to be cost-effective. Treatment options for DMO include macular laser treatment or antivascular endothelial growth factor (VEGF) injections, however, treatment is only recommended for patients with clinically significant macular oedema (CSMO), with non-CSMO patients deriving little additional benefit from treatment.

Under the screening programme, patients with early stage DR and suspected DMO are referred to hospital eye services, with a large proportion deriving no benefit due to absence of CSMO. Spectral Domain Optical Coherence Tomography (SD-OCT) produces three-dimensional images of the eye. It could relieve pressure on NHS services by correctly identifying those patients who are screen positive for DMO but do not have CSMO, limiting the number of referrals to hospitals. HERC researchers have recently investigated whether the addition of SD-OCT imaging to the screening pathway is cost-effective compared to hospital eye service follow-up.

Using a Markov model we simulated the progression of individuals with early stage DR and DMO following DR screening over 12 months. The model was informed by patient-level data from the Gloucestershire Diabetic Eye Screening Service linked to the local digital surveillance programme and hospital eye service follow-up between 2012 and 2015.

For patients with early stage DR and DMO following DR screening, assessment using SD-OCT was found to be cost-saving when compared to the hospital eye service pathway. These savings, estimated at £76 (95% CI: £70 to £81) per patient, were driven by the fact that 80% of patients did not require referral to the hospital eye service, so could be safely monitored at an SD-OCT follow-up clinic or discharged back to screening.

This was the first study to show that the use of SD-OCT in the digital surveillance pathway of the English NHS Diabetic Eye Screening Programme is both effective and cost-effective.

For more information: **HERC**
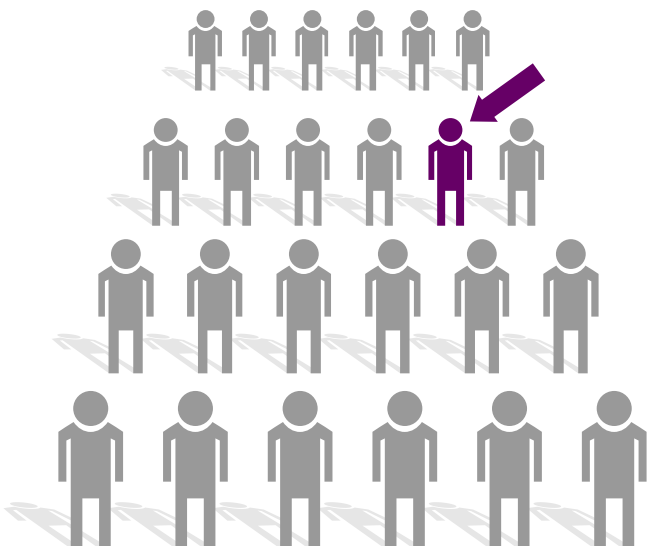
Comparing methods for analysing partial factorial trials

Project team: Helen Dakin, Alastair Gray

Partial factorial trials compare two or more pairs of treatments on overlapping patient groups, randomising some (but not all) patients to more than one comparison. For example, some patients may be randomised to drug A or its placebo, others randomised to drug B or its placebo (illustrated for a hypothetical trial in the table below), and further patients randomised simultaneously to A or its placebo and to B or its placebo. Although the design has been used in several high-profile trials, including the United Kingdom Prospective Diabetes Study and the Women's Health Initiative, analysing this type of study raises additional challenges for health economists and there has been little or no previous research on the best way to analyse the results.

The Knee Arthroplasty Trial (KAT) is a partial factorial randomised trial comparing three aspects of knee replacement design: bearing (mobile versus fixed), backing (metal versus solid polyethylene) and patella (resurfacing versus no resurfacing). HERC researchers compared four different methods for analysing the KAT study:

1. Ignoring interactions and analysing the trial "at-the-margins".

2. Focusing on the patients randomised to more than one comparison "inside-the-table".

3. Using the "Bayesian bootstrap" to estimate interactions while analysing data from all patients.

4. Analysing the entire trial population "as treated".

We observed interactions between the different types of knee replacement being compared in KAT and found that both standard errors and the treatment providing best value for money differed between the four analyses.

We concluded that researchers analysing partial factorial trials should explore interactions and test whether the results are sensitive to the methods used. At-the-margins may give a useful indication of average results if interactions are negligible or if the proportion of patients receiving different treatments is very similar to routine clinical practice, but may be misleading in other situations. The Bayesian bootstrap provides a useful way to allow for interactions while making use of the whole sample. This could be used for analyses of clinical endpoints or economic evaluations.

For more information: **HERC**

Hypothetical partial factorial trial (n=400)

		Number of patients				
		Randomised in Comparison A		Not randomised in Comparison A		*Total*
		Placebo of A	*Drug A*	*Did not have A*	*Received A*	
Randomised in Comparison B	*Placebo of B*	40	40	30	40	150
	Drug B	40	40	28	42	150
Not randomised in Comparison B	*Did not have B*	10	11			
	Received B	40	39			
	Total	130	130			

> "...researchers analysing partial factorial trials should explore interactions and test whether the results are sensitive to the methods used

Spotlight on PATRICK FAHR

I joined HERC and the University of Oxford as a DPhil student in October 2017 to undertake research on the economics of genomic medicine. Supervised by Sarah Wordsworth and James Buchanan, the focus of my thesis will be on economic evaluations of next-generation sequencing (NGS) technologies in rare disease diagnostics using big data from the 100,000 Genomes Project. The 100,000 Genomes Project was set up by Genomics England with the principle objective to sequence 100,000 whole genomes from patients that suffer from rare diseases and cancer. Scientific discoveries generated from this project will subsequently support the successful implementation of genomic medicine in the NHS. My main interest lies in understanding the costs involved when patients with rare genetic disorders follow long diagnostic odysseys with predominantly meagre diagnostic success rates. Additionally, I am interested in the usability of linked datasets such as routinely collected health data and genomic data in economic evaluations of NGS technologies.

Prior to joining HERC, I was part of a market access team at a contract research organisation within the pharmaceutical industry, living in Mexico City and working across Latin America. Before that, I undertook an MSc in Public Policy and Human Development at the United Nations University / Maastricht University, The Netherlands. Living in Oxford now, I cannot put into words how much I have so far appreciated the City of Oxford, the University of Oxford and the Nuffield Department of Population Health / HERC. My social highlight so far has been the unofficial HERC trip to Snowdonia – sleeping with ten people in an old, cold and very dirty barn was so much fun! I am very much looking forward to at least two more years at HERC.

Staff News — Welcome to:

Koen Pouwels, who joined HERC in January 2019 as a Senior Researcher from Public Health England. Koen will be working with Sarah Wordsworth on the antimicrobial resistance portfolio of projects, in particular modelling the long term costs and effects of antimicrobial resistance.

Jungseok Lee, who joined HERC as a Senior Researcher in February 2019. He will be working with José Léal and Jane Wolstenholme on a cost-effectiveness model to evaluate the impact of implementing a smart handheld technology capable of monitoring blood counts from a single drop of blood into routine oncology care.

Mitchell Burden, who is a foundation doctor on a 4-month rotation in HERC working with Alastair Gray and Filipa Landeiro on a systematic review of the literature on economic models for Alzheimer's disease as part of the ROADMAP project.

Christopher Bennett, who is a foundation doctor on a 4-month rotation in HERC working with Alastair Gray and Filipa Landeiro on a systematic review on resources used and costs incurred by people with predementia or dementia as part of the ROADMAP project.

Carlos Wong, who is visiting Sarah Wordsworth from February to May 2019, from the University of Hong Kong. Carlos will be evaluating the short-term and long-term cost-effectiveness of bariatric surgery compared to a non-surgical group in terms of cost per life-years gained and cost per QALY gained for patients with different levels of obesity.

Lars Asphaug, who is a doctoral research fellow at the University of Oslo visiting HERC on a 3-month placement. His doctoral research is on the economic evaluation of diagnostic technologies. Whilst at HERC, he will work with James Buchanan and Sarah Wordsworth on a project investigating whether traditional evaluation methods for diagnostics can be applied in the case of genetic testing.

HERC Seminars
Convenor: Stephen Rocks

HERC runs a series of seminars with invited speakers from the health economics community who talk on a wide range of applied and methodological topics.

In November, **Dr Guido Erreygers**, Professor of Economics at the Faculty of Business & Economics, University of Antwerp, was invited to HERC to present his research on: *A Direct Regression Approach to Decomposing Socioeconomic Inequality of Health.*

In December, **Dr Tommi Tervonen**, Research Scientist and Consultant at Evidera, London, visited HERC to present his work on: *Multi-Criteria Decision Analysis for Comparative Value Assessment throughout the Drug Lifecycle.*

In February, **Dr Dan Howdon**, Senior Research Fellow in Health Economics, Leeds University visited and presented his work on: *Implications of non-marginal budgetary impacts in health technology assessment.*

Details of forthcoming talks can be found on the HERC website: **http://www.herc.ox.ac.uk.** To be added to our mailing list for future seminars, email us at **herc@ndph.ox.ac.uk**

Presentations

4th Annual Primary Care Research Symposium
Aylesbury, January 2019
Ines Rombach, Marvi Iftikhar
How missing and spurious data can affect trial results

Health Economics Group Seminar Series
Newcastle University, November 2018
Seamus Kent
Total diet replacement as a scalable population approach to tackling obesity

Economics and Finance Seminar Series
University of Durham, November 2018
Laurence Roope
Gravitational Allocation Problems

Health Economists' Study Group
York, January 2019
Philip Clarke
Moving beyond the threshold: Using a competitive mechanism alongside economic evaluation to allocate health care resources

Health Economics Research Unit Seminar Series
University of Aberdeen, January 2019
Seamus Kent
Food on prescription: should total diet replacement programmes be provided by the NHS?

Division of Epidemiology and Public Health Seminar Series
University of Nottingham, February 2019
Mara Violato
The impact of diagnosis on health-related quality of life and costs in people with coeliac disease: a UK population-based longitudinal perspective

Centre for Health Economics Seminar
University of York, February 2019
Philip Clarke
The origins of health economic evaluation

Oxford Health Economics Workshop 2019

HERC is hosting a University-wide health economics workshop on the afternoon of **Thursday 23 May 2019** at the **University of Oxford Old Road Campus in Headington.** The workshop will provide economists and health economists from across Oxford with a forum to present current research and discuss future collaborations, (for example, the organisation of the UK Health Economists' Study Group (HESG) meeting, which is likely to be held in Oxford in summer of 2020/2021).

If you are interested in participating in this workshop, please contact Philip Clarke (**philip.clarke@ndph.ox.ac.uk**) or Laurence Roope (**laurence.roope@dph.ox.ac.uk**). For more general enquiries please contact **herc@ndph.ox.ac.uk**. Further details will be available on our website soon.

Recent Publications

1. Becchetti L, Pelligra V, **Salustri F**. *The impact of redistribution mechanisms in the vote with the wallet game: experimental results.* Soc Choice Welf. 2018. 51:595-619. doi:10.1007/s00355-018-1130-8

2. Blakely T, Kvizhinadze G, et al. [includes **Clarke P**]. *Health system costs for individual and comorbid noncommunicable diseases: An analysis of publicly funded health events from New Zealand.* PLOS. 2019. doi:10.1371/journal.pmed.1002716

3. Braithwaite T, Calvert M, et al. [includes **Gray A**]. *The use of patient reported outcome research in modern ophthalmology: impact on clinical trials and routine clinical practice.* Patient Relat Outcome Meas. 2019. 10:9-24. doi:10.2147/PROM.S162802

4. Cholesterol Treatment Trialists' (CTT) Collaboration [includes **Mihaylova B**]. *Efficacy and safety of statin therapy in older people: a meta-analysis of individual participant data from 28 randomised controlled trials.* Lancet. 2019. 393(10170):407-415. doi:10.1016/S0140-6736(18)31942-1

5. Doble B, Welbourn R, et al. [includes **Wordsworth S**]. *Multi-centre micro-costing of roux-en-y gastric bypass, sleeve gastrectomy and adjustable gastric banding procedures for the treatment of severe, complex obesity.* Obes Surg. 2018. doi:10.1007/s11695-018-3553-9

6. Ee Png N, Dritsaki M, et al. [includes **Gray A**]. *Economic Evaluation plan of a Randomised Controlled Trial of Intra-nodular Injection of Anti-TNF and Placebo among Patients with Early Dupuytren's Disease: Repurposing Anti-TNF for Treating Dupuytren's Disease (RIDD).* Wellcome Open Res. 2018. doi:10.12688/wellcomeopenres.14936.1

7. Gallacher J, de Reydet de Vulpillieres F, et al. [includes **Gray A**]. *Challenges for Optimizing Real-World Evidence in Alzheimer's Disease: the ROADMAP Project.* J Alzheimers Dis. 2019. 67(2):495-501. doi:10.3233/JAD-180370

8. Ganesh A, **Luengo-Fernández R**, Wharton RM, Rothwell PM. *Ordinal vs dichotomous analyses of modified rankin scale, 5-year outcome, and cost of stroke.* Neurology. 2018. 91(21). doi:10.1212/WNL.0000000000006554

9. Ganesh A, **Luengo-Fernández R**, Pendlebury ST, Rothwell PM. *Long-term consequences of worsened poststroke status in patients with premorbid disability.* Stroke. 2018. doi:10.1161/strokeaha.118.022416

10. **Kent S,** Jebb SA, et al. [includes **Gray A, Mihaylova B**]. *Body mass index and use and costs of primary care services among women aged 55–79 years in England: a cohort and linked data study.* Int J Obes (Lond). 2018. doi:10.1038/s41366-018-0288-6

11. **Leal J, Luengo-Fernández R**, et al. *Cost-effectiveness of digital surveillance clinics with optical coherence tomography versus hospital eye service follow-up for patients with screen-positive maculopathy.* Eye (Lond). 2018. doi:10.1038/s41433-018-0297-7

12. Mehanna H, Robinson M, et al. [includes **Gray A**]. *Cetuximab Versus Cisplatin with Radiotherapy for Low-risk Human Papilloma Virus Associated Oropharyngeal Cancer.* Lancet. 2018. doi:10.1016/S0140-6736(18)32752-1

13. Mostafa SA, Coleman RL, et al. [includes **Gray AM**]. *Simulating the impact of targeting lower systolic blood pressure and LDL-cholesterol levels on type 2 diabetes complication rates.* J Diabetes Complications. 2019. 33(1):69-74.

14. **Rombach I, Gray AM**, et al. *Correction to: multiple imputation for patient reported outcome measures in randomised controlled trials: advantages and disadvantages of imputing at the item, subscale or composite score level.* BMC Med Res Methodol. 2018. 18:107. doi:10.1186/s12874-018-0563-1

15. **Rombach I**, Merritt N, et al. [includes **Gray AM**]. *Cost-effectiveness analysis of a placebo-controlled randomized trial evaluating the effectiveness of arthroscopic subacromial decompression in patients with subacromial shoulder pain.* Bone Joint J. 2019. 101-B:55-62. doi:10.1302/0301-620X.101B1.BJJ-2018-0555.R1

16. Taggart DP, Benedetto U et al. [includes **Gray A**]. *Bilateral versus Single Internal-Thoracic-Artery Grafts at 10 Years.* N Engl J Med. 2019. 380:437-46. doi:10.1056/NEJMoa1808783

17. Wild J, El-Salahi S, et al. [includes **Tsiachristas A**]. *Preventing PTSD, depression, and associated health problems in student paramedics: Protocol for PREVENT-PTSD, a randomised controlled trial of supported online cognitive training for resilience versus alternative online training and standard practice.* BMJ Open. 8:e022292. doi:10.1136/bmjopen-2018-022292

18. Yang Y, Abel L, et al. [includes **Buchanan J**]. *Use of decision modelling in economic evaluations of diagnostic tests: an appraisal and review of health technology assessments in the UK.* PharmacoEconomics Open. 2018. doi:10.1007/s41669-018-0109-9

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