Welcome to the 25th issue of the HERC newsletter

As usual, this issue contains the latest news about research at HERC, along with details of recent publications, seminars, presentations and other HERC activities. In addition, we open this month with news of a change in leadership at HERC. Further details are provided below by Alastair Gray, and on page two by Philip Clarke.

A message from our departing Director,
Professor Alastair Gray

In January 2019 I will be standing down as Director of HERC and handing over that role to Philip Clarke, who (re)joined us in August of this year. Philip will be taking a forward look on page two of this newsletter, so it falls to me to be more retrospective.

Prior to HERC’s formation, health economics was not completely absent in Oxford. Miranda Mugford was in the National Perinatal Epidemiology Unit, and Alistair McGuire and Paul Fenn were at the Centre for Socio-Legal Studies, then based in Wolfson College. But there was no focal point, and my good fortune was to get the support of Martin Vessey, head of the then Department of Public Health, in creating and hosting a new group, and of Muir Gray, then Director of Research and Development at Anglia and Oxford NHS Executive, who provided the pump-priming funding. In 1996 HERC got going, quickly recruited Nikos Maniadakis and Andy Briggs, and grew. By our 10th birthday we had grown to 18 staff, and now have over 40 staff and students.

I and the group have been very lucky to have had the unwavering support of four successive Heads of Department: Martin Vessey got us started, Ray Fitzpatrick successfully steered us through various reviews and reorganisations, Harold Jaffe gave our research a more international dimension, and now Rory Collins has integrated us physically and academically into the Nuffield Department of Population Health. We have also been fortunate in the excellent admin support our HERC office has unfailingly provided.

Above all, we could not have thrived without the efforts of all my colleagues, past and present. I have been very lucky to work with such a group of loyal and hard-working people, and with our associates and visitors, and our doctoral and MSc students. I’m also lucky to be handing over to Philip, and am completely confident that under his leadership the group will go from strength to strength. Meanwhile I look forward to working alongside Philip and continuing my research and teaching.

Alastair
A message from our new Director, Professor Philip Clarke

My involvement with HERC dates back almost two decades, having worked for six years in the Centre prior to taking up appointments at the Universities of Sydney and Melbourne in Australia. I have a diverse range of research interests, which focus not only on ways to improve health care and research efficiency, but also on ways to improve access to health care and thereby reduce health inequalities. I am also known for developing computer simulation models that can be used to inform health economic evaluations.

Under Alastair’s leadership, HERC has grown considerably over the last few years, not only in the number of researchers, but in the scope of work it undertakes. HERC has also benefited from being embedded within the Nuffield Department of Population Health and being co-located with the Big Data Institute. This, combined with HERC’s strong links across the University of Oxford and external collaborations, means that HERC has tremendous opportunities to access primary data from individual patients, which in turn informs and characterises much of its research.

While continuing to do what the centre does well (e.g. conducting economic evaluations alongside clinical trials), I believe HERC can build on its key strength in computer simulation modelling. Although HERC has developed models for diabetes and renal disease, these will need to be updated and extended, and we are looking for opportunities to develop new simulation models for other diseases to help inform economic evaluations world-wide.

I am also keen to collaborate closely with existing researchers within HERC and form collaborations to develop several new programmes of research, such as:

- Developing new statistics to routinely monitor health inequalities both within and across countries;
- Finding cost-effective ways to reduce health inequalities;
- Conducting economic research on research i.e. finding ways to increase the efficiency of the allocation of research funding and improving the design of RCTs.

These new directions complement our existing research programme and will allow HERC to tackle new challenges in the coming years.

Philip

Mount Hood Diabetes Challenge Network

The Mount Hood Diabetes Challenge Network has organised regular diabetes computer simulation modelling conferences since 1999. The most recent conference was held in October 2018 in Düsseldorf, Germany and was hosted by researchers from the German Diabetes Centre (Deutsches Diabetes-Zentrum).

The Mount Hood conference has a different format to traditional conferences in that a major focus are challenge sessions. These involve up to 15 developers of health economic diabetes models who run prespecified simulations and then compare and contrast their results. Researchers from HERC participated with the UKPDS Outcomes Model and the SHARP CKD-CVD Model.

This year the challenges focused on the ability of models to predict recent clinical studies such as EMPA-REG which tested the effectiveness of a new class of drugs for lowering blood glucose levels in type 2 diabetes, the sodium–glucose cotransporter 2 (SGLT2) inhibitor. Other challenges looked at the sensitivity of simulation models to assumptions regarding the impact diabetes has on quality of life, and a comparison of diabetes models with other chronic disease models that include people with diabetes.

Nine researchers from HERC participated in the conference and gave several presentations over the three days. The next bi-annual conference will be held after the American Diabetes Association meeting in June 2020 in Chicago, USA.

Presentations at the 9th Mount Hood Challenge 2018

Philip Clarke
- Growing old gracefully? The QALY at 50
- The event rate and costs associated with major complications of diabetes in China: a comparative analysis

José Leal
- Pre-diabetes model using Chinese data
- Challenge 2: UKPDS Outcomes Model

Mi Jun Keng
- Impact of variation in type 2 diabetes management on health outcomes and healthcare costs

Joel Smith
- Identifying those who benefit from treatment: an open challenge for diabetes economic models

Iryna Schlackow
- Challenge 3: SHARP CKD-CVD model

For more information: HERC
Handling missing outcome data in RCTs using patient reported outcome measures

**Project team:** Ines Rombach, Alastair Gray, Oliver Rivero-Arias

Missing data can introduce bias in the results of randomised controlled trials (RCTs), but are often unavoidable in pragmatic studies, particularly when patient reported outcome measures (PROMs) are used. We have performed a range of simulation studies to generate guidance on best practice when analysing data with incomplete PROMs outcomes.

Firstly, we compared multiple imputation (MI) approaches for multi-item PROMs, comparing imputation at the item, subscale or composite score level. We concluded that differences between the imputation approaches are likely to be small in realistic settings. Imputation at the subscale or item level has theoretical advantages in settings where more individual PROMs items are missing, rather than the entire questionnaire (unit non-response). However, MI at the item level is often infeasible in realistic settings due to the complexity of the imputation models, and low numbers of observations in some of the item levels resulting in issues with perfect prediction. Further details on this research are published in *BMC Medical Research Methodology*.

A further simulation study, published in *Patient Related Outcome Measures*, considered the comparative performance of maximum likelihood (ML), MI and inverse probability weighting (IPW) to handle missing composite PROMs scores in longitudinal follow-up. MI produced more accurate results when the MI model took into account post-randomisation data, but performed similarly to ML otherwise. IPW performed worse than ML and MI in all simulation scenarios.

Choosing the most appropriate methods for handling missing data is essential for the accurate reporting of RCT results, but does not lessen the importance of taking active steps to minimise the occurrence of missing data in the design and conduct of RCTs. Since all of the investigated approaches for handling missing data assume data to be missing at random, the performance of appropriate sensitivity analyses to assess the impact of missing data when changing the underlying assumptions about the missing data mechanism remains imperative.

For more information: "Finding the most appropriate methods for handling missing data is essential... but does not lessen the importance of taking active steps to minimise the occurrence of missing data in the design and conduct of RCTs."

Are people with lifestyle-related chronic disease more inclined to gamble with their health?

**Project team:** Thomas Rouyard, José Leal, Alastair Gray

People diagnosed with a lifestyle-related chronic disease such as Type-2 diabetes (T2D) must decide whether to adopt a healthier lifestyle or not, considering both the benefits (better health outcomes in the long run) and the costs (more commitments in their daily life, such as exercising regularly). In real life, physicians observe low rates of adherence to healthy lifestyles in these populations. One hypothesis to explain this trend is that these patients have different underlying risk preferences. Putting it simply, they may be more inclined to “gamble with their health” than the average person.

HERC researchers have conducted a study to measure the risk preferences of both people living with T2D and controls. Focusing on a specific trade-off between health outcomes and behaviour change incurred by the management of T2D, they found that patients express strong risk aversion in this context. In other words, evidence suggests that risk seeking behaviour (the “taste for gambling”) does not explain lack of adherence to a healthy lifestyle in T2D populations. One hypothesis to explain this trend is that these patients have different underlying risk preferences. Putting it simply, they may be more inclined to “gamble with their health” than the average person.

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These results suggest that non-adherence to a healthy lifestyle may alternatively be explained, at least partly, by an underestimation of the risks associated with T2D. In the medical literature, it has been shown that people with T2D largely underestimate their risks of developing complications and that better risk communication interventions are needed. It was previously thought that such interventions are doomed to fail because patients are naturally inclined to gamble with their health. We have shown that this is not the case, i.e. more effective risk communication interventions may increase adherence to a healthy lifestyle. Future work at HERC will explore how risks can be better communicated to people with lifestyle-related chronic disease.

For more information: "More effective risk communication interventions may increase adherence to a healthy lifestyle."
All of these papers focused on the overarching issue of how to appropriately consider and assess the value of NGS technologies.
Can we reduce demand for antibiotic prescriptions? Or might our efforts backfire?

Project team: Laurence Roope, Sarah Wordsworth

Taking antibiotics when they are not necessary is a major concern, because it causes bacteria to become resistant to antibiotics. This means that, in the future, we may not be able to find antibiotics that can cure serious illnesses. Recent research from Public Health England found that at least 20% of all antibiotics prescribed by GPs in the UK are likely to be inappropriate. Flu-like conditions and other respiratory conditions are the most common reasons for inappropriate prescribing. It is thought that antibiotics are often given unnecessarily because GPs think their patients expect them.

In a recent HERC study, published in Eurosurveillance, we used an online survey to ask more than 2,000 adults from the UK questions about their attitudes to antibiotics. We found that nearly 40% of people would ask their doctor for antibiotics if they had flu-like symptoms that lasted for five days. Perhaps not surprisingly, these people tended to believe antibiotics would be effective in this situation, and to have low awareness of the problem of antibiotic resistance. This suggests that well-designed public information campaigns about inappropriate antibiotic use and antibiotic resistance might help reduce antibiotic requests for flu-like symptoms.

However, we found that providing information about unnecessary antibiotic use and antibiotic resistance might backfire, leading many people to actually be more likely to ask for antibiotics for flu-like symptoms. In fact, among people with low awareness of antibiotic resistance, many more said the information we provided would make them more likely – rather than less likely – to ask for antibiotics.

Our findings suggest that it is essential to carefully design and test messages about inappropriate antibiotic use and antibiotic resistance before using them in public health campaigns. Our team are therefore developing and testing new messages – in the hope that we can soon help people realise they can treat flu-like symptoms more effectively, and more safely, without antibiotics.

For more information: HERC

Spotlight on STEPHEN ROCKS

I joined HERC as a Researcher in February 2018 to work on an evaluation of child and adolescent mental health services (CAMHS) in the South of England, funded by the local CLAHRC and Clinical Commissioning Groups. This is very topical; CAMHS have been in the news frequently with issues around waiting times and access to care. Across England, services are changing as part of government-mandated local transformation plans. The changes are complex, involving new ways of working and engaging the community sector. Transformations are also phased in time. This gives us, as researchers, the opportunity to compare services where changes have been made with those yet to begin their transformations.

We are currently doing this: using routinely collected data and a difference-in-differences approach, supplemented with propensity score matching, to compare transformed CAMHS with those delivering a more conventional service. This approach will help us to assess whether the transformations meet their objectives, including allowing more people to access CAMHS and reducing waiting times. This is a mixed methods project and colleagues in the Department of Psychiatry and the Department of Primary Care are conducting qualitative research to get a fuller picture of the changes taking place. I am excited to work on this project. I enjoy the challenge of evaluating complex interventions, and consider it crucial that those commissioning the services have evidence to inform decisions going forward.

Prior to joining HERC, I was part of the evaluation team at the UK charity Citizens Advice. Before that I worked at a consultancy mainly on mixed methods evaluations for organisations such as the British Heart Foundation, Macmillan Cancer Care, and for local authorities. Being part of HERC gives me the opportunity to deepen my skills in health economics and I have thoroughly enjoyed my time in the department so far.

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 September, Dr John Buckell, Postdoctoral Associate, Health Policy and Management, Yale School of Public Health visited to give a presentation on: How do FDA policies impact demand for cigarettes and e-cigarettes in the US tobacco market? Predictions from discrete choice experiments.

In October, Michelle Tew, Research Assistant at the Centre for Health Policy, Melbourne School of Population and Global Health, University of Melbourne gave a seminar entitled: Estimating survival: Does patient reported quality of life matter? during a short academic stay at HERC.

In November, Dr Eleonora Fichera, Senior Lecturer in the Department of Economics at the University of Bath, gave a presentation on: Do consumers respond to “sin taxes” heterogeneously? New evidence from the tax on sugary drinks using retailer scanner data.

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@dph.ox.ac.uk

Commonwealth Fencing Championships

HERC Researcher Stephen Rocks is a keen fencer, a sport that he started when growing up in the Shetland Islands in the North of Scotland. In late November Stephen will travel to Australia to represent Scotland in the Commonwealth Fencing Championships, hoping to emulate his success in 2014 when he won a bronze medal. This is very exciting, but also expensive - the athletes have to cover their own costs. To raise money for this Stephen is running a prize draw featuring a range of goods donated by Shetland businesses. You can enter at https://www.justgiving.com/crowdfunding/prize-draw-stephen-fencing.
**Staff News – Welcome to:**

**Francesco Salustri** who joined HERC in September 2018 as a Senior Researcher in Munich, Germany, working on the behavioural and experimental network of the European Research Network on Economics of Health Care. Francesco is working on heterogeneous treatment effects in clinical trials and on the behavioural implications of ambiguity and risk attitudes in health related decision-making processes.

**Paolo Candido** who joined HERC as a Researcher in October 2018. Paolo is currently working with Ramón Luengo-Fernández and John Leek on modeling the economic impact of stroke in Europe. This study will assess the impact on nationwide costs and outcomes of investing in a number of priority areas including prevention strategies, pioneering new treatments and rehabilitative care interventions for stroke survivors.

**Sarah Briggs** who joined HERC in November 2018 as a DPhil student working with Sarah Wordsworth. Sarah was previously a Medical Oncology trainee, but is now working on the development of targeted approaches to bowed screening through incorporating genetic and environmental risk factors, and evaluating the cost-effectiveness of this approach.

**Ana Gobernati-Cruz** who joined HERC in October 2018, also as a DPhil student under the supervision of Sarah Wordsworth. Ana will conduct health economic analyses to understand how best to deploy whole genome sequencing technology for the diagnostics of infectious diseases in low- and middle-income countries.

**Mi Jun Keng** who joined HERC in October 2018 as a Researcher and has recently been successful in obtaining PhD status under the DPhil programme at the Nuffield Department of Population Health to develop a diabetes model using data from the ASCEND trial.

**Thomas Rouyard** on successfully completing his PhD entitled ‘A Health Economic Approaches to Personalised Risk Communication: nudging people with type 2 diabetes towards better self-management’ in September 2018.

**Claire Simonis** who also successfully defended her PhD entitled ‘Quantifying and Targeting Reduction in Uncertainty within a Cost-Effectiveness Analysis’ at the University of Cambridge in October 2018.

**Mara Violato** who has been awarded the title of University Research Lecturer. This is conferred on researchers who can demonstrate substantial independent research achievements, commitment to teaching, and a sustained and continuing contribution to the general work of the Medical Sciences Division.

**Sarah Wordsworth** who joined HERC as a Research Fellow in June 2018. Sarah has been awarded a 2018 Doctoral Scholarship to work on successfully defending her DPhil entitled “A Behavioural Economic Approach to Personalised Medicine” at the University of Newcastle, September 2018.

**Seamus Kent** who is a total diet replacement cost-effective for the routine treatment of obesity?

**Presentations by members of HERC**

- **European Society of Cardiology Congress 2018**
  - **Bobby Mihaylova** and **Kamran Behravesh**
  - **Apololos Tsaiachristas**

- **UK-China Workshop on the Economic Analysis of Large Medical Databases**
  - University of Peking, China, August 2018

- **UK Obesity Congress**
  - University of Newcastle, September 2018

- **Golden Helix Summer School**
  - Syros Island, Greece, September 2018

- **International Summit on Population Genomics**
  - London, September 2018

- **5th U-Px Personalised Medicine Day**
  - Liverpool, September 2018

**Recent Publications**

7. Nauj M, Buse J, et al. [includes Gray A]. Health-related quality of life assessed with EQ-5D in people with type 2 diabetes participants in the LEADER trial. Diabetes, Obesity and Metabolism. 2018. 10:1111/dob.13547

**45th Annual Meeting of the European Society for the Study of Diabetes (EASD)**

- Zander Nasmey, October 2018
- Alastair Gray

**Frauke Becker**

- Lifetime cost-effectiveness simulation of exenatide once-weekly in type 2 diabetes: evidence from the EXSCEL trial [Poster]

**Liam Mc Morrow**

- Comparison of medical resources, costs, and health utilities among patients with CHD and impaired glucose tolerance in the acarbose cardiovascular evaluation trial (ACE) [Poster]

**World Stroke Congress 2018**

- Montreal, Canada, October 2018
- Ramón Luengo Fernández

**Presentation of projects in 2019**

A longitudinal study of child mental health in the UK: the role of income and other risk factors – supervised by Mara Violato, Claire Carson, and Cathy Crosswell (University of Reading). Quality of life in informal caregivers of people with dementia – supervised by Alastair Gray, Filipa Landeiro and Chris Butler (Nuffield Department of Clinical Neurosciences).

For more information on these projects, and to apply, please visit [HERC website](https://www.ercox.ac.uk)

**HERC is advertising two DPhil (PhD) projects for admission in 2019**

- A Health Economic Perspective on the genomics of rare diseases: evidence from genome sequencing technology for the UK [includes Violato M, Buchanan J].
- Economic Evaluation In Genomic Medicine [includes Wordsworth S, Buchanan J].

**Funding**

**Apostolos Tsaiachristas** and **Sarah Wordsworth** have recently been awarded funding by the EU for a project titled ‘Healthcare- and pharmacoeconomic models in support of the International Consortium for Personalised Medicine’ (iCoPerMED). The aim of this project is to provide guidance to the International Consortium for Personalised Medicine on state-of-the-art health economic modelling and on financing and payment strategies for rapid uptake of personalised medicine.

**Thomas Rouyard** has been awarded a 2018 Doctoral Transition Innovation Fellowship, funded by the European Institute of Innovation & Technology, to further develop and launch an innovative risk communication tool named PERCODA to help doctors in primary care better communicate risks of diabetes with poorly controlled diabetes.

**www.ercox.ac.uk**