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Evaluating the lifetime cost-effectiveness of population health interventions alongside clinical trials

Project team: Apostolos Tsiachristas and Alastair Gray

Most clinical trials of population health interventions have relatively short follow-up periods. However, decision makers are interested in the impact of these interventions throughout people's lifetimes, so providing decision-makers with relevant evidence is a challenge for health economists. We recently faced this challenge in an economic analysis conducted alongside the STRATEGIC trial, which investigated whether embedding a range of novel interventions within the cervical screening program in England could improve young women's receptivity to and uptake of screening.

We developed a methodological approach to measure the lifetime cost-effectiveness of the interventions by combining different research methods and data sources including: 1) a template to measure intervention costs; 2) combining trial data on screening uptake with data from the literature to estimate the healthcare costs of screening; 3) a systematic literature review to obtain information about the lifetime costs and QALYs associated with attending/not attending screening;

4) an assessment of the quality of the selected studies; 5) a meta-analysis to estimate pooled lifetime costs and QALYs, weighted by study quality; 6) a decision analytic model that combined all of this data to calculate the incremental cost per QALY gained for each intervention from an NHS perspective using a lifetime horizon; 7) sensitivity analyses to address uncertainty; and 8) a scenario analysis to estimate the nationwide impact of the interventions.

The incremental cost per QALY gained of all the interventions was below £10,000, but only timed appointments and unrequested Human Papilloma Virus self-sampling were likely to be cost-effective at a threshold of £20,000 per QALY gained. Further analyses suggested that introducing these interventions independently in England would yield 2,785 QALYs at an additional cost of £22m. However, further work is required to establish the optimum way of combining them.

Our approach has generated results which will help decision makers to improve the cervical screening programme in England and could be used to evaluate other population health interventions. Further work is required to establish the optimum way of combining trial-based results with extrapolations.

For more information: **HERC**



Our approach has generated results which will help decision makers to improve the cervical screening programme



Is restrictive blood transfusion after cardiac surgery cost-effective?

Project team: Sarah Wordsworth and Liz Stokes

Anaemia is common after cardiac surgery. Although red blood cell transfusion is the preferred treatment for acute anaemia, the level of anaemia at which the benefits of transfusion outweigh the risks (e.g. of infection due to immunosuppression) is unclear. Transfusion guidelines increasingly recommend restrictive transfusion (at a lower haemoglobin level) as safe and appropriate for most patient groups, but there is uncertainty around this strategy for cardiac surgery patients who may be less able to compensate physiologically for anaemia.

As reported in Issue 11 of this newsletter, to address this uncertainty, the Transfusion Indication Threshold Reduction (TITRe2) trial was conducted. This was a multicentre RCT funded by the NIHR Health Technology Assessment (HTA) Programme, comparing restrictive and liberal transfusion thresholds after cardiac surgery.

HERC researchers conducted the first full trial-based economic evaluation of alternative transfusion thresholds alongside the TITRe2 trial, and the results were recently published in *BMJ Open* and the *HTA* journal. While the costs associated with red blood cell transfusion were significantly lower in the restrictive group, mean healthcare costs from surgery to three months follow up were similar in the restrictive and liberal groups (£17,945 and £18,127 respectively). Detailed resource use data were collected, particularly around complications, and this was a large trial (n=2,003), so we are confident that there was genuinely not a large difference between the two groups. Outcomes from surgery to three months were measured in QALYs, and these were also effectively identical in the two groups. Partly due to the small differences, there was great uncertainty around the ICER.

From an economic perspective, we concluded that there is no difference between the two groups. Although a restrictive threshold saves blood, a scarce resource, and reduces the costs associated with transfusion, there is no evidence to suggest that a restrictive blood transfusion threshold reduces overall NHS costs. This is an important message for policy makers, since it goes against what is often assumed.

For more information: **HERC**



...there is no evidence to suggest that a restrictive blood transfusion threshold reduces overall NHS costs



The impact of socioeconomic factors on the uptake of disease prevention measures

Project team: Peter Eibich and Alastair Gray

We are pleased to announce that HERC Senior Researcher Peter Eibich has recently been awarded a three-year Research Fellowship by the Wellcome Trust to study the impact of socioeconomic factors on the uptake of disease prevention measures.

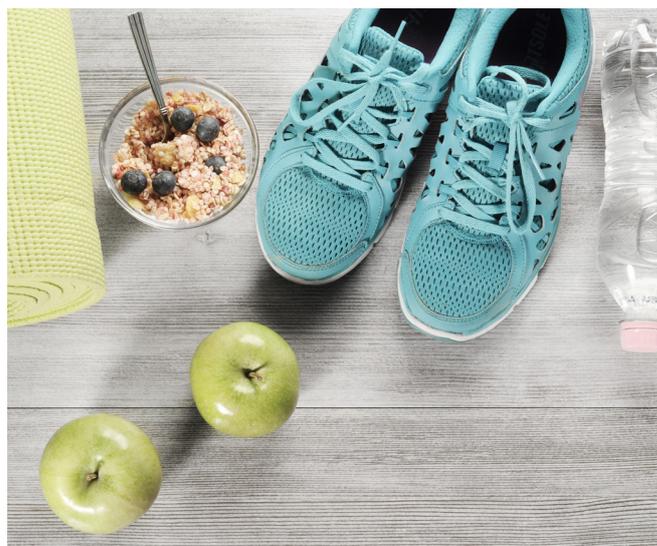
Population ageing is likely to result in an increase in the burden of non-communicable diseases such as cardiovascular diseases, cancer or type 2 diabetes for which age is a major risk factor. However, many of these diseases can be prevented; for example, according to the World Health Organization, at least one third of all cancer cases are preventable. In addition, early detection (e.g. through screening) can reduce the risk of later complications and mortality. Therefore, prevention and early detection play a major role in maintaining the health of an ageing population.

However, uptake of healthy behaviours and early-detection programmes by older adults is often below desired levels. For example, more than two-thirds of older adults in the US fail to meet government guidelines for physical activity. Similarly, uptake of bowel cancer screening in England between 2012 and 2015 was just 58% with large regional variation.

Peter's project aims to investigate the social and economic factors that affect uptake of healthy behaviour and screening programmes among individuals aged 50 and above. As part of this project, Peter will develop a new health economic model which will be used to derive hypotheses on the relationship between uptake of prevention and socioeconomic factors such as employment status. In the second part of the project, he will use econometric methods that allow the identification of causal relationships to test these hypotheses on international datasets, including for instance the English Longitudinal Study of Ageing. Peter will focus in particular on factors such as voluntary work that are associated with time constraints.

Keep an eye on future editions of the HERC newsletter to hear more about this exciting work.

For more information: **HERC**



HERC DPhil (PhD) projects for 2017

The Nuffield Department of Population Health is offering an extensive list of research projects available to potential DPhil students applying for admission in October 2017.

There are four projects available at HERC, summarised below. For more information about these projects, and to apply, please visit, <https://www.ndph.ox.ac.uk/study/dphil-population-health/2017-DPhil-research-projects-list/herc-projects>

Deadline for applications is 12:00 noon UK time on Friday 6th January 2017.

Conducting economic evaluations of perinatal interventions from a family perspective

Supervisors: Oliver Rivero-Arias and Helen Dakin

Perinatal and maternal health interventions invariably affect the quality of life and economic well-being of the whole family. Despite interest from NICE and the literature, most economic evaluations focus on NHS costs and the benefits for the child. This project aims to explore the theoretical and practical challenges involved in taking a family perspective and to develop methods to measure and aggregate the benefits and costs of interventions across different family members. The project will provide training and experience in literature reviews, preference elicitation, trial-based economic evaluation, econometric analyses and decision-analytic models.

For more information: <https://www.ndph.ox.ac.uk/study/dphil-population-health/2017-DPhil-research-projects-list/conducting-economic-evaluations-of-perinatal-interventions-from-a-family-perspective>

Linking genomic and clinical data in health economic evaluations: identifying challenges and exploring potential solutions

Supervisors: James Buchanan and Sarah Wordsworth

Whole genome sequencing (WGS) is a technique that determines the complete DNA sequence of an organism's genome. Few economic evaluations of WGS have been undertaken to date due to issues surrounding data availability and study design. 'Big data' initiatives such as the 100,000 Genomes Project in the UK could transform the way that economic evaluations of genomic interventions are conducted, but there are a number of challenges that are yet to be resolved in terms of conducting such analyses. The aim of this project is to investigate these challenges and opportunities using data from the 100,000 Genomes Project, with an emphasis on rare diseases.

For more information: <https://www.ndph.ox.ac.uk/study/dphil-population-health/2017-DPhil-research-projects-list/linking-genomic-and-clinical-data-in-health-economic-evaluations-identifying-challenges-and-exploring-potential-solutions>

Unhealthy behaviour clusters, socio-economic background and health outcomes

Supervisors: Iryna Schlackow and Bobby Mihaylova

Smoking, alcohol consumption, poor diet and lack of physical exercise are leading risk factors for a multitude of chronic diseases. These behaviours, potentially determined by socio-economic characteristics, disease history or genetics, frequently co-exist. The project will use data, such as the UK Biobank and/or English Longitudinal Study of Ageing, to characterise behavioural clusters, assess their associations with health outcomes, and explore the heterogeneity of findings by socio-economic and other characteristics, with a view to supporting the development of novel public health initiatives.

For more information: <https://www.ndph.ox.ac.uk/study/dphil-population-health/2017-DPhil-research-projects-list/unhealthy-behaviour-clusters-socio-economic-background-and-health-outcomes>

Use of cholesterol- and blood pressure lowering interventions

Supervisors: Bobby Mihaylova and Iryna Schlackow

Cholesterol- and blood pressure-lowering medications, shown to cost-effectively reduce cardiovascular risk and recommended in clinical guidelines, are at the forefront of cardiovascular prevention. However, their use has remained suboptimal even in countries with comprehensive healthcare provision and the debate is ongoing on whether such drug interventions have a complementary or substitute role for personal health behaviours. The project will investigate the role of socioeconomic, behavioural and cognitive factors in the use of cardiovascular preventive interventions using population surveys from UK and Europe.

For more information: <https://www.ndph.ox.ac.uk/study/dphil-population-health/2017-DPhil-research-projects-list/use-of-cholesterol-and-blood-pressure-lowering-interventions>

Spotlight on FRANCESCO FUSCO



After visiting HERC as a PhD student in January 2014 I subsequently joined as a post-doctoral researcher in November 2015. I am currently involved in projects ranging from orthopaedics to cancer research. The TOPKAT study is a multicentre randomised clinical trial (RCT) funded by NIHR which is investigating the cost-effectiveness of partial knee replacement.

This project will initially assess the drivers of costs and quality of life up to one year after knee surgery, with a full economic evaluation then taking into account the outcomes up to five years after surgery. The FOXFIRE study is an add-on multicentre RCT in patients with liver metastases from colorectal cancer. In this study I will evaluate the costs and outcomes associated with adding radio-embolization to standard care (i.e. chemotherapy).

Before joining HERC I completed my PhD at Scuola Superiore Sant'Anna in Pisa, Italy, on innovation management in healthcare. My PhD project was funded by Telecom Italia and contributed to the development of an innovative knee telerehabilitation system. I was responsible for the development of the business model and the assessment of the economic impact of the new system. This economic evaluation was based on a Markov model which used data from the Knee Arthroplasty Trial to conduct survival analysis.

My experience at HERC has been very rewarding. First of all, I have been able to publish my PhD paper which was also well-received in social media. I was also able to further develop my decision and survival modelling skills by refining the work of FOXFIRE and TOPKAT. In addition, I have enjoyed taking part in non-research related activities such as teaching and public engagement. I have benefited greatly from these experiences and I am looking forward to new challenges that will help me to further improve as a researcher.

Staff News – Welcome to:



David Jones:
David joined HERC in October 2016. Prior to this appointment he completed an internship at The Global Fund researching the effect of Harm Reduction services on HIV prevalence in Injecting Drug Users. David will be working alongside the RADICAL trial on the cost-effectiveness of non-invasive rapid assessment of chronic liver disease using Magnetic Resonance Imaging with LiverMultiScan.



Mi Jun Ken:
Mi Jun also joined HERC in October 2016. She recently graduated from LSE with a MSc in Operational Research, and also has a Mathematics degree. She will be working on the REVEAL study, assessing long term health and economic effects of Anacetrapib for cardiovascular disease prevention.



Winnie Mei:
Winnie recently joined HERC as a researcher in health economics after working as a medical statistician at the Clinical Trials Research Unit in Oxford for over 2 years, where she worked on the China Kadoorie Biobank study. Winnie will be working with Bobby Mihaylova on an economic evaluation of Anacetrapib on reduction of CVD, as well as the LiverMultiScan study.



Stefania Manetti:
Stefania is an academic visitor from Sant'Anna School of Advanced Studies in Pisa, Italy, visiting HERC for 3 months until December 2016. Stefania is working with José Leal to update a cost-effectiveness decision model for secondary hip fracture prevention, and also considering the impact of using different sources of hospital costs.

HERC Seminars

Convenor: Apostolos Tsiachristas

The HERC seminar series resumed in September 2016, when Apostolos Tsiachristas (Senior Researcher) took over as the new Seminar Convenor from Laurence Roope.

In September, it was our great pleasure to welcome **Philip Clarke**, Professor of Health Economics at the Melbourne School of Population and Global Health, University of Melbourne who gave a talk entitled: *A Brief History of Economic Evaluation*.

In October, **Catia Nicodemo**, Research Fellow Centre for Health Service Economics & Organisation, Department of Economics, University of Oxford visited us to give a talk on: *The determinants of GP referrals and elective hospital admissions: a practice level study*.

Finally, in November **James Hammit**, Harvard University & Toulouse School of Economics, presented on: *Valuing Non-fatal Health Risks: Monetary and Health-Utility Measures*.

Details of forthcoming talks can be found on the HERC website: <http://www.herc.ox.ac.uk/upcoming-events>

To be added to our mailing list for future seminars, email us at herc@dph.ox.ac.uk

Presentations by members of HERC

International Summer School on Integrated Care
Oxford, June 2016

Apostolos Tsiachristas
Defining outcomes, measuring performance and putting it to practical use
Financing integrated care and aligning key processes

EIT Health Summer School
Oxford, August 2016

Apostolos Tsiachristas
Economic evaluation of healthcare interventions for rare cancers

German Economic Association Conference
Augsburg, September 2016

Peter Eibich
Retirement, intergenerational time transfers and fertility

Centre for Public Health, Queen's University Belfast
Belfast, September 2016

Richéal Burns
Cost-effectiveness of cancer screening: Results from the PROSPECTIV Study

Cairnes School of Business and Economics, NUI Galway
Galway, September 2016

Richéal Burns
Economic burden of malignant blood disorders across Europe

Mt Hood Diabetes Challenge
Switzerland, September 2016

Helen Dakin
Combining parameter and sampling uncertainties within diabetes clinical outcome simulation models

Alastair Gray
Can delaying onset of diabetes be cost-effective? A simulation study based on NAVIGATOR data

José Leal
Life-expectancy and costs for people with type 2 diabetes

Challenges and opportunities for decision modelling from the onset of pre-diabetes onwards

Helix Foundation Summer School Conference: Cancer Genomics and Individualized Therapy

Greece, September 2016
Sarah Wordsworth
The economics of cancer genomics: is it cost-effective?

NDPH DPHI Poster Prize Competition 2016
Oxford, October 2016

Seamus Kent (winner of the Best Poster prize)
Hospital costs in relation to body mass index in over 1 million middle-aged and elderly women in England

Filipa Landeiro
Delayed hospital discharges and social isolation among elderly hip fracture patients in England

Ines Rombach
The current practice of handling and reporting missing outcome data in 8 widely-used PROMs in RCT publications: A review of the current literature

European Union Geriatric Medicine Society Conference
Lisbon, October 2016

Filipa Landeiro
Delayed discharges and social isolation in countries with ageing populations: England vs Portugal

ISPOR 19th Annual European Congress
Vienna, November 2016

Sarah Wordsworth
Health-economic evaluation of genomic technologies: which issues arise?

General Practice Research in Infections Network Conference
Oxford, November 2016

Jane Wolstenholme
A systematic review and cost effectiveness decision model of the early use of antibiotics for at risk children with influenza

UK Stroke Forum conference
Liverpool, November 2016

Kusal Lokuge
Procedural risks of carotid endarterectomy and carotid artery stenting have improved since 2005: results from a systematic review of observational studies

Recently Funded

Alastair Gray is collaborating with John Gallacher of the Department of Psychiatry, University of Oxford, Martin Knapp at the LSE and 22 other collaborators on an EU funded study entitled: *Real world Outcomes across the Alzheimer's disease (AD) spectrum for better care: Multi-modal data Access Platform (ROADMAP)*. This study aims to benefit AD patients and their caregivers by 1) using use-case based pilot studies to assess tools and methods of data integration for patient outcomes that are scalable, transferable and useful for disease modelling, and 2) developing tools and methods for stakeholder engagement, understanding the ELSI context, and evaluating the HE and budget impact, of a real-world evidence approach in AD. The initial pilot study will last two years with a further follow-up study planned if all goes well.

PUBLICATIONS

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Tsiachristas A, Smith AD. *B-vitamins are potentially a cost-effective population health strategy to tackle dementia: Too good to be true?* Alzheimer's and Dementia: Translational Research and Clinical Interventions. 2016; 2(3):156-161

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