Driven by widespread antibiotic use, bacteria are becoming increasingly resistant to treatment, and the pipeline for new antibiotics is dry. Recent reports estimate that antimicrobial resistance will cause up to 10 million annual deaths globally by 2050 if no action is taken.

As pressure mounts to secure international commitments to tackle the problem, it is useful to consider what we can learn from another major global challenge – climate change. HERC researchers – in collaboration with colleagues in Oxford, Exeter, London, the Netherlands, Germany and Sweden – considered this topic in a recently published paper in Science.

In theory, carbon and antibiotic consumption could be reduced to ‘optimum’ levels, reflecting their social costs, via taxes or quotas. However, estimating these optimum levels is extremely complex. Rather than waiting for optimum policies to curb resistance, we should agree ambitious but pragmatic targets for reducing antibiotic use without delay.

A system in which GP practices are taxed on each antibiotic they prescribe, or a tax is applied at a local or national level, might provide an effective incentive for reducing prescriptions. The revenue raised could then be invested in antibiotic development. An alternative may be to establish a regulatory body that gives prescribers permits or quotas for prescribing, then lets the market determine the price. Taxes and quotas could also be used to discourage unnecessary use of antibiotics in animals and reinvest in research and development. However, if the cost of antibiotics increases, it will be vital to develop mechanisms to reduce the risk that they will only be used by those who can afford them.

A key obstacle to developing new antibiotics is that the end product will be held back for as long as possible. This gives little incentive to developers, whose rewards depend on sales volumes. New ways are needed to make antibiotic development profitable, decoupling the rewards for developing new antibiotics from the volumes that will be sold.

There is a great opportunity for economists, across many different fields, to engage with this pressing global problem; we hope that they rise to this challenge.

For more information: HERC

An alternative may be to establish a regulatory body that gives prescribers permits or quotas for prescribing, then lets the market determine the price.
Improving health-related quality of life (HRQoL) is a key goal when managing chronic diseases such as diabetes. As a result, patient-reported outcome measures are increasingly being collected during clinical trials. However, few of the diabetes outcomes trials reported in recent years have so far published quality of life information. In the Liraglutide Effect and Action in Diabetes: Evaluation of cardiovascular outcome Results (LEADER) trial, 9,340 patients with type 2 diabetes at high risk of cardiovascular disease were randomised and followed up for a median of 3.8 years. The EQ-5D-3L survey instrument was administered at baseline and every 12 months in a subset of 3014 patients from Canada, Denmark, Germany, Ireland, Italy, Netherlands, Spain, Sweden, the UK and the USA.

We compared changes in utility index scores and visual analogue scale (VAS) scores from baseline to 36 months in participants randomised to liraglutide or placebo, and assessed which complications had the greatest impact on HRQoL.

At 36 months, we found that the EQ-5D utility index had deteriorated less in the liraglutide group (−0.058) than in the placebo group (−0.082), a modest but significant difference. A significant difference was also observed in the VAS score. These differences appeared to be driven mainly by shifts in the domains of mobility and self-care.

The main events contributing to poorer HRQoL were stroke, heart failure, malignant neoplasm and confirmed hypoglycaemia. But even after adjusting for all key factors and events into account, a small estimated treatment difference was still observable in the EQ-5D index score.

LEADER is the first trial that we are aware of in a patient population of this type to report a modest but significant benefit in patient-reported health status using the EQ-5D with an antihyperglycaemic agent (liraglutide) compared with placebo. This benefit may be of clinical relevance and requires further study. It also demonstrates the value of including measures such as EQ-5D at more than one time point in such studies.

For more information:

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 March, Dr Benjamin Craig, Associate Professor, Department of Economics, University of South Florida, visited HERC to present his work on ‘Health Preference Research: past, present and possible future.

In May, Dr Padraig Dixon, Research Fellow, Bristol Medical School, Population Health Sciences, was invited to HERC to present his work on ‘The casual effect of adiposity on hospital costs: Mendelian Randomization analysis of over 300,000 individuals from the UK Biobank.

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

Funding

Borislava Mihaylova, Alastair Gray and Iryna Schlackow were recently awarded NIHR HTA funding for a 3-year project entitled “Cost-effectiveness of statin therapies evaluated using individual participant data from large randomised clinical trials”. In this project, jointly developed by the University of Oxford (HERC/CTSU) and Queen Mary University of London, detailed assessment will be performed of the net effects and cost-effectiveness of statins in different categories of people using data from the Cholesterol Treatment Trials’ Collaboration (~28 large randomised trials), the UK Biobank and the Whitehall II study.

Total diet replacements for the routine treatment of obesity

Project team: Seamus Kent, Boby Mihaylova

Despite widespread recognition of the impact of obesity on people’s health and on healthcare services, there are few effective interventions for the routine treatment of obesity.

Two recent clinical trials – DIRECT and DROPLET – have demonstrated that low-energy total diet replacement (TDR) programmes, delivering 810-830 kcal/day, are safe and effective interventions to reduce weight. In DROPLET, the commercially provided TDR programme led to an extra 7.2kg weight loss at 12 months compared to usual lifestyle behavioural support.

HERC researchers collaborated with colleagues at the Nuffield Department of Primary Care Health Sciences to estimate the long-term effectiveness and cost-effectiveness of the TDR programme studied in DROPLET. This was done by projecting the impact of the weight loss observed at 12 months in the study on obesity-related diseases and mortality over people’s lifetime using the PRIMEtime-CE Obesity model (freely available at: https://github.com/seamuskent/PRIMEtime-CE-Obesity). An assumption was made that all weight loss was regained at five years following TDR.

The TDR programme was projected to reduce the incidence of obesity-related diseases, particularly type-2 diabetes, improve quality of life and increase length of life. The higher intervention cost (£762) was only partially offset by reductions in subsequent healthcare costs (£100). The TDR programme was estimated to cost £13,000 for every additional year of life lived in full health, and is therefore likely to be cost-effective in the UK.

In light of the recent clinical and economic evidence, the use of, and funding for, such programmes for the routine treatment of obesity in the NHS should be considered.

For more information:
Statins reduce cardiovascular morbidity and mortality in people over 75

Project team: Boby Mihaylova

Despite overwhelming evidence that statins reduce the risk of heart attacks, strokes and cardiovascular deaths in a wide range of people, uncertainty about their benefits in older people has persisted. Cardiovascular risk increases markedly with age and virtually all people over 75 are at high risk; however, fewer than half of them are taking statins and many stop treatment with advancing age.

Boby Mihaylova collaborated with colleagues from the Universities of Oxford and Sydney, as part of the Cholesterol Treatment Trialists’ Collaboration (CTT), to review and synthesize the data from nearly 187,000 participants in 28 large randomised clinical trials of statin therapy. The study, published in the Lancet, showed that statin therapy produced similar proportional reductions in cardiovascular risk among people older than 75 years as among those younger than 75, and these benefits far outweighed any rare side-effects. Similar risk reductions were noted among older people with and without previous cardiovascular disease, though the evidence is more limited in older people without previous cardiovascular disease.

All statins are now generic and available for less than 10 pence per day. At these prices, current evidence suggests that statins are likely to be very cost-effective in all people considered for treatment. However, with a large and growing share of the population considered for treatment, further evidence is required to strengthen recommendations with a large and growing share of the population considered for treatment. In a new HTA-funded project, co-led by Boby Mihaylova and Colin Baigent (CTT and University of Oxford), detailed analyses of the net effects and cost-effectiveness of different statin regimens in different people, including older people with and without previous cardiovascular disease, are being developed using the individual participant data in statin trials and UK population cohorts.

For more information: HERC

Cost-effectiveness in a placebo surgery randomised controlled trial

Project team: Ines Rombach, Alastair Gray

HERC recently conducted the cost-effectiveness analysis of the Can Shoulder Arthroscopy Work (CSAW) placebo surgery trial. This study investigated the effectiveness of subacromial decompression in patients with subacromial shoulder pain (pain on raising the arm), a common condition linked to reduced quality of life and socioeconomic burden. The surgical procedure removes the bone spur thought to be the cause of this condition, and its use in the UK has increased sevenfold between 2000-2010, despite many patients responding to conservative treatment.

Consenting participants were randomised to subacromial decompression, placebo surgery (arthroscopy only without the removal of bone and soft tissue) and no treatment. The trial found a statistically significant but not clinically important difference in the outcomes between the surgical groups and the no treatment comparator. No difference was found between subacromial decompression and arthroscopy only, putting into question the value of this procedure for this patient population.

For the cost-effectiveness analysis, we carefully considered the potential interpretation of the results; arthroscopy only was offered in the trial to investigate any placebo surgery effects, but is not a valid treatment in this patient population. As such, even if arthroscopy was shown to be cost-effective, it could not be recommended for use in these patients. Given this, we focused our cost-effectiveness analysis on the comparisons with the subacromial decompression.

We found no evidence of subacromial decompression being cost-effective over no treatment over the 12 months of trial follow-up. Extrapolation to two years indicated that subacromial decompression could be cost-effective in the longer-term, but these results were very sensitive to the assumptions made about costs and quality adjusted life years beyond the follow-up of the trial.

For more information: HERC

The updated HERC Database of Mapping Studies is now available

This includes 38 new studies published before January 2019 describing 82 mapping algorithms, including new source instruments, such as the Glasgow Outcome Scale, Kessler Psychological Distress Scale and 22-item Sino-Nasal Outcome Test (SNOT-22). Version 7 includes a total of 182 studies reporting 386 mapping algorithms, including 42 mapping to EQ-5D-5L. The database can be filtered by disease area or source/target instruments to quickly identify mapping studies that may provide data inputs for economic evaluation and assess the novelty of new mapping studies. The database can be accessed at https://www.herc.ox.ac.uk/downloads/herc-database-of-mapping-studies.

Spotlight on CLAIRE SIMONS

I returned to HERC in January 2018 to work on, in the first instance, a monitoring project alongside Boby Mihaylova and Iryna Schlackow. This work aims to identify the optimal monitoring strategy for people with reduced renal function in primary care making use of large, UK based, routine healthcare sources of individual patient datasets to help develop the models. These models project the long-term cardiovascular events, quality of life, survival and healthcare costs of people with reduced renal function and can be used to evaluate the cost-effectiveness of CVD preventive interventions in this population.

Going forward, I will be working alongside Boby and Iryna on a project estimating the cost-effectiveness of statin therapies in different populations using individual participant data from large randomised clinical trials.

Prior to January 2018, I was a PhD student at the HERC Biostatistics Unit, University of Cambridge. My thesis developed statistical methods to quantify uncertainty and target where reducing this uncertainty would be most beneficial in a CEA. This would enable policy decisions, based on the CEA models, to be better informed. I focused in particular on two under-explored areas of uncertainty – adherance to interventions and stratification of the optimal treatment decision by continuous disease measures. I hold a MMATH in Maths and Statistics (University of Oxford) and an MSc in Health Economics (University of York) and was also an NIHR Research Methods Fellow in Health Economics in HERC between 2012 and 2014.

Since returning to HERC all members of staff and students have made me feel welcome. I am looking forward to further developing my skills as a researcher through my current and future projects.
**Welcome to:**
understanding health behaviours and econometric modelling.

**Congratulations to:**
Liam Mc Morrow, who joined HERC as a Senior Researcher in April 2019, after completing his PhD in health economics at the University of Aberdeen. Liam worked on the ACE trial, a large multicentre randomised control trial in China evaluating the effect of acarbose on patients with prediabetes and a history of cardiovascular disease. He also worked on a PHE-funded, EU public private consortium funded by the Innovative Medicines Initiative, evaluating novel biomarkers to manage complications with prediabetes and diabetes. In all his work Liam has been able to demonstrate his strong health economics skills. Liam has been awarded funding from EIT Health-startup accelerator the HealthPoint Fund to develop a digital health innovation that helps people with diabetes to manage their condition by embedding community health. We wish Liam much happiness and success in the future.

**Farewell to:**
Darren Barber who for the last two years, held the position of Administrator and Assistant to Professors Alastair Gray and Philip Clarke. As well as contributing greatly to the production of ten editions of the newsletter, Darren was involved in a wide range of Unit activities from providing PA support, to administering HERC’s three day Applied Methods training course to organizing a large part of HERC researchers to climb Ben Nevis. He was a valued member of HERC who will be greatly missed by all. Darren has joined the Metropolitan Police, where we wish Darren much happiness and success in the future.

**Recent Publications**