Personalised Medicine and Resource Allocation Conference Co-Hosts

Ingrid Slade

Ingrid Slade is the Director of the Centre for Personalised Medicine, an innovative partnership between St Anne's College and the Wellcome Trust Centre for Human Genetics, University of Oxford, which aims to provide a focus for multidisciplinary interaction, dissemination of knowledge and enhancement of the educational experience of students, faculty, healthcare professionals and the public more broadly. Ingrid trained in medicine at the University of Bristol and went on to specialty training in Clinical Genetics at Great Ormond Street, London. She undertook a PhD at the Section of Genetics and Epidemiology at the Institute of Cancer Research, London, identifying and characterising genes that confer susceptibility to childhood tumours. Ingrid began specialty training in Public Health Medicine in 2011 in order to pursue her academic interest in the implementation and evaluation of genomic medicine within the national healthcare setting. Ingrid is on the Programme Committee of the Mainstreaming Cancer Genetics Programme; a Wellcome Trust funded initiative that aims to make genetic testing part of routine cancer patient care. Her time is divided between the Health Economics Research Centre and Ethox (a bioethics research centre), in the Nuffield Department of Population Health where she works on the themes of resource allocation and priority setting applied to the integration of genomic medicine across the NHS.

Sarah Wordsworth

Sarah Wordsworth is Associate Professor of Health Economics at the Health Economics Research Centre, in the Nuffield Department of Population Health, University of Oxford and a Fellow at St. Anne's College, University of Oxford. After several years working at the Health Economics Research Unit (University of Aberdeen), she came to Oxford in 2003 to develop a research programme on the economics of genetic and genomic technologies. Of particular interest are the economics of translating genomic high-throughput technologies from research into clinical practice, especially in cancer and infectious diseases such as TB. In 2006, she was awarded a fellowship by the National Institute for Health Research to explore the use of economic evaluation in evaluating genomic technologies in the NHS. Sarah works closely with the Oxford Biomedical Research Centre, where she evaluates the translation and implementation of genomic technologies, such as targeted panels, whole exome and whole genome sequencing. Her other interests include costing methodology (which was the focus of her PhD awarded in 2004) and trial based evaluations in the areas of cancer, eye disease, blood transfusion, cardiac surgery and surgery for obesity. She teaches on a range of undergraduate and postgraduate university courses and also teaches advanced cost-effectiveness analysis methods to health economists and policy makers.

Kathryn Phillips

Personalised medicine and resource allocation – an international perspective

Abstract
The need to systematically consider the value of new genetic technologies is inescapable, but challenging. This presentation will discuss the role of health economics, focusing on both the methodological and political opportunities and challenges and how these may vary across countries. I will draw particularly on "takeaways" from the research being done by the *University of California San Francisco Center for Translational and Policy Research on Personalized Medicine* (TRANSPERS). Our Center is focusing on how to address the benefit-risk tradeoffs of new genetic technologies - particularly gene panels and whole genome sequencing – as they move into clinical care and health policy.

Biography
Kathryn A. Phillips is Professor of Health Economics and Health Services Research and Founding Director of the UCSF Center for Translational and Policy Research on Personalized Medicine (TRANSPERS). Kathryn focuses on the translation of new technologies into improved patient outcomes and its impact on clinical care, health economics, and health policy. Her core specialty is personalized (or precision) medicine. Kathryn's work spans multiple disciplines, including basic, clinical and social sciences, and brings together leading experts in academia, industry, healthcare, payers, and government.

Katherine Payne

The challenges of integrating health economics evidence into policy in the area of genomics

Abstract
This presentation will start by clarifying some of the different applications of genomics in the context of personalised medicine. The presentation will take a UK perspective to describe some current examples where economic evidence is used to inform decision making related to the allocation of healthcare resources. The presentation will then use examples of current policies relevant to genomics and personalised medicine to illustrate some of the potential methodological, technical,practical and organisational challenges of integrating health economics evidence into policy development.

Biography
Katherine Payne was awarded a personal chair in health economics at the University of Manchester in August 2010. She has over 17 years of experience working as an academic health economist with different research groups. She has an honorary position with Nowgen – A Centre for Genetics in Healthcare. In September 2007, Katherine was awarded a five-year Research Councils UK Academic Fellowship in Health Economics to focus on the evaluation and valuation of genetic technologies including genetic-based diagnostics and pharmacogenetic tests. Ongoing and recent projects include: evaluating models of service delivery for people with an inherited form of blindness; identifying and costing pathways of care for people with inherited ataxia; building an economic model to identify the most appropriate interval for breast cancer screening; preliminary economic evaluation of high-throughput whole genome sequencing technologies and economic evaluations of pharmacogenetic testing. Katherine has been a member of the NICE Technology Appraisal Committee since October 2003.

Wolf Rogowski

Priority setting for new genetic tests - experiences from the EuroGentest project

Abstract

One clinical area which is directly affected by the exploding body of genetics knowledge is clinical genetic services: the number of diseases that can be tested for has risen from less than 200 in 1993 to more than 4,000 in 2015. In consequence, decisions need to be made about which tests should be funded by public health care payers. Funded by the EU-project "EuroGentest" and in collaboration with experts in genetics, ethics, and health economics, the European Society for Human Genetics therefore explored the topic of priority setting for genetic tests. This presentation briefly summarizes this project which consisted of five steps: first, the development of a theoretical (needs-based) framework for priority setting; second, the operationalization of the multiple criteria in this framework; third, the identification of tentative weights for the criteria by means of a discrete-choice experiment; fourth, the development of a tentative rank order of testing case studies; and fifth, a process of stakeholder deliberation oriented at the principles of accountability for reasonableness to discuss the previous steps among clinicians, patient representatives, and experts. The results are presented and implications for the prioritization of genetic tests are discussed.

Biography

Wolf Rogowski is a health economist at the Helmholtz Center Munich, Institute of Health Economics and Health Care Management in Germany. Since August 2009, he has been head of the institute's research unit "Translational Health Economics". He holds a Ph.D. from Ludwig-Maximilians Universität in Munich and has held visiting fellowships at the Centre of Health Economics at the University of York (UK), the Hastings Center in Garrison, New York (USA) and the Harvard School of Public Health, Boston (USA). Focusing on genetic testing and personalized medicine, Wolf serves as a member of the European Society for Human Genetics' Professional and Public Policy Committee and the scientific advisory board of the Journal of Community Genetics.

Wolf explores the process of translational medicine from a health economics perspective. This includes: the application of cost-effectiveness and value of information analysis to new health technologies; the empirical and theoretical assessment of methods and procedures applied in decision making; and the development of instruments for decision support. He has a particular interest in the intersection of ethics and economics in medical innovation.

Adrian Towse

The economics of next-generation sequencing – how should platform technologies be valued?

Abstract

Platform technologies are used to perform genetic testing. The term is usually used to refer to Next Generation Sequencing (NGS) platforms such as the FDA cleared Illumina. They are distinguished by their ability to rapidly examine many genes simultaneously, using a single test, offering over previous technologies four main advantages: speed; cost of sequencing; sample size needed; and accuracy. The drivers of the cost of NGS are three: the pre-analytics and assay; the bioinformatics platform; and the evidence base for clinical utility. Of those three, only the cost of the assay is clearly decreasing raising questions as to how advantageous NGS will be in practice. Despite the absence of consensus on whether NGS is ready for the clinic or not, there is evidence suggesting that it would already be feasible to use NGS in some disease areas. We therefore need to develop an HTA approach for such platform technologies where we assess their cost and clinical utility. We explore HTA issues. We look at two areas – lung cancer and schizophrenia – where there is evidence of genetic markers impacting treatment decisions. We also comment on the broader policy context. Specialist teams may need to be concentrated in fewer centres and incentives will need to be re-aligned. “Home brews” present a particular challenge in genomic testing, not only due to the variability in quality that they might introduce, but also because they create a clear disincentive to innovation.

Biography

Professor Adrian Towse is Director of the Office of Health Economics in the UK. Adrian’s current research includes the use of 'risk-sharing' arrangements between health care payers and pharmaceutical companies, including value-based pricing approaches; the economics of pharmacogenetics for health care payers and the pharmaceutical industry; economic issues that affect both R&D for and access to treatments for diseases prevalent in the developing world; the economics of medical negligence; and measuring productivity in health care. A visiting Professor at the London School of Economics and a Senior Researcher at the Nuffield Department of Population Health at the University of Oxford, Adrian also has been a Visiting Professor at the University of York. For ten years, he served as the Non-Executive Director of the Oxford Radcliffe Hospitals NHS Trust, one of the UK’s largest hospitals. Adrian currently is President of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR), for the 2014-15 term. Adrian joined the OHE in 1993. He holds an MA (Hons) in Politics, Philosophy and Economics from Keble College, Oxford; an MPhil in Management Studies from Nuffield College, Oxford, and the Oxford Centre for Management Studies; and is a Member of the Chartered Institute of Management Accountants.

James Buchanan and Jilles Fermont

Methodological issues surrounding the health economic evaluation of genomic technologies and a case study of these issues in the research setting

Abstract
This presentation considers the methodological challenges associated with conducting economic evaluations in genomics. The issues fall into several categories including choosing an appropriate analytical approach, and the challenges associated with measuring costs, outcomes and effectiveness. Each category is discussed in turn, with examples provided. We then consider whether genomics poses an exceptional challenge in health economics, given these methodological issues. Finally, we present a case study which uses the example of multi-gene testing for lung and bowel cancer to illustrate some of these challenges, including issues surrounding rapid technological development, the non-existence of standard genomic testing practice, and the importance of incorporating all subsequent therapeutic decisions in analyses.

Biographies
James Buchanan joined the Health Economics Research Centre in September 2005, having completed his MA in Economic Development and Policy Analysis and his BA in Economics at the University of Nottingham. James is currently undertaking a DPhil (PhD) investigating issues related to the economic analysis of genomic diagnostic technologies for multifactorial genetic diseases in the UK NHS, based on a study evaluating targeted next generation sequencing in chronic lymphocytic leukaemia. Previous genetics projects have included the development of an economic modelling framework to evaluate novel genomic diagnostic tools in inflammatory bowel disease, a cost-effectiveness analysis of microarray technology in the NHS, and an economic evaluation of the use of genetic testing to identify gastrointestinal pathogens to improve hospital infection control practice.

Jilles Fermont is a research assistant at the Health Economic Research Centre, University of Oxford. Jilles primarily works on projects addressing the economics of genetic and genomic technologies such as high-throughput next-generation sequencing in cancer research and whole-genome sequencing in mycobacteria and humans for individual patient care. His research is funded from several sources such as the Health Innovation Challenge Fund and the Technology Strategy Board. In addition, Jilles is an honorary NHS researcher at the Oxford Molecular Diagnostics Centre. His research interests include economic evaluations, clinical trials, discrete choice experiments, cancer research, translational research, and genetic and genomic technologies.

Maarten J. IJzerman

Early Stage Modelling of the Health Economic Impact of Circulating Tumor Cells in the management of Cancer patients

Abstract

Previous studies have shown that the presence of circulating tumour cells (CTC's) or free circulating DNA in the blood has prognostic value regarding tumor metastasis and overall survival. However, current methods, like Cellsearch, only isolate small amounts of blood and therefore lack clinical utility. The EU funded CTCtrap (CTC therapeutic apheresis) project aims to isolate and characterize tumor cells circulating in whole blood to enable a real-time liquid biopsy for all cancer patients with metastatic disease regardless whether or not the disseminated disease has been clinically detected. Although it is expected that CTCtrap could have additional benefit in management of cancer patients the most appropriate use of CTCtrap in the diagnostic track CTCtrap is not clear. Early Health Technology Assessment aims to inform R&D about future use and benefits of medical technologies by making assumptions and uncertainties more explicit. In this presentation, early health economic modelling will be introduced to estimate the potential health impact of implementing CTC diagnostic technologies. The presentation will focus on the potential health impact of using CTCtrap in breast and prostate cancer.

Biography

Maarten IJzerman is professor of clinical Epidemiology & HTA and chair of the department Health Technology & Services Research at the University of Twente, the Netherlands. In 2013 and 2014 he has been the acting Scientific Director of MIRA, Institute for Biomedical Technology and Technical Medicine. Maarten received his MSc in 1993 in Biomedical Health Science at the University of Nijmegen and a PhD in Biomedical Engineering at the University of Twente in 1997. Maarten and his team work on methods to evaluate the benefits of diagnostic and imaging technologies and on the application of outcomes research and decision analytic models to predict health economic impact of medical technologies in development. The early assessment research program intends to further enhance the revenues of public and private spending in biomedical research. An important methodological contribution is made in the use of multi-criteria decision models to elicit stakeholder- and patient preferences for health outcomes and technology.

He has more than 130 peer-reviewed articles in the intersection of engineering, medicine and outcomes research. Maarten is a visiting adjunct professor at Case Western Reserve University in Cleveland (USA) and serves on numerous national and international boards and scientific committees. He is a member of the ISPOR board of directors and is a member of the ISPOR Health Science Policy Council. He is chair of the Committee for revising the Dutch Pharmacoeconomic guidelines (ZINL) and co-chair of the ISPOR taskforce Multi-Criteria Decision Analysis (MCDA). He is a member of the ISPOR taskforces on Simulation Modeling and Statistical Analysis of Conjoint studies. Since 2013, he initiated GITHE (Global Initiative for

Translational Health Economics). A joint collaboration between the MIRA Research Institute of the University of Twente (the Netherlands), Antoni van Leeuwenhoek Hospital - Netherlands Cancer Institute (The Netherlands), the Fred Hutchinson Cancer Research Center in Seattle (USA), the University of York (UK), UMIT in Hall (Austria) and CRP-Santé and EPEMED (both based in Luxembourg). Originating from their research program, Maarten IJzerman initiated the University spin-off company PANAXEA b.v. in 2010.

Frances Flinter

Commissioning Clinical and Laboratory Medical Genetics services in the NHS

Abstract
Medical Genetics (which includes clinical and laboratory genetics) is commissioned as a specialised service by NHS England rather than locally by individual Clinical Commissioning Groups. This should enable providers to offer similar services nationally as the scope of the services commissioned is standardised and the 17 providers in England are assessed by nationally agreed quality measures, dashboards and standards. The Medical Genetics Clinical Reference Group (CRG) membership includes both senior clinical and laboratory members, as well as representatives of professional groups such as the British Society of Genetic Medicine, senior commissioning and public health leads and 4 Patient and Public Engagement Representatives.

The Medical Genetics CRG works closely with the UK Genetic Testing Network, which accepts and assesses applications called 'gene dossiers' from individual labs that wish to add new genetic tests to their portfolio. Evidence of the scientific validity as well as the clinical validity and utility of new tests is reviewed before tests that are approved are recommended to the commissioners for funding in the next financial year. In the past, most genetic tests were paid for by the Regional Genetics centres but with the increasing movement of genetic testing into mainstream medicine, much work has been done to re-allocate budgets so that the clinician requesting a test does so at an appropriate time in the patient's pathway – and pays for it. Economic evaluation of the entire pathway is required before the potential contribution of genetic testing can be properly assessed and there are many examples where the carefully targeted use of genetic testing can actually save the NHS money, as well as enhancing patient care by reducing the time it takes to make a diagnosis, enabling cascade testing to relevant family members and, in some cases, enabling truly personalised, precision medicine.

Biography
Professor Frances Flinter is a Consultant Clinical Geneticist and the Caldicott Guardian at Guy's & St Thomas NHS Foundation Trust. She has a personal chair in Clinical Genetics at King's College, London. In addition Frances is Chair of the Medical Genetics Clinical Reference Group, which is responsible for developing the national specialised service level strategy together with service specifications and policies for NHS clinical and laboratory Medical Genetics services in England.

Mike Parker

Ethical aspects of genomic medicine with particular reference to 100,000 genomes project and the role of social justice in thinking about ethics and genomics

Abstract

In this presentation I will introduce the ethical issues and governance challenges presented by large scale genomics research projects using the 100,000 genomes project as a case study. I will then go on to suggest that these new forms of research present an important challenge to the way in which we understand autonomy and paternalism in research. Following on from Nuremberg and Helsinki a view has emerged that the best way to 'protect' research subjects is through high standards of consent and limiting the kinds of activities to which people are 'allowed' to consent because of a commitment to duties of care. This has led to an over emphasis on informed consent and the idea that autonomy is only possible with full understanding. What this has done in practice, I'll argue, is to undermine autonomy. Respecting people as moral agents means respecting their ability as competent adults to make decisions under conditions of uncertainty and in which the future is less than fully explained and transparent i.e. like it is in most areas of everyday life. I agree with Onora O'Neill and Neil Manson that the key factors respecting autonomy at the time of consent are those such as not deceiving people, not coercing them and so on. Information is never complete but people ought to be able to consent to open-ended activities such as biobanking even if the implications for them are unclear as long as they are not being deceived etc. But where does this leave protection and the duty of care? I'll argue that genomic research and biobanking raise really important questions about: health inequality, exploitation, commercialisation, privacy, discrimination, social justice etc. I think these issues are extremely important and that the approach to research ethics which focuses on individual informed consent - as protection - has actually substituted a contract based (consumer) approach to research ethics for one which takes social justice issues seriously. If we believe that individual informed consent can provide protection then we don't need to address justice issues. I disagree with this. I think that these issues need to be taken head on and separately from consent. So, we need non-discrimination legislation, we need guarantees of high levels of security and confidentiality and we need greater equality of access. It is not enough to rely on consent. We also need to recognise the importance of commercial and private input into medical research and the public interest in this. But this needs to be managed to ensure that there really is pubic benefit and that industry has a conscience.

Biography

Mike Parker is Professor of Bioethics and Director of the Ethox Centre at the University of Oxford. One of his main research interests is in the ethical aspects of the clinical use of genetics. He is a member of the Nuffield Council of Bioethics Working Group on the collection, linking, use and exploitation of biological and health data, the Data Access Committee of the Wellcome Trust Case-Control Consortium, and the Medical Research Council's Ethics, Regulation and Public Involvement Committee. Professor Parker also chairs Genomics England's ethics committee as well as being an ethics consultant to UK Biobank.

He has previously been a member of a number of national and international committees and working parties including the Ethics in Practice Committee of the Royal College of Physicians and the Department of Health's Committee for the Ethical Aspects of Pandemic Influenza.

Roger Crisp and Theron Pummer

Distributive Ethics, Health Care Allocation, and Personalised Medicine

Abstract

First we will introduce ethics and the reliance on judgments in ethical theory. Next, we will discuss the QALYs approach to health care allocation, and the connection between health and well-being. We will turn to three competing ethical principles concerning the interpersonal distribution of well-being: utilitarianism, egalitarianism, and prioritarianism. Finally, we will outline some respects in which personalised medicine brings with it threats of translating economic inequalities into health inequalities (and vice versa), as well as how it could be used as a tool for decreasing health inequalities.

Biographies

Roger Crisp is Uehiro Fellow and Tutor in Philosophy at St Anne's College, and Professor of Moral Philosophy at the University of Oxford. His work falls principally within the field of ethics, including metaethics, normative ethics, applied ethics, and the history of ethics. His latest book, *The Cosmos of Duty*, will appear in June 2015. He has been a member of the Clinical Ethics Committee at the John Radcliffe Hospital, and served on various working parties on health-related issues at the BMA and the Nuffield Council on Bioethics.

Dr Theron Pummer is a Plumer Junior Research Fellow in Philosophy at St Anne's College, University of Oxford, as well as a Research Associate for the Oxford Uehiro Centre for Practical Ethics and the Population Ethics Project at the Future of Humanity Institute (within the Faculty of Philosophy). He specializes in ethical theory, and is particularly interested in problems about the nature, aggregation, and distribution of well-being, the relevance of numbers in ethics, and the normative significance of persons.

Submitted Abstracts

Economic evaluation of gene panels and sequencing technologies: what can we learn from CEAs of whole-body CT screening?

Christine Y. Lu, PhD[1] Michael P. Douglas, MS[2] Kathryn A. Phillips, PhD[3]

1. Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, Massachusetts, USA
2. University of California at San Francisco Center for Translational and Policy Research on Personalized Medicine (TRANSPERS), Department of Clinical Pharmacy, San Francisco, California, USA
3. University of California at San Francisco Center for Translational and Policy Research on Personalized Medicine (TRANSPERS), Department of Clinical Pharmacy; UCSF Philip R. Lee Institute for Health Policy; and UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, California, USA

Whole-body CT scans and whole genome sequencing (WGS) share a similar concept of examining virtually any part of the body to detect a tumor or other abnormality, or predict disease risk. A literature review was conducted to identify articles reporting economic evaluation of whole-body CT scans in order to inform methodological approaches to conducting economic evaluations of WGS. We found 4 articles reporting cost analysis or economic evaluation involving whole-body CT. Common challenges for economic evaluations of whole-body CT and WGS include: limited use of the societal perspective, including only a small range of relevant cost categories, use of disease-specific measures that do not represent many relevant outcomes, poor data on the link between surrogate outcomes and survival, adjusting for rates of false-positives and costs of additional testing for false-positive results, and lack of attention on patient and clinician behavioral uncertainty after knowing test results. Evaluations of whole-body CT generally assumed diseases are independent of each other. Evaluations did not consider: (i) accidental findings because of low prevalence and that false-positive and true-positive results may have offsetting effects, (ii) quality of life due to lack of data, and (iii) personal utility because the benefit to quality of life with the peace of mind that comes from knowing one is disease free may be offset by the detriment caused by anxiety due to a false-positive result. Evaluations inconsistently adjusted for deleterious effects of radiation exposure from CT. We have identified several approaches used in economic evaluations of whole-body CT scans that may deserve discussion in order to refine methodological approaches to conducting economic evaluations of WGS.

Individualised cost-effectiveness analysis in risk-based screening: practical and ethical?

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1. School of Medicine, University of Nottingham
2. School of Economics, University of Nottingham

Personalised medicine can raise practical and ethical dilemmas. We argue that there is one form of personalised medicine - risk-based screening - that can be practically and ethically implemented. There is necessarily a relationship between an individual's risk of disease onset and the cost-effectiveness of screening them for that disease. The expected cost-effectiveness of screening is likely to have a positive relationship with an individual's level of risk. Assuming that risk increases with time, it follows that intervals for recurrent screening should be shorter for people with a higher level of risk. By including individual risk in net benefit calculations, it is

possible to estimate individualised cost-effectiveness results. These can be used to optimise policy by selecting the shortest screening recall period at which net benefit is positive. We present a practical means of delivering a screening programme capable of this, involving the use of a risk calculation engine and automatic generation of invitations to screening. Different approaches to individualised cost-effectiveness analysis have different ethical implications. Programmes that discriminate based on differences in costs or health outcomes are not ethically justifiable due to concerns for non-discrimination. However, we argue that non-discrimination rules should not apply to individual risk in the case of screening. This is because screening does not confer health benefit, and capacity to benefit is instrumental. Risk-based screening can operate within existing standards of distributive justice and the prevailing philosophy of health economics. We discuss implications and applications for genomic medicine and individualised cost-effectiveness analysis more broadly.

Ethics of equality and cost-effectiveness—implications for personalised medicine

Leah Rand
Ethox Centre, Oxford University

In practice resource allocation for healthcare is a matter of making trade-offs between individuals and populations. The ethics of this is often contrasted as a conflict between the principles of equality and cost-effectiveness. Equality focuses on each person receiving a fair share of the opportunities available at health and to be healthy. However, limited resources mean that it is not possible for each person to receive all the healthcare from which she would benefit. A cost-effectiveness, or utilitarian based, approach aims to maximize the healthcare benefits available to each person. In a situation of limited resources, such as faces health systems today, these two approaches will necessarily conflict; equality, epitomizing care of the individual, must also work in relation to cost-effectiveness for populations of patients. Personalised medicine brings out this conflict in new ways by making us think about how to optimise healthcare for an individual, but this must be balanced against the needs of all the individuals who make up the population. I will discuss this tension, particularly as it plays a role in the National Institute of Health and Care Excellence's (NICE) deliberations. How we conceive of this problem will also have implications for how personalised medicine and genomics are addressed.

Cost-effective Allocation of Resources for Type-2 Diabetes Prevention between High-risk Subgroups

Penny Breeze[1], **Chloe Thomas[1],** Hazel Squires[1], Alan Brennan[1], Colin Greaves[2], Peter Diggle[3], Eric Brunner[4], Adam Tabak[4], Louise Preston[1], Jim Chilcott[1]

1. ScHARR, University of Sheffield,Sheffield, UK
2. University of Exeter Medical School, St. Luke's Campus, Magdalen Road, Exeter, UK
3. Medical School, Lancaster University and Institute of Infection and Global Health, University of Liverpool
4. Epidemiology & Public Health, University College London

Type-2 diabetes is a complex disease with multiple risk factors and health consequences. We have developed a microsimulation model that can evaluate the effectiveness and cost-effectiveness of diabetes prevention interventions, either in the general population or in subgroups at high risk of diabetes in the UK. Within the

model individual patients follow metabolic trajectories (for BMI, cholesterol, systolic blood pressure and glycaemia), develop diabetes, complications of diabetes and related disorders including cardiovascular disease (CVD), and eventually die. Disease trajectories are stratified by baseline characteristics. Lifetime costs and quality-adjusted life-years are collected for each patient under both a standard care scenario and a diabetes prevention intervention scenario that modifies metabolic trajectories.
Six high risk subgroups with the following characteristics were chosen for analysis: South Asian origin; Low socioeconomic status; BMI > 35, HbA1c test results > 6; Finnish Diabetes Risk Score (FINDRISK) > 0.1 and adults aged 40-65. Diabetes prevention interventions are most cost-effective in South Asians followed by those of low socioeconomic status, due to the reduction in CVD rather than lower diabetes incidence. Intervening in the HbA1c > 6 group results in the largest reduction in new cases of type-2 diabetes, followed by those with FINDRISK > 0.1. These results have implications for the allocation of public health resources between different subgroups at risk of type-2 diabetes, and demonstrate the ability of the model to estimate the benefits of flexibly specified interventions for highly specific population subgroups.

Cost effectiveness of screening for HLA-A*31:01 prior to initiation of carbamazepine in epilepsy

Catrin O Plumpton[1], Vincent LM Yip[2], Ana Alfirevic[2], Anthony G Marson[2], Munir Pirmohamed[2], Dyfrig A Hughes[1]

1. Centre for Health Economics and Medicines Evaluation, Bangor University, Wales, UK
2. Department of Molecular and Clinical Pharmacology, University of Liverpool, Liverpool, UK

Carbamazepine causes severe cutaneous adverse drug reactions that may be predicted by the presence of the HLA-A*31:01 allele in northern European populations. There is uncertainty as to whether routine testing of patients with epilepsy is cost-effective. We conducted an economic evaluation of HLA-A*31:01 testing from the perspective of the National Health Service in the UK. A short-term, decision analytic model was developed to estimate the outcomes and costs associated with a policy of routine testing (with lamotrigine prescribed for patients who test positive) versus the current standard of care which is carbamazepine prescribed without testing. A Markov model was used to estimate total costs and quality-adjusted life-years (QALYs) over a lifetime to account for differences in drug effectiveness and the long term consequences of adverse drug reactions. Testing reduced the expected rate of cutaneous adverse drug reactions from 780 to 700 per 10,000 patients. The incremental cost effectiveness ratio for pharmacogenetic testing versus standard care was £12,808 per QALY gained. The probability of testing being cost-effective at a threshold of £20,000 per QALY was 0.80, but the results were sensitive to estimated remission rates for alternative antiepileptic drugs. Routine testing for HLA-A*31:01 in order to reduce the incidence of cutaneous adverse drug reactions in patients being prescribed carbamazepine for epilepsy is likely to represent a cost-effective use of healthcare resources.

Opportunities and challenges in diagnostic embryo selection during assisted reproduction: Practical and conceptual issues

Mark Connolly [1,2], Hans-Joerg Fugel [1], Nikolaos Kotsopoulos [1,2], Maarten Postma [1]

1. Unit of PharmacoEpidemiology & PharmacoEconomics, Department of Pharmacy, University of Groningen, The Netherlands
2. Global Market Access Solutions (GMAS), St-Prex, Switzerland

In recent years several diagnostic technologies have been developed to identify the most suitable embryo(s) to transfer during assisted reproduction in order to improve live birth outcomes, and optimizes resource allocation decisions. Personalised medicine in reproductive healthcare poses specific opportunities and challenges not faced by traditional areas of interventional medicine, namely that diagnostic testing does not determine the future use of targeted therapies; rather it determines the viability of specific embryos for transferring and likely implantation. Consequently, improved embryo selection offers the opportunity to transfer the optimal embryo to improve success and minimize the need for subsequent treatments. Furthermore, identification of optimal embryos can also reduce the need for multiple embryo transfers which could reduce complication costs associated with multiple pregnancies. As with other areas of personalised medicine, diagnostic testing costs are of concern, although improved embryo selection leads to the reduction in future costs and the need for future interventions. Challenges associated with embryo diagnostics stem from concerns over manipulation to obtain designer babies, and what to do with embryos that are likely to be of lower quality. We describe a recent cost-effectiveness analysis applied to a theoretical embryo diagnostic procedure and its influence on the cost per live birth. The case study will be used to illustrate unique features of cost-effectiveness analysis of personalised medicine in reproductive healthcare and influence on resource allocation.

Personalised Medicine and the Moral Obligation to Change

Angeliki Kerasidou

The Ethox Centre, Department of Population Health

Doctors and public health professionals are hoping that genetics will open the door to better and more effective disease prevention strategies. The expectation is that if people are aware of their risk factors for disease, they would take responsibility of the lifestyle and health choices and adopt changes that will improve their long term health outcomes. This way, '[p]reventing disease will also become the responsibility of the patient. He will know what the risks he takes if he smokes, over-eats or leads a sedentary life style. The risks will be personalized based on his own genetics' (Steakley, 2012).

It seems reasonable to assign personal responsibility to people for their actions. As long as the action is freely and autonomously chosen, one should not be acquitted of the cost of freedom that comes with being a free and autonomous agent. But is it possible to argue with certainty that health-related actions are always freely and autonomously chosen? And even if we can prove this, would it be fair if a national health system rewarded those who make the 'right' choices and penalised those who make the 'wrong' ones?

In this presentation am going to explore the notions of personal autonomy and responsibility within the context of personalised medicine and public health and will draw some conclusions on what this might mean for the national health system.

Session Chairs

Sarah Wordsworth

Ingrid Slade

Gurdeep Sagoo
Gurdeep Sagoo is a Health Economist and Epidemiologist at the PHG Foundation, Cambridge. As a health economist and epidemiologist with expertise and experience in the design and conduct of diagnostic test accuracy reviews, meta-analysis and economic evaluation of genomic technologies, Gurdeep has a rare combination of methodological and applied skills covering genetics, genetic epidemiology and health economics. Gurdeep is involved in several projects evaluating diagnostic exome sequencing within clinical genetics services and pathogen genome sequencing for informing and managing outbreaks within hospital settings.

Gurdeep is a co-founder and joint coordinator of the Health Economics @ Cambridge group, a pan university and Cambridge wide interest group in health and economics, set up in 2014. He is also an honorary Health Economist at Guy's and St Thomas' NHS Foundation Trust, London and an Honorary Health Economist at Cambridge University Hospitals NHS Foundation Trust, Cambridge.

Mark Sheehan
Mark Sheehan is the Oxford Biomedical Research Centre (BRC) Ethics Fellow at the Ethox Centre in the Nuffield Department of Population Health, University of Oxford and a Research Fellow at the Uehiro Centre for Practical Ethics in the Faculty of Philosophy, University of Oxford. He is also Dean and a Senior Research Fellow in Philosophy at St. Benet's Hall, University of Oxford. He received a PhD in Philosophy from The Graduate Center of the City University of New York, where his thesis was on the nature of moral judgements. Prior to coming to Oxford he was a lecturer in the Centre for Professional Ethics at Keele University, Ethics Fellow at the Mt. Sinai Medical School, New York and Adjunct Lecturer in the Philosophy Department at The City College of New York.

In addition Mark is a National Research Ethics Advisor for the National Research Ethics Service, a member of the Nuffield Council on Bioethics Working Group on research in children and a member of the NICE Highly Specialised Technology Evaluation Committee. He also sits on the University's Social Sciences and Humanities Inter-Divisional Research Ethics Committee, the Ethics Committee of the Royal College of General Practitioners and is a member of the Thames Valley Priorities Committee in the NHS. Mark is an Associate Editor of the Journal of Medical Ethics.