2023

Presentations from New Fellows

28 September 2023

The Academy of Medical Sciences

Programme: Thursday 28 September 2023

16.00 **Welcome**
Professor Paul Stewart FMedSci
Vice President (Clinical), Academy of Medical Sciences

Presentations from new Fellows:

16.05 **On the 'knife-edge' - balancing innovation and evaluation in surgery**
Professor Marion Campbell FRSE FMedSci
Vice Principal (Research) and Professor of Health Services Research, University of Aberdeen

16.30 **Epilepsy: Informing complex decisions, managing, and improving safety**
Professor Tony Marson FMedSci
Professor of Neurology, University of Liverpool

16.55 **Making early intervention for eating disorders earlier, bolder, and brainier**
Professor Ulrike Schmidt FMedSci
Professor of Eating Disorders, King's College London

17.20 **The design of novel drugs with generative AI**
Professor Andrew Hopkins FRS FRSE FMedSci FLSW
Chief Executive Officer, Exscientia.ai

17.45 **Close**

Presentations from new Fellows

On the `knife edge' - balancing innovation and evaluation in surgery

Professor Marion Campbell FRSE FMedSci

More than 11 million surgical procedures are conducted in the UK every year at the cost of over £5bn to the NHS, and the backlog of patients waiting for elective surgical treatment post Covid continues to grow (>800,000 currently waiting for orthopaedic procedures, >500,000 for ENT etc). Generating the evidence to inform what surgical procedures are most effective is now more critical than ever. Surgery is a high-tech specialty where innovation thrives. New developments can emerge from the introduction/refinement of new surgical procedures to the integration of emerging technologies such as robot assisted surgery. Innovations often develop iteratively, can be fast moving, and can diffuse organically into practice. Surgeons also experience learning curves as they adapt to new techniques. These issues all make formal evaluation challenging – yet there is a scientific and moral imperative to ensure that surgical techniques adopted into practice are truly beneficial. A lack of routine rigorous evaluation in the past led to the adoption of some surgical techniques that were later shown to lack any discernible benefit and in some cases harm. Surgical research was famously described as a 'comic opera' in the '90s and the field was challenged to do better in terms of evaluative research. Over recent years, the surgical evaluation landscape has undergone significant transformation. In this presentation I will outline some of the recent advances in the field including developments in innovative trial design, use of surgical placebos, integration of the patient voice and incorporation of implementation science and health systems thinking to surgical evaluation, and how they are being applied to state-of-the-art technologies such as robotic and digitally assisted surgery.

Marion Campbell is Professor of Health Services Research and co-Director of the RCSEng Aberdeen Surgical Trials Centre at the University of Aberdeen. Marion is a medical statistician, clinical trialist and methodologist. Her main research interests are in the design, conduct and analysis of clinical trials especially complex trial design. She has majored on the evaluation of surgical interventions and the development and use of innovative surgical trial design. Her wider research has also led to the major advances in the design and conduct of cluster trials now widely used across clinical and healthcare research. She has published on clinical trials methodology including surgical evaluation, cluster trials, pragmatic trials and trials reporting. She has served on many national and international funding agencies and committees, including MRC, NIHR and was a REF2021 panel member. She is an elected Fellow of the Royal Society of Edinburgh, the Faculty of Public Health, and the International Society for Clinical Trials. Her work also contributed to the award of a Queens Anniversary Prize to the University of Aberdeen for sustained excellence in health services research.

Epilepsy: Informing complex decisions, managing risk and improving safety.

Professor Tony Marson FMedSci

Epilepsy is a common neurological condition (prevalence 0.5-1%) that affects people across the age spectrum and has highest incidence in the young and the old. It is associated with massive burden to individuals and wider society and remains uniquely stigmatising. Whilst we recognise a large number of epilepsy syndromes, treatment policies (particularly in adult practice) recognise two broad groups of patients, those with

focal epilepsy and those with generalised epilepsy. Given that epilepsy is a long-term condition, treatment should be guided by results from long term clinical trials, such as the NIHR HTA Standard and New Antiepileptic Drug trials, which identify lamotrigine as a first line treatment for focal epilepsy and valproate for generalised epilepsy, where around 60-70% of participants enter a remission from seizures over time. There are many risks to consider for people that have had seizures, one being the risk of seizure recurrence. Clinical trial data can be modelled to help estimate seizure recurrence risk, such as analyses of the Multicentre Study of Early Epilepsy and Single Seizures trial which underpins DVLA and European driving regulations. Another important risk to consider is teratogenicity of anti-seizure medications. Cochrane systematic reviews highlight the risks associated with valproate exposure in utero; 10% risk of major malformations and 30-40% risk of neurodevelopment syndrome. For women of child-bearing age with generalised epilepsy there is a challenging benefit harm trade off to consider and regulators have put pregnancy prevention scheme in place. More recently concerns have been raised about use of valproate in men, where it may be associated with reduced fertility and major malformations in children fathered by men taking it, and also a possibility of transgenerational effects. A pregnancy prevention scheme for men is about to be rolled out. But are our services currently configured to provide coordinated and safe care? The National Audit of Seizure Management in Hospitals would suggest not. If we are to deliver safe care we urgently need to mobilise data across primary and secondary care to enable safer care.

Tony Marson leads the epilepsy research group in Liverpool where he is Professor of Neurology at University of Liverpool and Honorary Consultant Neurologist at The Walton Centre NHS Foundation Trust. His work has focussed on informing treatment decisions for people with epilepsy and improving the delivery and implantation of care, all of which are the focus of this presentation. He is also a founding member of international genomics consortia aiming to identify the genetics architecture of the epilepsies and genetic determinants of treatment response. He has led the largest pragmatic trials in epilepsy (MESS, SANAD, SANAD II), established and led the Cochrane Epilepsy Group as Coordinating Editor, led National Audit of Seizure Management in Epilepsy and the NHS England epilepsy pathway programme. He is currently Secretary General of the European Academy of Neurology.

Making early intervention for eating disorders earlier, bolder, and brainier.

Professor Ulrike Schmidt FMedSci

Eating disorders are deadly and disabling disorders, typically starting in adolescence or emerging adulthood, i.e. during a developmentally sensitive time. Thus, they have the potential for seriously derailing young people's life trajectories. There is a clear rationale and growing research evidence supporting the need for and effectiveness of early intervention for eating disorders. There is also enthusiastic support from people with lived experience, clinicians, researchers and policy-makers alike for the concept. During the last 10 years we have developed, tested and nationally implemented across England an early intervention model called FREED (First Episode Rapid Early Intervention for Eating Disorders). Yet, much more needs to be done to make authentic early intervention a reality for all young people with eating disorders. In this talk I will present our approach and focus on recent areas of development, such as initiatives to improve early detection

and help-seeking. I will also present findings from our ongoing work designed to better understand illness and recovery trajectories and to develop personalised or precision treatments for young people with eating disorders.

Ulrike Schmidt is Professor of Eating Disorders at King's College London and a Consultant Psychiatrist at the South London and Maudsley NHS Foundation Trust. A key focus of her research is the development of brief scalable interventions. She has led the development of MANTRA, a NICE-recommended psychotherapy and of FREED, a multi-award winning early intervention programme. She has also pioneered the use of novel brain-directed treatments in eating disorders. She leads the large UKRI-funded EDIFY consortium on early intervention for eating disorders. She has written some 450 peer-reviewed papers and many other publications. Ulrike has led/contributed to multiple national and international initiatives, trying to improve eating disorders policy and practice.

The design of novel drugs with generative AI

Professor Andrew Hopkins FRS FRSE FMedSci FLSW

The discovery of a new medicine remains an expensive challenge. Drug design can be considered a problem of data and decision making and thus amenable to machine learning. We have now progressed multiple drugs into clinical trials that have been extensively designed using machine learning and generative artificial intelligence (AI) algorithms.

The use of AI to design drugs is a learning process where we start with the patient - by understanding what would make a good drug for a particular disease to define the objectives we want to design towards. Molecular generative AI algorithms enable the exploration of chemical ideas – searching for molecular designs that could solve all the desired objectives. We then make a test of just a few of these ideas to see how the predictions match the real-world observations in laboratory experiments. We then learn from the experimental data, feeding it back into the algorithms to improve the models.

The advantage of using AI in the drug design process is that we have seen that it allows us to learn faster. What we have experienced is, for the drug candidates that we have nominated for clinical development, we have needed to conduct about 90% fewer experiments than conventionally would be the case.

Andrew Hopkins is the Founder and Chief Executive of Exscientia plc, where he has pioneered the use of artificial intelligence and machine learning to design new medicines.

Andrew led the teams that discovered the first drugs to enter human clinical trials which were designed with the extensive use of machine learning and AI generative methods. Exscientia plc listed on the NASDAQ in October 2021 and is recognised as the most successful UK university spin out company of the past decade. For its end-to-end AI-driven precision medicine platform, Exscientia won the Prix Galien USA for Digital Health in 2022 and the Prix Galien UK in the same category in 2023.

Andrew holds an honorary Professorship at the University of Dundee, where he previously held the Chairs of Medicinal Informatics and Translational Biology. He served as the Director of the Scottish Universities Life Science Alliance and co-founded the European Lead Factory. Prior to the University of Dundee, he spent a decade at Pfizer leading various informatics groups. Andrew received his DPhil in biophysics from the University of Oxford and LLD from the University of Dundee.