The Alumni Summit

The Alumni Summit Report

9–10 July 2015, Saïd Business School, Oxford, UK

www.alumnisummit.com

Oxford Academic Health Science Network

About the Oxford AHSN

The Oxford Academic Health Science Network unites regional NHS, universities, businesses, patients and public to achieve two goals – improving health and generating economic growth in our region.

As catalysts of change, we strive to reduce variation in the quality of care. Our aim is that innovative ideas and technologies are rapidly and universally introduced into clinical practice. This will advance patient safety, improve patient outcomes and experience, and ensure the NHS is more sustainable and efficient.

Collaboration underpins the Oxford AHSN concept and change programmes. We work with partners to embed projects into local systems and plans, building acceptance and sustainability.

BELS
British Expats in Life Sciences

About BELS

BELS (British Expats in Life Sciences) is a network that connects and fosters relations and interaction among an enthusiastic group of UK expatriates who are involved in the health and life sciences globally.

BELS enables this talent base to strengthen connections with the UK to mutually benefit the expats, UK affiliates, and the UK health and life sciences sector.

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SAID BUSINESS SCHOOL

Summary

The first Alumni Summit, organized by Oxford Academic Health Science Network (AHSN) and British Expats in Life Sciences (BELS), aimed to debate the opportunities and challenges afforded by cutting-edge UK science and technology, and their role in changing the face of health care in the 21st century.

Acknowledged world-class experts in medicine, life sciences and technology, industry leaders and researchers, regulators and politicians shared insights and opinions in frank, open and stimulating discussion. Delegates agreed that the UK has academic and clinical centres of excellence, data collections and a National Health Service (NHS) that are the envy of the world. However, rapid change is needed to ensure that patients benefit from innovations emerging from the combined strengths of our national assets and our flourishing life science industry.

Keynote speaker Professor Sir John Bell GBE (Regius Professor of Medicine, University of Oxford) threw down the gauntlet, commenting: "To be transformational, we need to make bold steps."

Sir John highlighted the unique position of bioscience not only in Oxford and the South East but across the UK, in terms of the powerful academic research resource, highly integrated healthcare system and coordinated response to funding.

Speaking at the Alumni Summit dinner, George Freeman MP (Minister for Life Sciences) agreed. "Something very special is going on here in Oxford in this AHSN. AHSNs have such a big part to play, to be the delivery arm to unlock the power of research and Academic Health Science Centres, and link them to local health economies."

Co-hosts Oxford AHSN and BELS were delighted with the outcomes.

Nigel Gaymond (Founder and Chief Executive Officer, BELS) commented: "We've exported so much talent overseas. It's always been in my mind to bring some of these guys back and it's been a spectacular success. People have been exposed to a whole range of issues from big data to regulation. Some have been taken out of their immediate comfort zones but I think they understand this is a highly collaborative industry and they need to know what's going on and to be connected right across the whole paradigm."

Dr Nick Scott-Ram MBE (Commercial Director, Oxford AHSN) looked forward. "We see this as a start, not an end, and a process where we hope the relationships with those who have come here can be strengthened and built to foster long-term collaborations."

This report draws out key points from each session. Video interviews with participants and slide presentations may be accessed at www.alumnisummit.com.

Something very special is going on here in Oxford in this AHSN.

George Freeman MP, Minister for Life Sciences

The UK is already and can become a global leader in this new area of precision medicine.

Professor Richard Barker OBE, Chairman, Precision Medicine Catapult

Could phase 1 be the new phase 3?

Dr Sean McCarthy, Chief Executive, CytomX Therapeutics

The 100 000 Genomes Project is the most exciting and revolutionary project happening in the world today.

Sir John Chisholm, Executive Chairman, Genomics England

Social innovation will come from companies who are adapting and making emotional connections with people through technology.

Lord Paul Drayson, Chairman and Chief Executive, Drayson Technologies Group

We have catalysed science, we have catalysed translational research.

Chas Bountra, Professor of Translational Medicine, University of Oxford

This is an unprecedented moment for innovation.

Alex Snow, Deputy Chairman, Oxford Sciences Innovation

The whole medical system will be turned inside out in the next 10 years. Hospitals will be on the outside and care will move to our homes.

Dr Dan Mahony, Fund Manager, Polar Capital

Collaboration and trust between academia, scientists, industry and health care is paramount.

Peter Ellingworth, Chief Executive, ABHI

UK life sciences sector: priorities, progress and plans

With 4400 companies employing an estimated 183 000 people and having a turnover of more than £50 billion per annum, the UK life sciences sector is one of the strongest globally. We are, however, a small country. "If we want to be competitive and make progress, we have to work together," emphasized Professor Sir John Bell (University of Oxford).

In 2009, the UK Government established the Office for Life Sciences to develop the life sciences sector. The current UK Government maintained this commitment and appointed a Minister for Life Sciences (George Freeman) in 2014.

UK clusters

Clusters of high-tech industry exist across the UK (*Figure 1*). Scottish Enterprise has contributed to life sciences discoveries in Dundee, Glasgow and Edinburgh. The Northern Powerhouse (Liverpool and Manchester) and Swansea and Cardiff are also key innovation centres; however, an 'arc of innovation' in the South East dominates activities. Oxford, Cambridge and London form the 'Golden Triangle', the largest cluster in Europe and the third largest globally.

Professor Sir John Bell

FIGURE 1. UK high-tech industry clusters

South East cluster (Golden Triangle): Oxford, Cambridge and London

- More than 500 life sciences small- and medium-sized enterprises
- More than 1200 life sciences companies
- Five top 20 medical schools
- Strong and broad non-life-sciences technology economy
- Three major research facilities (Sanger, Crick and Harwell)

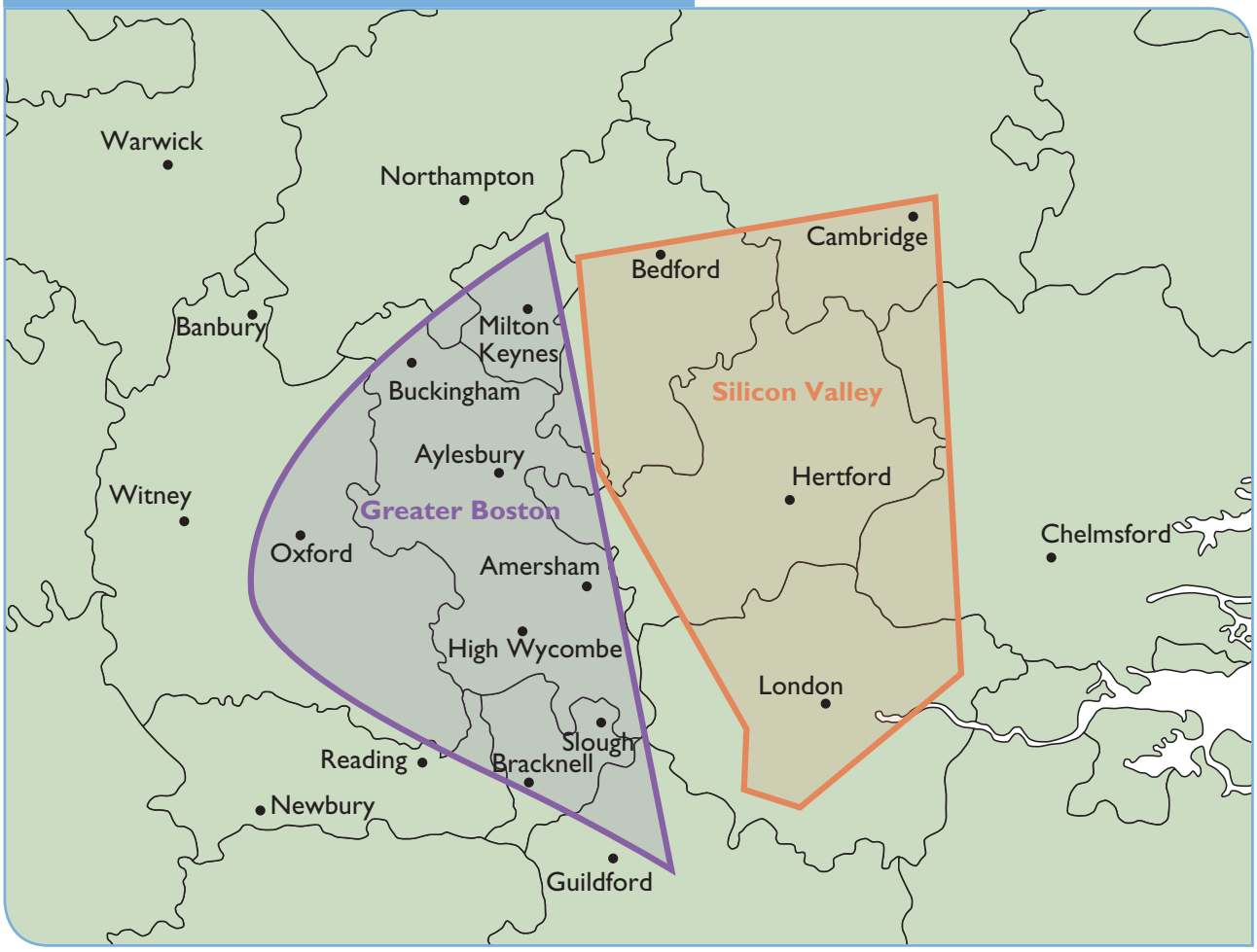
Professor Sir John Bell demonstrated the potential strength of the 'Golden Triangle' by superimposing the approximate geographical extent of two major US clusters (*Figure 2*). Silicon Valley covers an area the size of London and Cambridge, while the Greater Boston cluster is similar in size to the Thames Valley. Individually, the Oxford, Cambridge and London regions are isolated, but improved connectivity could strengthen the 'Golden Triangle'.

Competitive advantage

The UK has five major universities in the top 11 of the *Times Higher Education* World University Rankings: University of Oxford, University of Cambridge, Imperial College London, University College London and King's College London. The Office for Strategic Coordination of Health Research is a unique grouping of funders who have generated £3.5 billion per year to support UK biomedical science. Valuable national assets have emerged in the Oxfordshire region, including the UK Biobank, the National Institute for Health Research BioResource, WGS500 and the University of Oxford Big Data Institute.

> ***The UK has a remarkable position in genetics analysis. We need to be a country that applies genetic science to real patients before anyone else.***
>
> ***It's people that make clusters operate.***
>
> Professor Sir John Bell

FIGURE 2. Geographical extent of two major US high-tech industry clusters: Silicon Valley and Greater Boston



Oxford response to global, national and local priorities

The NHS is contributing to a thriving life sciences economy in the UK; however, there is growing recognition of fragmentation and variation in the healthcare system. Professor Gary Ford highlighted that a top-down approach is not working. Care needs to begin with patients and their families.

Fifteen AHSNs have been established by NHS England. The Oxford AHSN draws expertise from academia, industry and the NHS to improve health outcomes and to support economic growth in the region (*Figure 3*). Their investment in Best Care Clinical Networks has improved clinical outcomes. For example, in 2014–2015, the Anxiety and Depression Clinical Network improved regional recovery rates for people experiencing anxiety and depression from 48% to 58%, while the national rate remained constant (45%).

Professor Gary Ford

FIGURE 3. Oxford AHSN: a large entity

£5 billion annual NHS spend
3.3 million people
65 000 NHS employees
2000 general practitioners
550 healthcare and life sciences organizations
326 general practices
12 clinical commissioning groups
12 district and county councils
11 NHS trusts and commissioners
9 universities
4 counties: Bedfordshire, Berkshire, Buckinghamshire and Oxfordshire
4 local enterprise partnerships

AHSN, Academic Health Science Network; NHS, National Health Service

Innovation adoption

In 2014–2015, the Oxford AHSN focused on 10 innovations with the potential to have a large impact on patient outcomes and healthcare costs:

- atrial fibrillation (AF) detection and management in primary care
- community-based asymptomatic AF screening using hand-held electrocardiograms
- intermittent pneumatic compression sleeves to reduce deep vein thrombosis risk in stroke care
- portable bladder scanners to reduce the risk of catheter-acquired urinary tract infections
- consistency in drug therapy for patients with Alzheimer's disease
- electronic management of blood transfusions to improve patient safety
- intraoperative fluid management to expedite recovery from surgery
- best practice disease-modifying therapies for patients with rheumatoid arthritis
- recovery support for individuals with eating disorders
- remote gestational diabetes management.

Professor Gary Ford (Oxford AHSN) concluded that the Oxford AHSN is presenting the NHS with the challenge of supporting rapid adoption of innovation and creation of a patient-centred system.

Keynote speaker
Professor Sir John Bell GBE (Regius Professor of Medicine, University of Oxford, UK)

Speaker
Professor Gary Ford CBE, FMedSci (Chief Executive Officer, Oxford AHSN, UK)

Panellists
Dr Stuart Collinson (Executive Chairman, Arcturus Pharmaceuticals, CA, USA)
Dr Stephen Hill (President and Chief Executive Officer, Targacept, NC, USA)
Dr Sean McCarthy (Chief Executive Officer, CytomX Therapeutics, CA, USA)
Marc Owen (Chairman, Celesio AG, Germany)

Moving towards a digital revolution in health care

Genomics, proteomics and big data are at the leading edge of a digital revolution in health care. Whole genome sequencing (WGS) could answer key medical questions and transform the NHS. The Oxford AHSN is at the centre of efforts to share data, engage with patients and industrialize this technology.

Professor Gil McVean (University of Oxford and Genomics plc) described how WGS has afforded insights into disorders and provided targets for therapeutic intervention. It is a powerful research tool, but can it be integrated into mainstream health care?

Molecular diagnosis

The WGS500 study recruited individuals with a range of disorders, in whom previous genetic testing had failed. Sir John Chisholm (Genomics England) outlined the collaboration between the Wellcome Trust Centre for Human Genetics, the technology company Illumina and the local NHS to facilitate WGS in 500 patients and their families. New genes, new phenotypes for known genes and new candidate genes have been identified. The study has demonstrated the clinical utility of the technique, providing definitive diagnoses for one-third of patients (Taylor JC *et al. Nat Genet* 2015;47:717–26).

A new era of population-scale genomic studies has emerged (Table 1). Genomics England has adopted a multi-sector approach to develop the 100 000 Genomes Project. The organization has selected 11 regional Genomic Medicine Centres to collect data for target cancers and rare inherited diseases, and a sequencing partnership has been agreed with Illumina. The Genomics England Clinical Interpretation Partnership has assembled more than 2500 clinical and scientific minds to interpret the data, while pharmaceutical and biotechnology companies have formed the Genomics Expert Network for Enterprises Consortium. Partners specializing in bioinformatics and analytics will provide platforms for handling data.

TABLE 1. Population-scale genomic studies

	Population	Country
Genomics England	100 000	UK
Geisinger-Regeneron	100 000	USA
UK Biobank	500 000	UK
China Kadoorie Biobank	500 000	China
Million Veteran Program	1 000 000	USA

Data complexity is hindering the integration of genomics into health care

Genomics plc was founded by leading academics from the Wellcome Trust Centre for Human Genetics, with the support of Genomics England. Genomics plc has raised more than £10 million from institutional investors and recruited high-tech, domain-specific analysts and commercial software developers. Their sophisticated algorithms and software solutions aim to realize the potential of genomic medicine.

Big data for dementia

Professor Simon Lovestone (University of Oxford) outlined initiatives to capture existing genomic and clinical data for patients with dementia.

The Dementias Platform UK (DPUK) has assembled data on more than 20 pre-existing cohorts of patients with dementia, a total of over 2 million participants for research in dementia. This includes a UK Biobank core subgroup of over 10 000 people with repeated neuroimaging to add to the planned 100 000 with whole body imaging. The UK Biobank has also assessed cognitive function through a short web-based test. Other elements of the DPUK include the 'Deep and Frequent Phenotyping' feasibility study aiming to identify biomarkers for early-stage Alzheimer's disease, and the UK Clinical Record Interactive Search (UK-CRIS) system enabling researchers to access electronic medical records for pseudonymized research. Further details are available at www.dementiasplatform.uk

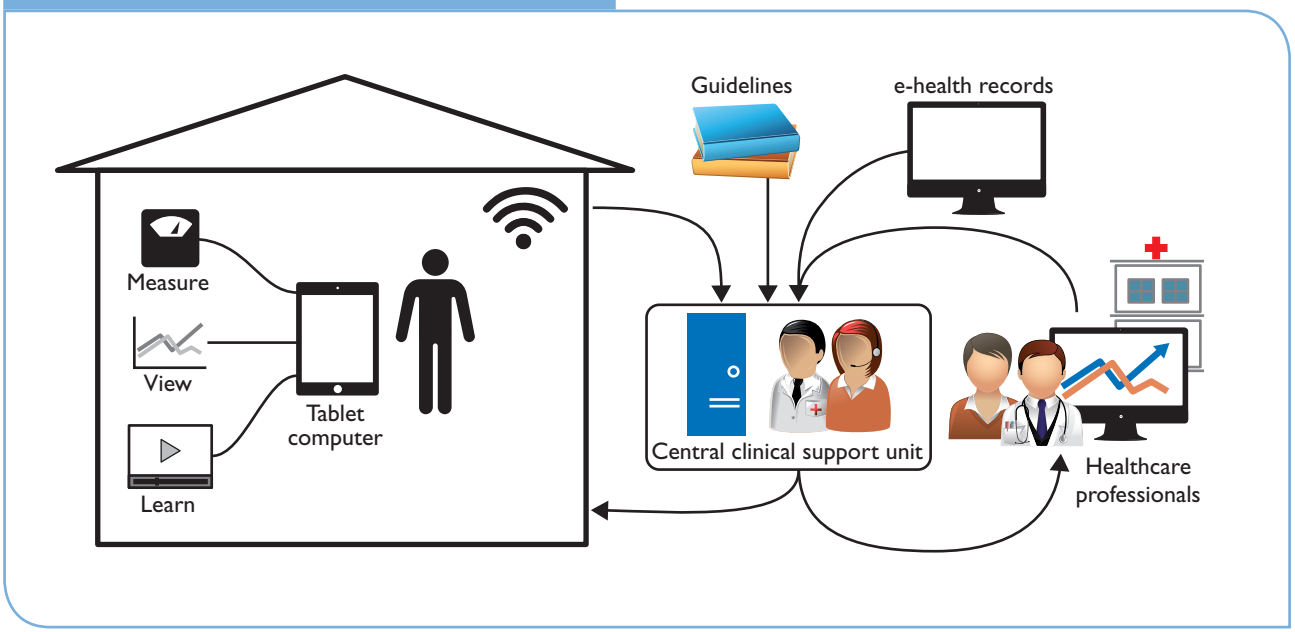
> ***The 100 000 Genomes Project is the most exciting and revolutionary project happening in the world today.***
>
> Sir John Chisholm

Digital health

Professor Kazem Rahimi (The George Institute for Global Health) outlined the SUPPORT-HF study that developed a user-friendly heart failure risk prediction system that can be used at home (*Figure 4*). Equipped with simple tablet technology and wirelessly linked sensor devices, patients can monitor their blood pressure, heart rate, oxygen levels and weight. Data are processed centrally and can be used to predict the risk of their condition deteriorating, supporting early intervention by healthcare providers.

Professor Kazem Rahimi

FIGURE 4. Personalized, integrated digital health



Proteomics approach

Dr Stephen Williams (SomaLogic) proposed that "for most diseases we care about there may never be a genetics revolution". Protein analysis may help to build a complete picture of disease states.

Technology failure has hindered a 'proteomics revolution'. Existing tools can measure large numbers of abundant proteins or small numbers of less abundant proteins, but not both. SomaLogic have utilized genetic technology to perform large-scale interrogation of proteins over a wide dynamic range. Their SOMAscan® platform was used in a large proteomic study that investigated protein biomarkers to predict the risk of future cardiovascular events, including heart failure, myocardial infarction and stroke. SOMAscan® outperformed the existing Framingham risk model across all event types.

Linking proteomic data to other sources of health information could improve diagnosis and help patients and healthcare providers to make informed treatment decisions, achieve appropriate lifestyle changes and manage medical resources.

Dr Stephen Williams

> ***When can we develop a Proteomics England?***
>
> Professor Chas Bountra

Chair

Professor Gil McVean (Wellcome Trust Centre for Human Genetics, University of Oxford and Genomics plc, UK)

Speakers

Sir John Chisholm (Executive Chairman, Genomics England, UK)
Professor Simon Lovestone (Professor of Translational Neuroscience, Department of Psychiatry, University of Oxford, UK)
Professor Kazem Rahimi (Deputy Director, The George Institute for Global Health, Oxford, UK)
Dr Stephen Williams (Chief Medical Officer, SomaLogic, CO, USA)

Panellist

Andrea Mensah (Senior Director, Health Sciences Global Business Unit, Oracle, CA, USA)

The changing face of diagnostics

Precision medicine can improve patient outcomes and resource utilization across medicine, from specialist areas such as oncology to care in the community. The digital revolution is transforming diagnostics, as a session chaired by Dr John Jeans (Office for Life Sciences) heard. Increased processing power is bringing next-generation sequencing into routine clinical care while, with the right technology, the simple webcam could also play an important role.

Next-generation sequencing

Dr Anna Schuh (University of Oxford) outlined the clinical utility of targeted next-generation sequencing, providing examples from haematology and cancer.

Conventional diagnostic tests for rare congenital anaemias may involve the use of electron microscopy, which is expensive and not always available. Less expensive methods may lack specificity and sensitivity. In a study involving 57 individuals with rare congenital anaemias, targeted next-generation sequencing resulted in a change in care for 42% of patients, including the avoidance of bone marrow transplantation.

Dr Schuh also described a multigene platform to predict response to cancer treatment. The test, which yields results in 6 days, detects more mutations and requires less DNA than conventional technology. Stratifying patients to the most effective targeted agents has the potential to prolong remission and reduce side effects. Importantly, targeted next-generation sequencing can be offered at a cost similar to that of conventional diagnostic techniques.

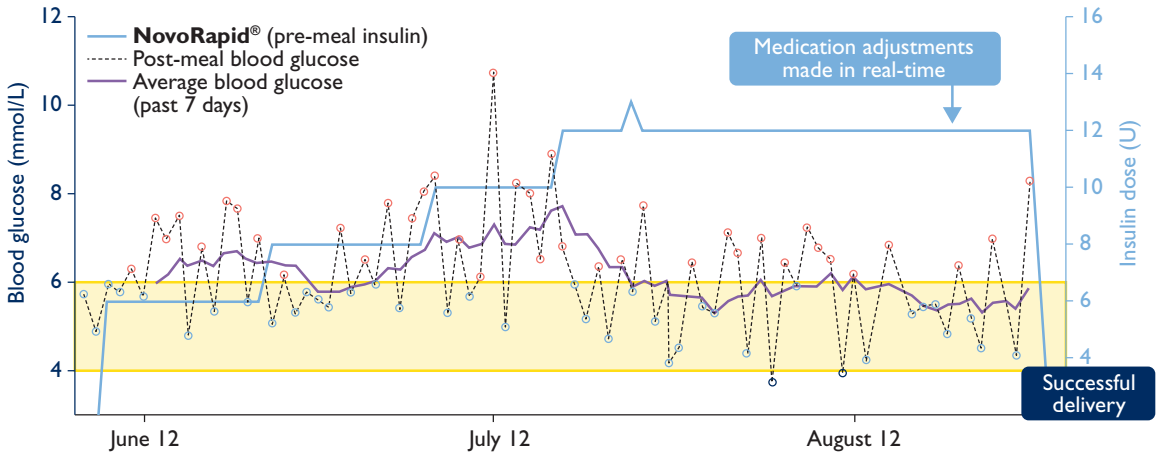
Remote monitoring

Professor Lionel Tarassenko (University of Oxford) discussed the use of digital health technology in remote monitoring of patients with chronic diseases.

The number of cases of gestational diabetes mellitus is rising steadily, placing demands on resource-limited services. Professor Tarassenko has developed GDm-health, a system that transmits readings from a Bluetooth-enabled blood glucose meter to a smartphone application. Women can annotate their data with comments regarding mealtimes and medication, review historical data and request advice from a midwife. Results are automatically sent to a secure website allowing healthcare professionals to monitor patient progress (*Figure 5*).

Care can be tailored to risk, patient and carer preference

FIGURE 5. GDm-health: real-time medication adjustments in response to blood glucose levels



Yellow shaded area denotes target blood glucose levels.

The impact of GDm-health on clinical outcomes and service utilization is being assessed in an ongoing randomized clinical trial (NCT01916694). The Oxford AHSN is helping to implement this technology across NHS trusts in the region.

Healthcare professionals can also use telecommunications technology to evaluate, diagnose and treat patients remotely. Professor Tarassenko explained how the addition of webcam sensing for non-contact monitoring of vital signs has the power to transform telemedicine.

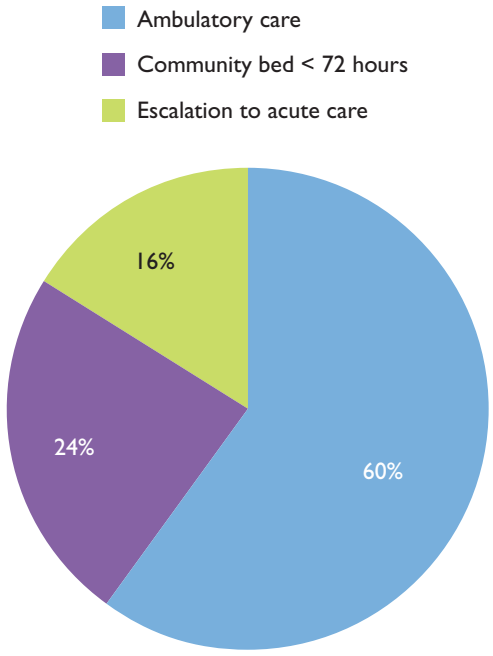
Optimizing care delivery

Professor Dan Lasserson

Point-of-care diagnostic technology is used to enable rapid, acute ambulatory care outside the hospital setting. Professor Dan Lasserson (University of Oxford) described the award-winning Emergency Multidisciplinary Unit (EMU) at Abingdon Community Hospital. The EMU is a "medical home for a population of patients who are frail," he remarked.

The EMU provides patients with access to medical, nursing, and social care assessments. Although patients referred to the EMU may have complex medical needs, most are successfully diagnosed and treated without hospital admission (*Figure 6*). Community beds are available for patients requiring overnight care. Patients requiring escalation to acute hospital care can be referred with a diagnosis and care plan already in place. Collaborators with the Oxford AHSN Out of Hospital Care Clinical Network hope to implement this innovative care model more widely.

FIGURE 6. Emergency Multidisciplinary Unit: analysis of care pathways



Chair

Dr John Jeans CBE (Life Science Champion, Office for Life Sciences, University of Oxford and Genomics plc, UK)

Speakers

Dr Anna Schuh (Director of Molecular Diagnostics, Department of Oncology, University of Oxford, UK)
Professor Lionel Tarassenko CBE (Head, Department of Engineering Science, University of Oxford, UK)
Professor Dan Lasserson (Associate Professor, Department of Primary Care Health Sciences, University of Oxford, UK)

Panellist

Dr Teresa Wright (Principal Medical Director, Genentech, CA, USA)

From ideas to approval: accelerating development pathways

We are at an unprecedented point in the evolution of our healthcare system. The NHS is delivering world-class patient care but demand is outstripping supply. Exponential growth of innovation across life sciences is placing increasing demands on regulatory authorities and health technology assessment agencies.

Novel clinical study designs

Precision medicine is creating increasingly stratified patient populations. In this new healthcare environment, could more effective clinical trial designs be devised to provide earlier results in smaller patient populations, compared with current trials? Regulators must adopt a permissive approach and support innovation. Sir Michael Rawlins (Medicines and Healthcare products Regulatory Agency [MHRA]) said that the MHRA is "open to new ideas".

Traditional randomized, controlled studies are expensive and may not generate evidence that is applicable to real-world populations. In a study with an adaptive pathway design, drug effect sizes determined during an experimental phase form the basis for an initial, conditional marketing authorization. The subsequent observational phase generates real-world evidence to support progressive adaptations of the marketing authorization. Currently, the European Medicines Agency is investigating how adaptive pathways might be designed for different products and indications. The basket trial design shows particular promise in oncology, where tumour molecular heterogeneity presents a challenge. Patients expressing the same specific molecular marker (i.e. in the same 'basket') receive the same targeted therapy, independent of their tumour histology. Other options to consider are umbrella, Mendelian randomization and step-wedge study designs.

> ***We may see drugs licensed for people with specific mutations rather than specific conditions.***
>
> Sir Michael Rawlins

Novel statistical analysis

Frequentist statistics has dominated the design and analysis of clinical trials for over 60 years. Bayesian analysis is an alternative approach that relates to the probability of what is already known, what the new evidence shows and what can be inferred. It does not require a null hypothesis or generate a *p* value; however, Bayesian analysis is computationally difficult to perform and has not been widely accepted by drug regulatory authorities.

Companion diagnostics

Professor Gillian Leng (National Institute for Health and Care Excellence [NICE]) explained that commercial companies or senior clinicians may notify NICE of new companion diagnostic products. Ideas are reviewed by a Medical Technology Advisory Committee before being directed to the appropriate diagnostic assessment programme. Companion diagnostics may be developed simultaneously with a drug, come to market many years after drug approval or already be available. For NICE, the ideal situation is to develop co-dependent pharmaceuticals and diagnostics that can be considered as a 'package' for assessment of clinical- and cost-effectiveness.

Companion diagnostics can facilitate the stratification of patient populations and improve clinical outcomes, but are unlikely to generate cost savings.

Communication

Early communication to all stakeholders is important. In particular, reporting of adverse events needs to improve in order to provide clear, balanced, real-world evidence of safety and efficacy. While Internet forums provide platforms to increase patient voice and connectivity, it is important not to discriminate against those who are not familiar with this medium. All patients should be regarded as being (or soon to become) empowered, knowledgeable advocates and there should be no barriers to communication.

Sir Michael Rawlins

> ***Patient dialogue has to change.***
>
> Sir Michael Rawlins

Peter Ellingworth

> ***Innovation is growing exponentially. The question is often can we afford new therapies? We should be asking what the consequences are without them.***
>
> Peter Ellingworth

Chair

Peter Ellingworth (Chief Executive, Association of British Healthcare Industries, UK)

Speakers

Sir Michael Rawlins FMedSci (Chairman, Medicine and Healthcare products Regulatory Agency, UK)
Professor Gillian Leng CBE (Deputy Chief Executive, National Institute for Health and Care Excellence, UK)

Panellists

Dr Dominic Behan (Executive Vice President, Chief Scientific Officer, Arena Pharmaceuticals, CA, USA)
Professor Brendan Buckley (Chief Medical Officer, ICON, Ireland)
Dr Timothy Clackson (President of Research and Development and Chief Scientific Officer, ARIAD Pharmaceuticals, MA, USA)

Crowdsourcing science through open innovation partnerships

Only one in three molecules for cancer therapy that reaches phase 3 trials subsequently enters the market. Of the last 71 drugs launched for the treatment of solid tumours, only 30 showed clinically meaningful efficacy. Why is drug discovery so inefficient, and is crowdsourcing science the solution? The Oxford Structural Genomics Consortium, a public–private partnership, has demonstrated the power of open-access research in addressing these issues.

Minimize duplication

Secrecy, competition and duplication exist during the early stages of drug discovery as pharmaceutical companies, biotechnology companies and academic groups work in parallel on the same few ideas. This is a waste of resources, and is bad for carers and patients, noted Professor Chas Bountra (University of Oxford). Disease heterogeneity and complexity, a lack of biomarkers and a reliance on animal models are issues that need to be addressed. How can we design better drugs when we often do not know how currently used drugs work?

The Oxford Structural Genomics Consortium (SGC) has engaged with 10 large pharmaceutical companies each contributing US$8 million. Sharing expertise and resources, the consortium generates high-quality reagents from novel human proteins. These compounds are made freely available to academia and industry and are now being evaluated in primary human cell assays.

Data and knowledge are shared immediately to minimize duplication

Success story

Professor Bountra outlined an example to demonstrate the remarkable impact of this approach. In 2010, *Nature* published an article on JQ1, a potent and selective small-molecule inhibitor of bromodomain and extraterminal domain (BET)-family bromodomains (Filippakopoulos P *et al. Nature* 2010;468:1067–73). In collaboration with Harvard Medical School, Oxford SGC demonstrated the role of JQ1 in nuclear protein in testis (NUT)-midline carcinoma, a rare and aggressive cancer. Subsequently, this high-quality inhibitor was freely shared with more than 1000 laboratories globally. Collaborators identified targets for JQ1 in other cancers, as well as in sepsis, fibrosis, chronic obstructive pulmonary disease (COPD), cardiac hypertrophy and male contraception.

The *Nature* publication had a remarkable impact in academia and industry. In only 4.5 years, the article was cited nearly 800 times and over 200 articles were published on the JQ1 target. To date, six pharmaceutical companies have generated six proprietary molecules that are undergoing 14 clinical studies. Tensha Therapeutics (Boston, MA, USA) has secured US$15 million to take novel molecules related to JQ1 to the clinic.

The Oxford SGC has succeeded by bringing together the best of industry with the best of academia

"We have catalysed science, we have catalysed translational research," said Professor Bountra. The SGC aims to build stronger links with patient organizations. Through collaborations with academics and entrepreneurs they hope to help establish biotechnology companies across the UK. Their most ambitious project is to push the pre-competitive boundary to phase 2a to fast-track new targets into the clinic and marketplace. Other ongoing projects are shown in Table 2.

Professor Chas Bountra

> ***Drugs are discovered in patients, not in animal models, not in cell lines.***
>
> Professor Chas Bountra

TABLE 2. Current Structural Genomics Consortium projects

Funding source	Cost	Objective
Brazilian Government	US$9 million	Development of novel protein kinase inhibitors at SGC-UNICAMP
Wellcome Trust	£9 million	Generation of 'target-enabling packages' for high-priority genes in cancer, metabolism and neuroscience
Innovative Medicines Initiative	€42 million	ULTRA-DD: development of novel targets in autoimmune and EFPIA companies and inflammatory diseases using patient-cell-derived assays
Alzheimer's Research UK	£10 million	Establishment of a Drug Discovery Institute to identify new drug targets for dementias

EFPIA, European Federation of Pharmaceutical Industries and Associations; SGC-UNICAMP, Structural Genomics Consortium–Universidade Estadual de Campinas; ULTRA-DD, Unrestricted Leveraging of Targets for Research Advancement and Drug Discovery.

Creating opportunities

Participants in the meeting believed that there is an untapped 'treasure chest' of potent and selective compounds that have failed in their primary indication but may be effective elsewhere. "Those assets are out there, so it's a question of how to get at them," said Dr Rupert Vessey (Celgene). Can organizations be encouraged to donate these compounds for further evaluation? Using the innovative collaborative approach of the SGC, they could be resurrected.

> ***From my perspective, when we've tried to interact with collections of academic institutions, they still compete with one another.***
>
> Dr Rupert Vessey

> ***High-quality tools that let you have confidence in the results takes a lot of subjectivity and non-scientific influences out of choosing an indication.***
>
> Professor Ben Whalley

Keynote speaker

Professor Chas Bountra (Professor of Translational Medicine, University of Oxford, UK)

Panellists

Dr Martino Picardo (Chief Executive, Stevenage Bioscience Catalyst, UK)
Dr Rupert Vessey (Senior Vice President, Translational Development, Celgene, NJ, USA)
Professor Ben Whalley (Professor and Neuropharmacology School Director of Research, University of Reading, UK)

Precision medicine: evolution and revolution

The precision medicine landscape in the UK is promising but fragmented. The newly established Precision Medicine Catapult aims to make the UK the most attractive location in the world to develop precision medicine. We have a wide range of unique national assets to achieve this, but better coordination of these resources is required.

Professor Richard Barker (Precision Medicine Catapult) chaired a session exploring initiatives to fast-track precision medicine in the UK. These include population-scale biomedical data collection, as well as new approaches to develop vaccines and to manage cancer and airway diseases.

Big data

Professor Martin Landray (University of Oxford) emphasized that "drugs are discovered, evaluated and used in patients". He commented that bringing together data with sufficient scale, breadth, length and depth would advance understanding of disease, help to develop treatments and improve health care.

Large numbers can provide clarity

The UK Biobank has recruited 500 000 NHS patients in 3.5 years and collected information across a broad range of functions (Table 3).

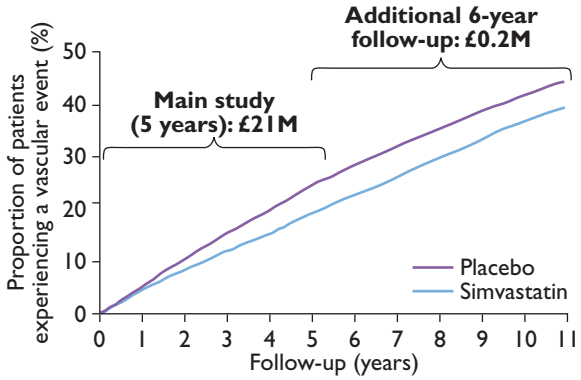
TABLE 3. UK Biobank baseline assessments

Assessment	Number of patients
Consent/questionnaire	500 000
Respiratory function	450 000
Diet (online)	200 000
Cognition (online)	120 000
Physical activity	100 000
Exercise/electrocardiogram	95 000
Retinal imaging	60 000
MRI/DEXA	5000
Multimodal brain MRI	5000

DEXA, dual-energy X-ray absorptiometry; MRI, magnetic resonance imaging.

Longitudinal data can provide information on long-term efficacy and safety. In the 5-year Heart Protection Study (20 536 patients), individuals receiving the cholesterol-lowering drug simvastatin experienced fewer vascular events than did those receiving placebo. Persistent benefits were evident throughout a 6-year post-trial period (*Figure 7*).

FIGURE 7. Heart Protection Study (N = 20 536): risk of vascular events during the main study and extended follow-up



Costs indicate the funding required to conduct the main study and extended follow-up.

Vaccine technologies

Professor Adrian Hill (University of Oxford) explained that at least 15 pathogens have caused disease outbreaks in the past 15 years. No licensed human vaccinations exist for any of these infectious diseases. In August 2015, the World Health Organization approached the Jenner Institute (University of Oxford) to develop a vaccine to respond to the Ebola virus disease outbreak in West Africa. The time required to reach phase 3 trials was impressive, taking months rather than years.

> ***Clinicians often only see a snapshot of the problem. We need to understand phenotypes at scale.***
>
> Professor Martin Landray

There is huge interest in the use of immunotherapy for cancer. The Jenner Institute is utilizing an approach involving amplification of natural T-cell responses to develop a vaccine for prostate cancer. Window-of-opportunity trials allow the new therapy to be evaluated alongside the standard treatments that patients are receiving. Immunopeptidome analysis will allow immunotherapy to be specifically targeted to peptides presented by tumours. Local spin-out companies such as ProImmune and Immunocore will play essential roles in this rapidly expanding field.

Cancer management

Professor Gillies McKenna (University of Oxford) proposed that precision cancer therapy could help to achieve a 75% 10-year disease-free survival rate for patients.

Intratumour heterogeneity and the acquisition of resistance limit patient response rates to molecularly targeted cancer therapies

Most patients who have been disease free for 10 years have undergone surgery or received radiotherapy. Cancer surgery has progressed towards minimally invasive interventions, and there is a drive to increase the precision and to reduce the toxicity of radiotherapy. Opening in 2018, the Precision Cancer Medicine Institute at the University of Oxford will provide research facilities to investigate new therapeutic techniques. A partnership with ProNova Solutions will bring the first proton therapy research facility to the UK. The institute will focus on patients with early-stage cancers.

Airway disease

Professor Ian Pavord (University of Oxford) outlined how inflammatory phenotyping could help to identify patients with respiratory disease who are likely to respond to treatment or to experience specific adverse events.

In patients with asthma, airway dysfunction drives day-to-day symptoms. More severe exacerbations, which respond poorly to conventional inhaled therapies, are associated with eosinophilic airway inflammation. In June 2015, the US Food and Drug Administration approved mepolizumab for the treatment of severe asthma in adults. Previously, this anti-interleukin-5 monoclonal antibody was almost discarded as a candidate for asthma treatment. In patients with recurrent asthma exacerbations and evidence of eosinophilic inflammation, mepolizumab produced a 50% decrease in the rate of exacerbations. No improvements in symptoms were observed (Haldar P *et al. N Engl J Med* 2009;360:973–84).

Long-term inhaled corticosteroid treatment of patients with COPD has been associated with cases of pneumonia; however, although the risk of COPD exacerbations, like asthma exacerbations, increases with blood eosinophil count, it has been shown that pneumonia occurs only in patients with the lowest eosinophil counts.

> ***The UK is already and can become a global leader in this new area of precision medicine.***
>
> Professor Richard Barker

Chair

Professor Richard Barker OBE (Chairman, Precision Medicine Catapult, UK)

Speakers

Professor Adrian Hill (Director of the Jenner Institute, University of Oxford, UK)
Professor Martin Landray (Professor of Medicine and Epidemiology, University of Oxford, UK)
Professor Gillies McKenna (Head of Department of Oncology, University of Oxford, UK)
Professor Ian Pavord (Professor of Respiratory Medicine, University of Oxford, UK)

Tackling cancer: priorities, progress, plans

Despite rising costs, the UK Government is tightening spending on cancer care. Professor Sarah Blagden (University of Oxford) proposed that industry and academia should work together to implement participation in clinical trials into the routine care of patients with cancer. Currently, clinical trial legislation is too inflexible to meet this challenge.

The largest drop-off in drug development occurs between phases 1 and 2, due to lack of efficacy, safety concerns and other commercial reasons. Trials need to be more imaginative and adaptive.

Professor Blagden proposed that it would be beneficial to conduct larger phase 1 studies that recruit more representative patient populations. Investment in pharmacokinetic and pharmacodynamic analyses at phase 1 would help to identify and validate biomarkers. In the UK, 18 Experimental Cancer Medicine Centres have facilities to perform such complex studies. These centres could form an effective consortium and market themselves worldwide.

Transfer the decision point to phase 1

Biologic therapies

Early cancer biologics, such as interferons and interleukins, were intended to influence patients' natural immune response to cancer cells. Identification of specific tumour antigens enabled the development of monoclonal antibodies that could deliver targeted cancer therapy. Dr Sean McCarthy (CytomX Therapeutics) explained that immunotherapy is shifting the paradigm of cancer care. More patients are seeing tumour regression and cancer remission rather than delayed progression.

CytomX Therapeutics has developed Probodies™, fully recombinant masked antibodies that remain inert in healthy tissue but are activated through protease activity in the tumour microenvironment. This prodrug strategy aims to increase the therapeutic index of immunotherapy.

Dr McCarthy asked if "phase 1 could be the new phase 3"? Several US Food and Drug Administration initiatives have created a favourable regulatory landscape to improve patient access to new therapies. For example, Breakthrough Therapy designation expedites the development and review of drugs for serious or life-threatening conditions that demonstrate strong early signals of clinical efficacy. With this designation, the cancer therapy Keytruda® received approval based on phase 1 data after only 3.5 years in development.

Post-marketing experience

As survival rates for cancer have improved, the post-marketing period has become critical for monitoring adverse events associated with new drugs. Dr Timothy Clackson (ARIAD Pharmaceuticals) emphasized that accelerating development should not compromise benefit–risk assessments.

Chair

Professor Sarah Blagden (Department of Oncology, University of Oxford, UK)

Speakers

Dr Timothy Clackson (President of Research and Development and Chief Scientific Officer, ARIAD Pharmaceuticals, MA, USA)

Dr Sean McCarthy (Chief Executive Officer, CytomX Therapeutics, CA, USA)

Tackling diabetes: a global epidemic

A global epidemic of diabetes is threatening the economic development and stability of many countries. In China, half the population have diabetes or pre-diabetes. Professor Rury Holman (University of Oxford) emphasized that mass screening would not be effective in the management of this chronic disease. Treatments need to be targeted appropriately.

Diabetes research

With approximately 48 000 patients participating in clinical studies, the Oxford Centre for Diabetes, Endocrinology and Metabolism (OCDEM) Diabetes Trial Unit (DTU) is the largest of its kind worldwide. In addition to performing multinational clinical outcome trials, the DTU has a translational research group that designs and conducts trials to evaluate new therapeutics and devices. OCDEM also has a leading Human Islet Isolation Unit that provides islets for research and clinical use.

> ***To tackle the global epidemic in diabetes, we need to become a lot cleverer in who we treat, when and how.***
>
> Professor Rury Holman

Weight management

Obesity can lead to serious complications, including type 2 diabetes. Dr Dominic Behan (Arena Pharmaceuticals) provided an overview of the development of Belviq® (lorcaserin HCl), a first-in-class, selective 5-HT_{2C} receptor agonist approved for long-term weight management. G-protein-coupled 5-HT_{2C} receptors play a crucial role in the hormonal control of food intake and energy balance. In a phase 3 programme, lorcaserin provided consistent weight-loss benefits without the side effects associated with activation of other 5-HT receptors.

Achieving a 5% weight loss is important in diabetes management and prevention

Lorcaserin improves glycaemic control and reduces the use of anti-diabetic medications in patients with type 2 diabetes. It has also been shown to decrease the onset of type 2 diabetes in obese patients without the disease.

The forgotten organ

The human gut microbiome contains more than 100 trillion microorganisms and 400-fold more genes than the human genome. Dr Alessandra Cervino (Enterome Bioscience) outlined how sequencing and mapping of total faecal bacterial gene content allows identification of 'metagenomic signatures' associated with a disease. This approach has helped to increase understanding of the role of the gut microbiome in several diseases, including type 1 and type 2 diabetes, and obesity.

Companies have focused on the potential health benefits that can be derived from interfering with the composition of the gut microbiome. Strategies include the use of prebiotics, probiotics, synthetic communities, targeted therapeutics and faecal transplants.

> ***There has been an explosion in the literature on the human gut microbiome over the past 5 years.***
>
> Dr Alessandra Cervino

Chair

Professor Rury Holman (Director, Diabetes Trial Unit, University of Oxford, UK)

Speakers

Dr Dominic Behan (Executive Vice President, Chief Scientific Officer, Arena Pharmaceuticals, CA, USA)
Dr Alessandra Cervino (Head of Discovery, Enterome Bioscience, France)

Tackling infection: rapid response

Whole genome sequencing and other new technologies could transform the diagnosis and management of infectious diseases in our lifetimes. Faster identification of the causative microorganism and its antimicrobial susceptibility, coupled with novel treatments, should allow infections to be controlled with less selective pressure driving the emergence of resistance.

Transformative technology

By 2050, antimicrobial resistance is predicted to result in the death of 10 million people per year and incur an annual cost of US$100 trillion. Professor Derrick Crook (Oxford University Hospitals NHS Trust) explained that traditional approaches to infection control are lengthy, relying on culturing samples to identify species and strain, and to test antimicrobial susceptibility. WGS of pathogens can generate complete diagnostic, susceptibility and surveillance information in a single step, reducing costs compared with current approaches.

Rapid response

Professor Miles Carroll (Public Health England) explained that WGS has shown promise in tackling Ebola virus disease. The European Mobile Laboratory Project (developed by the Bundeswehr Institute of Microbiology, Germany) shipped a laboratory to the epicentre of the Ebola outbreak in Guinea in 2014. The unit has access to a portable, real-time genomic surveillance system to provide a rapid diagnostic service.

Overturning assumptions

Dr Ronnie Farquhar (formerly of Cubist Pharmaceuticals) outlined assumptions made about infection therapeutics in the 1980s, and whether they proved to be true.

- **Assumption 1** – addressable targets for killing bacteria and fungi could be broadened.
  False. New pharmacophores have been identified but the challenge remains to convert them into safe and effective drugs.
- **Assumption 2** – antimicrobial resistance would drive continued innovation.
  False. Few pharmaceutical companies retain a sizeable drug discovery and development effort, although SMEs (small- and medium-sized enterprises) are emerging to fill this gap.
- **Assumption 3** – healthy gut bacteria are of minimal importance.
  False. The gut microbiome is important to overall health, and the impact of disrupting it is starting to be understood.
- **Assumption 4** – there is little scope for innovation in antivirals.
  False. Innovative molecules and multidrug combinations have improved outcomes for patients infected with human immunodeficiency virus and hepatitis C virus, and generated billion-dollar returns for forward-thinking companies.

Dr Farquhar believes that an era of untreatable infections will be avoided, thanks to new molecules and targets, immunotherapies and combination therapies. Point-of-care diagnostics and renewed interest in narrow-spectrum antibiotics will drive microbiome-sparing regimens that will reduce resistance pressure and preserve human health.

Chair

Professor Derrick Crook (Professor of Microbiology and Consultant Microbiologist, Oxford University Hospitals NHS Trust, UK)

Speakers

Professor Miles Carroll (Head of Research, Public Health England, UK)
Dr Ronnie Farquhar (Former Senior Vice President, Discovery and Pharmaceutical Sciences, Cubist Pharmaceuticals, MA, USA)
Dr Sean McCarthy (Chief Executive Officer, CytomX Therapeutics, CA, USA)

Generating a step change in life sciences investment

Can we turn our world-class science into market-leading life sciences companies? Oxford is generating many potential spin-out and commercial opportunities; however, funding entire commercialization pathways remains a challenge, and no one organization can achieve it all.

Landmark partnership

In May 2015, Oxford Sciences Innovation plc (OSI) was established as the University of Oxford's partner to develop spin-out companies. OSI has raised £320 million through partnerships with major investors and will actively consider every commercial opportunity that the university generates. "There is a team, and there is capital," Alex Snow (OSI and Lansdowne Partners LLP) assured delegates.

What are investors in the life sciences sector looking for? Platforms providing multiple solutions are more likely to create commercial opportunities than single science solutions. A committed leadership group is crucial to guiding science through commercialization. Management teams that can adapt their commercial goals as the science evolves will achieve better outcomes than less flexible teams.

> ***The university feels more commercially minded than it did 15 years ago. The prize has gone up in multiples.***
>
> Alex Snow

Shawn Manning

US perspective

What is behind the success of biotechnology investment in the USA? Dr Heather Preston (TPG Biotech®) suggested that the USA has more experience than the UK and other European countries.

Investors and managers in the USA have demonstrated a higher risk tolerance than their counterparts in other countries, and there are more sources of capital

Dr Shawn Manning (Akesios Associates) emphasized the limited number of stocks available in the UK, while US investors can compile large portfolios. The US Affordable Care Act reformed health care by providing individuals with affordable quality health insurance. Although patient numbers have increased, the past year has seen an approximate 7% price increase for the most innovative compounds marketed in the USA. Dr David Brindley (Saïd Business School) highlighted the impact of the Jumpstart Our Business Startups Act on investment in the US biotechnology industry and the active role of patient groups.

> ***The primary function of a commercial business is to ensure a return to stakeholders. Have a plan A, have a plan B and have a plan C.***
>
> Dr Shawn Manning

Oxford advantage

Dr Dan Mahony (Polar Capital) reinforced Oxford's commitment to developing resources and infrastructure and its well-placed position to utilize the datasets generated by the UK's integrated healthcare system. Dr Richard Gill (Launchpad Venture Group) believes that the University of Oxford has a powerful competitive advantage and has attracted some of the best investors in the world. "If people from the west coast of America believe this, isn't it time we believed it as well?" he said.

Chair

Alex Snow (Deputy Chairman, Oxford Sciences Innovation, UK)

Speakers

Dr David Brindley (Fellow in Healthcare Translation, Saïd Business School, UK)
Dr Richard Gill (Board Director and Investing Member, Launchpad Venture Group, MA, USA)
Dr Dan Mahony (Fund Manager, Polar Capital, UK)
Dr Shawn Manning (Managing Director and Founder, Akesios Associates, UK)
Dr Heather Preston (Managing Director, TPG Biotech®, CA, USA)

Smart cities and smart cars: rising to urban challenges

Cities are using smart knowledge and technologies to address challenges such as air quality, traffic congestion and health care. Tackling these issues is becoming a growth industry, and the global market for this sector may be worth more than £250 billion annually by 2020.

Clean travel

We need to accept shared responsibility for the quality of the air that we breathe. Lord Paul Drayson (Drayson Technologies Ltd) outlined how people living in London will be able to use CleanSpace™ smartphone technology and personal AirTag air quality sensors to create a live picture of air quality. CleanSpace app users will be able to make informed travel choices and translate their 'CleanMiles' into rewards (*Figure 8*). This social network will generate 'big data' that could help to improve understanding of the triggers of respiratory disorders.

> ***Social innovation will come from companies who are adapting and making emotional connections with people through technology.***
>
> Lord Paul Drayson

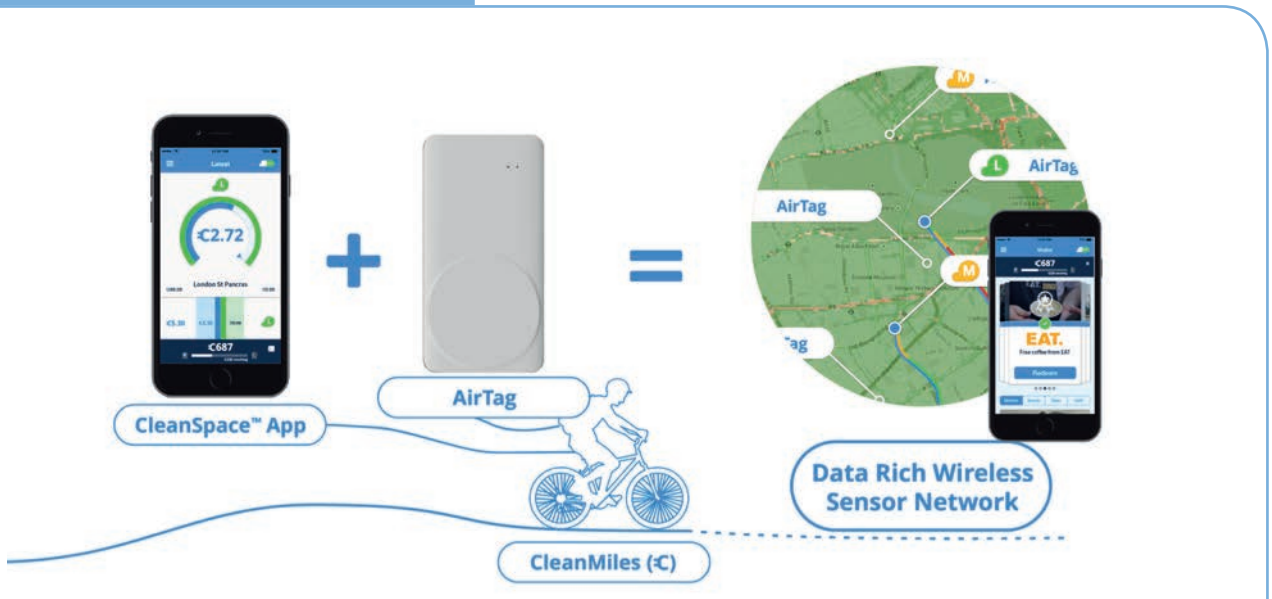
Smart Oxford

Dr Phil Clare (University of Oxford) described how smart cities are taking advantage of digital technologies to enhance wellbeing, reduce costs, increase sustainability and engage actively with citizens.

Oxford is a diverse and compact city that provides an ideal Petri dish to assess new technologies

Smart cities want to be more responsive and resilient to dynamic events, including flooding and traffic congestion. The Oxford Flood Network is a local initiative driven by citizens. Using their own sensors, residents provide early warning of changing stream and river levels. Automated vehicle trials are already taking place in Oxford, and the Mobile Oxford programme aims to transform the way that we use transport, technology and infrastructure.

FIGURE 8. CleanSpace™ technology



Digital therapeutics

Dr Caroline Hargrove (McLaren Applied Technologies) described the often complex care pathways of the current healthcare system as a 'pinball machine' in which there may be little to guide patients. Engineers at McLaren Applied Technologies see this as a design challenge. In a joint partnership with the University of Oxford, they hope to improve health outcomes, while reducing inequality and the costs of care. Expertise, technology and tools are available to improve a patient's lifestyle choices, diagnosis, treatment and recovery, but they need to be connected.

An efficient, data-driven framework for the healthcare system will benefit patients, healthcare providers and commissioners. Patients will benefit from 'digital project managers' to navigate through the best route of care. Healthcare providers can track patient progress through the system, while commissioners can assess whether targets are being met.

Lord Drayson concluded that "within health care and life sciences, we are going to need the equivalent of a standard operating system, and it is likely to be owned by a company".

Dr Caroline Hargrove

> ***Companies like Apple and Google are creating their own ecosystems. Change will be driven by users. If a system helps them, they will contribute by buying the product.***
>
> Dr Caroline Hargrove

Chair

Lord Paul Drayson (Chairman and Chief Executive, Drayson Technologies Ltd, UK)

Speakers

Dr Phil Clare (Associate Director, Research Services and Head of Knowledge Exchange, University of Oxford, UK)
Dr Caroline Hargrove (Technical Director, McLaren Applied Technologies, UK)

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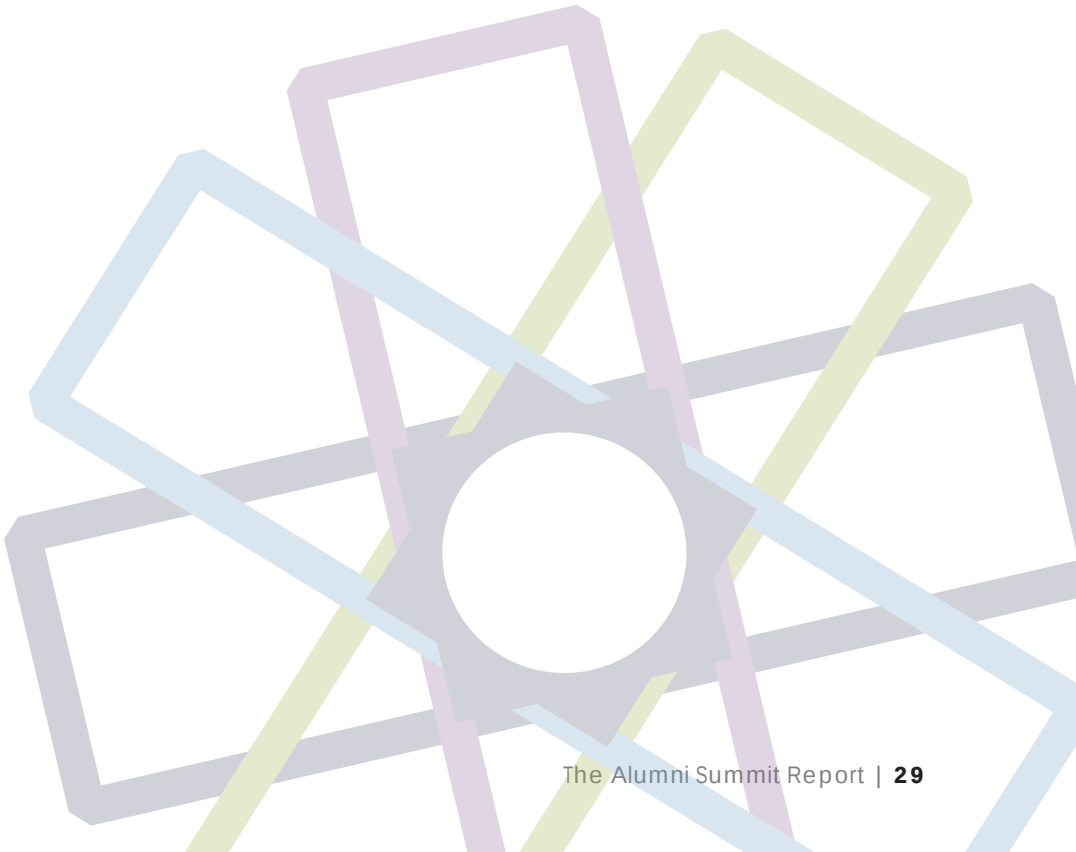

The Alumni Summit

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