



## **Stratified, personalised or P4 medicine: a new direction for placing the patient at the centre of healthcare and health education (May 2015)**

Summary of a joint FORUM meeting held on 12 May 2015.

Supported by the Academy of Medical Sciences, the University of Southampton, Science Europe and the Medical Research Council.



### **The Academy of Medical Sciences and the FORUM**

The Academy of Medical Sciences is the independent body in the UK representing the diversity of medical science. Our mission is to promote medical science and its translation into benefits for society. The Academy's elected Fellows are the United Kingdom's leading medical scientists from hospitals, academia, industry and the public service.

The Academy's FORUM was established in 2003 to deliver the strategic objective of 'linking academia, industry and the NHS' and to recognise the role of industry in medical research. We are grateful for the support provided by the members and are keen to encourage more organisations to take part. If you would like information on becoming a member please contact [FORUM@acmedsci.ac.uk](mailto:FORUM@acmedsci.ac.uk).

### **Medical Research Council**

The heart of the MRC's mission is to improve human health through world-class medical research. To achieve this, we support research across the biomedical spectrum, from fundamental lab-based science to clinical trials, and in all major disease areas. We work closely with the NHS and the UK Health Departments to deliver our mission, and give a high priority to research that is likely to make a real difference to clinical practice and the health of the population.

### **Science Europe**

Science Europe is an association of European Research Funding Organisations (RFO) and Research Performing Organisations (RPO), based in Brussels. Science Europe promotes the collective interests of the RFO and RPO. It supports its Member Organisations in their efforts to foster European research. It will strengthen the European Research Area (ERA) through its direct engagement with key partners. It works and partners with other entities such as the European Universities, the European Academies, the European Scientific Intergovernmental Organisations and the European Commission to develop a coherent and inclusive ERA. In its structures and actions it ensures that it takes into consideration the interests and opinions of researchers in all European research systems.

### **University of Southampton**

The University of Southampton is a world-class university built on the quality and diversity of our community. We are a research intensive university and a founding member of the prestigious Russell Group. Our successes are acknowledged in international and UK league table rankings and with prestigious awards. Our staff place a high value on excellence and creativity, supporting independence of thought, and the freedom to challenge existing knowledge and beliefs through critical research and scholarship. Through our education and research we transform people's lives and change the world for the better.

### **Disclaimer**

This document reflects views expressed at the meeting and does not necessarily represent the views of all attendees, the Academy of Medical Sciences or its Fellows, Science Europe, the University of Southampton or the Medical Research Council.

For further information, please contact Victoria Charlton, Head of Policy at the Academy of Medical Sciences ([victoria.charlton@acmedsci.ac.uk](mailto:victoria.charlton@acmedsci.ac.uk), (0)20 3176 2168).

All web references were accessed in June 2015.

© Academy of Medical Sciences 2015

## Contents

---

Summary	4
Introduction	6
The application of stratified approaches to healthcare	9
Next steps in the adoption of stratified medicines	18
Conclusion	28
Appendix I Programme	29
Appendix II Symposium delegates	31
Appendix III Summary of poster presentations	34

## Summary

---

The terms 'stratified', 'personalised' or 'precision' medicine all refer to the grouping of patients based on risk of disease, or response to therapy, using diagnostic tests or techniques.<sup>1</sup> This approach provides an opportunity for patients and healthcare providers to benefit from more targeted and effective treatments, potentially delivering more healthcare gain and improved efficiency for the healthcare system, while offering industry an expanded market for specialised treatments and the opportunity to benefit from the incremental value delivered by more effective products. The term 'P4' encompasses this personalised approach within a broader frame which also recognises the increasingly predictive, preventive and participatory nature of modern medicine. However, while such approaches have been under development for several years and are increasingly reaching the bedside, progress has been slower than anticipated; in particular, despite rapid advances in the research underpinning stratified medicine, barriers to its implementation in healthcare settings remain.

On 12 May 2015, the Academy of Medical Sciences, in partnership with the Medical Research Council, Science Europe and the University of Southampton, held a symposium on 'Stratified, personalised or P4 medicine' to explore these issues. Recognising the importance of cross-sector coordination, the meeting was held as part of the Academy's FORUM programme, which brings together leaders from across industry, academia and the NHS to accelerate progress through dialogue and collaboration. The aim of the meeting was to consider how stratified medicine can be applied across the spectrum of diseases, examine the issues of its implementation in healthcare settings and look to the future in preparing the healthcare community to embrace this targeted approach to therapy. This report provides a summary of the speakers' presentations and the discussions that followed.

The meeting brought together over 100 participants from across academia, industry, clinical practice, regulatory agencies, government, the NHS and the third sector. Over the course of the day, speakers described the many ways in which stratified approaches were now being used in healthcare settings, while exploring some of the challenges that were being faced. Subsequent discussion highlighted the potential ways in which the research community, the NHS and other stakeholders might take steps to resolve these issues.

Key themes arising included:

- The huge potential offered by P4 medicine and the many ways in which this potential is now being realised in the clinic. Examples include the application of stratified approaches to preventive healthcare, the use of 'omic technologies to better understand disease processes, and the increasing adoption of stratification for the delivery of highly effective, targeted therapies.
- The opportunity for 'big data' to transform medical science and its fundamental importance in the move towards increased personalisation. It was recognised that further organisational, technological and cultural changes will need to take place if the UK is to take full advantage of the data revolution currently underway.

---

<sup>1</sup> In this report, we use the term 'stratified medicine' to refer to this approach.

- The important role to be played by patients and the public in driving adoption of new medical approaches. It was argued that engaging these groups in the shift towards stratified medicine will necessitate an evolution of the 'social contract' that currently exists between patients and innovators, and patients and physicians, providing a societal mandate for wide-scale adoption.
- The significant barrier to further development and uptake of stratified medicines that continues to be posed by current drug and device pricing and reimbursement models. In particular, it was argued that volume-based pricing models – such as the current UK Pharmaceutical Price Regulation Scheme – do not well reflect the value often delivered by targeted treatments, and that the low price typically paid for companion diagnostics acts as a disincentive to their development.
- The need for the health system to evolve in order to keep pace with technological innovation and the new approaches to healthcare that this enables. While it was recognised that a large number of initiatives were currently underway to help facilitate the adoption of stratified medicine, participants continued to see a need for the NHS to adapt; in particular, to continue to develop a node-based healthcare infrastructure to facilitate regional adoption of innovative approaches.
- The requirement for both researchers and clinicians to have a robust understanding of genomics and other fields underlying stratified medicine, in order to better facilitate its adoption. It was noted that this will likely require both capacity building within the existing workforce and a new approach to the education of future generations.

## Introduction

---

*'It is more important to know what sort of person has a disease, than to know what sort of disease a person has'.<sup>2</sup> – Hippocrates*

The stratification of patients into groups in order to guide treatment decisions is not a new concept; every time that we attempt to diagnose the underlying cause of a fever as either bacterial or viral, in the hope of prescribing the intervention most likely to tackle the cause, we are effectively practicing stratified medicine. However, in recent years our understanding of both patients and their underlying conditions has significantly increased. Advances in our molecular understanding of the origins of disease have made increasingly targeted treatments possible, while advances in genome sequencing and molecular characterisation of patients have transformed our ability to identify those who will best respond to them. Thus, the reality of stratified, personalised or 'P4' medicine has entered a new phase.

These developments have come at an opportune time. In order to deal with the growing burden of non-communicable diseases and an ageing population under conditions of financial austerity, it seems likely that there will need to be a shift towards predictive and preventive healthcare and away from the current model of reacting to illness as it presents. This may require individuals to engage more actively in the 'co-production' of health, for example by taking action to minimise the risk of disease. As outlined in a recent article in the *Lancet*, *'such an approach has the potential to tackle the rising tide of chronic diseases and transform health care from disease-orientated provision to a true health maintenance service.'*<sup>3</sup> This change will potentially be enabled by the ongoing data revolution and the wealth of biological information that is now collected through diagnostic tests and, increasingly, emerging sources such as health 'apps'. These developments present both patients and clinicians with the opportunity to better understand risk factors and make informed decisions to counteract them. Increasingly, stratified approaches are likely to be a key feature of healthcare in the coming decades.

The Academy of Medical Sciences first outlined some of the challenges associated with a stratified approach in 2007, in the report of a meeting on 'Optimizing stratified medicines R&D: addressing scientific and economic issues'.<sup>4</sup> This outlined the potential benefits of stratified medicine and the barriers to its implementation, namely the lack of incentives for the development of companion diagnostics and challenges with regulation, pricing and reimbursement. Five years later, many of these issues remained and the Academy convened a two-day symposium focused on identifying solutions. The resulting report, 'Realising the potential of stratified medicine', included 18 recommendations covering infrastructure, regulation, pricing and reimbursement, and collaboration.<sup>5</sup>

---

<sup>2</sup> Murugan R (2015) *Comment: Movement towards personalised medicine in the ICU*, *The Lancet*, **3**(1), 10-12

<sup>3</sup> Horne R *et al* (2015) *A new social contract for medical innovation*, *The Lancet*, **385**(9974); 1153-1154

<sup>4</sup> The Academy of Medical Sciences (2007). *Optimizing stratified medicines R&D: addressing scientific and economic issues*.

<https://www.acmedsci.ac.uk/viewFile/publicationDownloads/120151486883.pdf>

<sup>5</sup> The Academy of Medical Sciences (2013). *Realising the potential of stratified medicine*.  
<https://www.acmedsci.ac.uk/viewFile/51e915f9f09fb.pdf>

In recent years, a variety of initiatives have been established to help address these issues and develop the UK stratified medicine landscape. This has included the formation of new Medical Research Council (MRC)-funded stratified medicine consortia, a network of molecular pathology nodes, four National Institute for Health Research (NIHR)-funded Diagnostic Evidence Cooperatives (DECs), which will help to generate information on the clinical and cost-effectiveness of *in vitro* diagnostic devices, and the launch of the 100,000 Genomes project. Increasingly, stakeholders from the NHS, industry and academia have come together to progress this field, as demonstrated by the expansion of the Innovate UK Stratified Medicines Innovation Platform to facilitate the development and adoption of stratified medicine in the UK.

However, obstacles to the implementation of stratified approaches remain and it is clear that the adoption of P4 medicine will require collaboration and communication across the clinical, commercial and research communities.<sup>6</sup> Bringing together these groups is a key objective of the Academy's FORUM programme, and, on 12 May 2015, a FORUM meeting was held to discuss this important subject. The aims of the meeting were to:

- Consider how the concept of stratified medicines can be applied across the spectrum of diseases, from cancer to rare diseases.
- Examine the issues of implementing stratified medicine in healthcare settings.
- Look to the future in preparing the healthcare community to embrace this new approach to therapy, including its incorporation into medical education.

The meeting, which was held in partnership with the MRC, Science Europe and the University of Southampton, convened over 100 delegates from across Europe spanning academia, industry, government, the NHS, charities, regulators and funding bodies, for a day of presentations and discussion. The agenda and full list of meeting participants can be found in Appendix I and II respectively. Promising developments in stratified medicine were presented, including work from the 100,000 Genomes project, the Farr Institute and the EU Innovative Medicines Initiative, alongside projects in the fields of oncology, the early life environment, asthma and rare diseases. In addition, posters were exhibited to showcase work by the MRC stratified medicine consortia, and by clinicians and academics from the University of Southampton and University Hospital Southampton (see Appendix III). Several talks expanded on the challenges highlighted in the Academy's 2013 report and considered recent developments in data integration and informatics, capacity building, diagnostic development and education.<sup>7</sup> Discussion throughout the day centred on the remaining barriers to adoption of stratified strategies across the healthcare and medical science sectors.<sup>8</sup>

## **Acknowledgements**

We would like to extend our thanks to the Medical Research Council, Science Europe and the University of Southampton for supporting this event, and to all those who attended

---

<sup>6</sup> Predictive, preventive, personalised and participatory. See, for example: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3678833/>

<sup>7</sup> The Academy of Medical Sciences (2013) *Realising the potential of stratified medicine*, <https://www.acmedsci.ac.uk/viewFile/51e915f9f09fb.pdf>

<sup>8</sup> This document reflects views expressed at the meeting and does not necessarily represent the views of all attendees, the Academy of Medical Sciences or its Fellows, Science Europe, the University of Southampton or the Medical Research Council.

and participated in the meeting. In particular, we would like to thank the four session chairs, Professor Sir John Tooke PMedSci, Professor Jens Lundgren, Professor Richard Trembath FMedSci and Professor John Iredale FRSE FMedSci, and Professor Stephen Holgate CBE FMedSci, for his assistance in planning and facilitating the meeting.

## The application of stratified approaches to healthcare

---

### Realising the potential of stratified medicine

In his introductory comments, Professor Sir John Tooke PMedSci highlighted the key findings of the Academy's 2013 report on stratified medicines and the notable developments that have occurred since, particularly across the UK.<sup>9</sup> He noted the substantial investment made by the MRC into the stratified medicine consortia and molecular pathology nodes, and the creation of four NIHR-funded DECAs to bridge the gap from invention to adoption in the diagnostics sector.<sup>10,11</sup> Sir John also highlighted the progress being made by the 100,000 Genomes project, which aims to deliver benefit to both patients and scientists while '*kick-starting the development of a UK genomics industry*'.<sup>12</sup>

In addition, Sir John noted the promise of the European Medicines Agency's adaptive licensing pilot scheme, which aims to accelerate provision of phase II drugs for unmet medical need, as an alternative to the current system of large, randomised controlled trial (RCT)-led market authorisation.

Finally, the importance of a new 'social contract' was emphasised, to bring the public on the journey of development and implementation of stratified medicine, to ensure that this approach is able to realise its full potential.

### The application of stratified approaches

Throughout the day, speakers showcased how stratified approaches had delivered healthcare benefits to date, and the potential that the future held. Some of these examples are detailed below.

### Stratification and preventive healthcare

The likelihood of a person developing a disease in their lifetime can sometimes be predicted according to their genetic sequence or clinical information from early life, allowing for stratification of patient populations into those more prone to developing a disease and those where intervention is less likely to be necessary. Ruling out predisposition for a condition can prevent unnecessary concern and potential intervention, to the benefit of both the patient and the healthcare provider. Several case studies (outlined in the following sections) were presented to demonstrate the value of such approaches.

<sup>9</sup> The Academy of Medical Sciences (2013). *Realising the potential of stratified medicine*. <https://www.acmedsci.ac.uk/viewFile/51e915f9f09fb.pdf>

<sup>10</sup> <http://www.mrc.ac.uk/news-events/news/minister-announces-14m-investment-in-stratified-medicine/>

<sup>11</sup> <http://www.nihr.ac.uk/about/diagnostic-evidence-co-operatives.htm>

<sup>12</sup> <http://www.genomicsengland.co.uk/about-genomics-england/>

### ***Genetic predisposition***

The 100,000 Genomes project was launched by Jeremy Hunt MP, Secretary of State for Health, in July 2013. It aims to sequence 100,000 genomes from NHS patients by 2017, focusing on patients with rare diseases and common cancers, and to establish the infrastructure required to store and use these data.

Professor Mark Caulfield FMedSci, Chief Scientist at Genomics England, explained that participants in the project benefit from a genetic diagnosis of their disease, both for themselves and for other family members. He presented the case of a family with a long history of kidney failure, in which genome sequencing of the father – who was already symptomatic – revealed the presence of a novel pathogenic mutation. This enabled clinicians to precisely test his daughter, who was shown not to carry the same mutation.

Without a genetic diagnosis, and the stratification that this facilitated, the daughter would have been repeatedly tested for signs of kidney failure via blood pressure measurements and urine assays, and would have likely carried the burden of uncertainty throughout her life. Thus, Professor Caulfield demonstrated how stratification based on genetic predisposition could provide reassurance to patients and their families, prevent unnecessary testing and treatment, and save time and money for the healthcare provider.

### ***Stratified public health***

Professor Cyrus Cooper FMedSci, Professor of Rheumatology and Director of the MRC Lifecourse Epidemiology Unit at the University of Southampton, argued that predisposition for non-communicable disease risk may exist from the beginning of the lifecourse, potentially enabling individuals to be stratified from birth in a way that could shape predictive and preventive approaches. He provided the example of seasonal vitamin D deficiency in pregnancy, which has been shown to predispose to osteoporosis in the unborn child. Since epigenetic biomarkers are stronger in effect size than fixed genetic markings, it is hoped that epigenetic profiling of cord cells taken at birth could be used to understand to which diseases a child is predisposed and help inform preventive and pre-emptive interventions. In this way, stratification can be extended to the wider domain of public health.

Cytomegalovirus (CMV) is another potential target for 'stratified public health'. CMV is one of the most common infections in immune-suppressed patients, developing in 30% of those who have recently undergone organ transplant. High-risk patients, if they can be identified, can be treated pre-emptively so that the infection does not lead to disease post-transplantation. However, for this to be effective, screening and allocation of patients to risk groups needs to be undertaken. Professor Jens Lundgren, Professor of Viral Disease at the University of Copenhagen and Rigshospitalet, reported that in a hospital with a high rate of incidence (50%) of CMV disease amongst those with infection, an algorithm had been developed as part of the PERSIMUNE ('Personalised Medicine of Infectious Complications in Immune Deficiency') study to generate alerts when the screening program was failing to adhere to the thresholds set. This reduced prevalence of CMV disease in transplant patients and as a result improved patient outcomes, reduced in-patient numbers and saved money. Professor Lundgren noted that using a real-time

algorithm alert system relies on clinicians trusting the computer program, which takes time and experience.

### **Using stratified medicine to better understand disease processes**

In addition to the benefit that stratification provides to the individual patient, the molecular pathology, clinical phenotyping and patient outcome data that results from this approach can be used to inform medical research for the benefit of all. Linking pathological changes in the patient to their symptoms, as well as how they respond to treatment, further informs research into the underlying mechanisms of both the pathological processes of diseases and the underlying differences in treatment response. This feedback of clinical data into medical research has been most evident in the field of oncology; however, other disease areas have also benefited in recent years. Particular advances made in cancer, asthma and genetic research were presented throughout the day.

#### ***Cancer***

The fight against cancer has increasingly embraced stratified approaches, both to identify the profile of genetic mutations within a particular tumour and to target its aetiology as it begins to spread.

Professor Peter Johnson FMedSci, Professor of Medical Oncology at the University of Southampton and Chief Clinician at Cancer Research UK, described how cancer develops as a result of an accumulation of genetic and molecular abnormalities. Profiling cancers on the basis of these abnormalities, using genomics, proteomics and metabolomics, can lead to the identification of specific 'signatures' which enables cancers to be categorised based on their genetic and molecular landscape rather than simply their site of origin. This has led to a fundamental redefinition of treatment approaches.

The site of origin of a cancer can also provide valuable information and often correlates with the degree and range of abnormality. For example, sites exposed to environmental mutagens or with a high turnover rate of cells (e.g. the lungs) tend to experience a high rate of mutation and can be associated with specific aetiology. To date, 21 different mutation signatures associated with different aetiology have so far been identified, including exposure to ultraviolet light, smoking tobacco and ageing.

Identifying the mutational and aetiological signatures present in each cancer enables their molecular pathology to be better understood and key drivers of proliferation identified. This carries benefits both for the individual patient and the wider population.

Whilst targeted treatments hold significant promise for cancer patients, drug resistance is a major issue. Professor Johnson highlighted that cancer cells are fast-replicating and heterogeneous in nature, providing the raw material needed for them to evolve very effectively when exposed to the selection pressure exerted by a single targeted treatment. The eradication of one population of cancer cells may therefore quite quickly lead to the establishment of another via selection for an alternative cancer-causing

mutation. In order to overcome this, multiple treatments targeting different mutations may be necessary. A recent focus of cancer research and drug development has been the immune system's action against cancer cells, leading to the development of promising new therapeutics that circumvent the risk of selecting for different mutations.

### ***Asthma***

Professor Ratko Djukanovic, Professor of Respiratory Medicine and Director of the Southampton NIHR Respiratory Biomedical Research Unit, highlighted the current paucity of knowledge regarding asthma aetiology. Asthma is largely regarded as a single disease and as such, current treatment options tend to address its symptoms rather than its underlying cause. Stratified approaches provide the opportunity to change this.

Professor Djukanovic presented the results of the U-BIOPRED project, a collaboration between clinicians, mathematical modellers and machine learning technologists to produce an unbiased approach to biomarker analysis, in order to better define the disease processes underlying asthma. This approach has revealed that asthma patients can be grouped according to patterns of differential gene expression and clinical phenotype. Mapping these groupings using algorithms and mathematical models helps visualise the statistically significant patterns in these complex data, revealing differences in survival rates between subsets of patients that do not necessarily present with different symptoms.

Professor Djukanovic suggested that using machine-learning to integrate genomics, proteomics and metabolomics with clinical data to inform diagnosis could enable clinicians to better predict patient outcome than using the traditional 'severe' and 'mild' categories of asthma. He hoped that this unbiased approach to big data analysis would transform the definition of asthma and its treatment ambitions by 2020.

### ***Sensory neuropathy***

Professor Mark Caulfield FMedSci, Chief Scientist at Genomics England, presented a second example from the 100,000 Genomes project involving two brothers with distal sensory-motor neuropathy – a generalised diagnosis defined by the loss of sensory and motor function as a result of nerve damage. Through genome sequencing, a novel mutation in a serine transporter was identified in both brothers, who were experiencing progressive disability as a result of their condition. This provided new understanding of disease aetiology and new treatment avenues for patients with this particular subset of the disease. In the future, Professor Caulfield suggested that patients with this mutation could be invited to participate in a trial to test whether L-serine, for example, was effective in treating this condition.

## **Using stratification for targeted therapies**

Building on a detailed understanding of the molecular basis of disease and the mechanisms involved, targeted therapies can then be developed to tackle the root cause of a disease. This both improves patient outcomes and reduces unnecessary side effects,

alongside increasing the efficiency of the healthcare system to ensure that the right therapy is chosen for the patient from the outset.

### **Cancer**

Several examples from oncology were presented by Professor Johnson, Professor Jonathan Knowles, Oxford University and Professor Andrew Morris FRSE FMedSci, University of Edinburgh, in which cancer patients carrying specific genetic mutations are being targeted by stratified medicines.

#### **Chronic myeloid leukaemia (CML)**

Until now, treatment for CML has been limited to bone marrow transplant and/or alkylating treatments. Refined profiling of the mutations in each case of CML has now enabled the development of novel therapeutics targeted at the underlying genetic causes of disease. One such drug inhibits a molecule that only exists in cancer cells and so is a truly targeted cancer therapy; this has transformed treatment for the 95% of CML patients who have this mutation.<sup>13</sup>

#### **Epidermal Growth Factor Receptor (EGFR)-positive lung cancer**

A clinical trial of gefitinib in 2004 showed no overall difference in efficacy between the drug and placebo. However, it was subsequently shown that those patients who had responded to the drug harboured the EGFR mutation, whereas non-responders did not. As such, gefitinib is now used to treat the molecularly-defined subset of lung cancer patients who test positive for the EGFR mutation.<sup>14,15</sup>

#### **Lymphoid malignancy**

In lymph node cancer, prognosis is related to the cell type in which the cancer originated. However, biopsies taken from patients are heterogeneous for cell types, making it difficult to establish the cell type in which the causative mutation arose. This can be addressed by analysing the pattern of gene expression in the biopsy to identify the cell-of-origin of the mutation, thereby enabling stratification of patients according to their cell-level diagnosis. A trial is currently ongoing to test whether molecular-guided therapy is an effective form of targeted treatment.<sup>16,17</sup>

#### **Acute myeloid leukaemia (AML)**

High throughput cell culture technology has also been used to inform treatment decisions for patients with AML. Professor Jonathan Knowles, visiting chair at the University of Oxford and Chairman of the Board at biotechnology company Immunocore, reported that the Finnish Institute for Molecular Medicine have developed an *ex vivo* cell culture platform to individualise treatment on the basis of drug sensitivity and resistance testing

<sup>13</sup> O'Brien SG *et al* (2003) *Imatinib compared with interferon and low-dose cytarabine for newly diagnosed chronic-phase chronic myeloid leukemia*, New England Journal of Medicine **348**, 994-1004

<sup>14</sup> Mok T *et al* (2009). *Gefitinib or carboplatin-paclitaxel in pulmonary adenocarcinoma*. New England Journal of Medicine **361**, 947-957.

<sup>15</sup> NICE Technology appraisal guidance [TA192] (2010)

<https://www.nice.org.uk/guidance/TA192/chapter/1-Guidance>

<sup>16</sup> <http://public.ukcrn.org.uk/Search/StudyDetail.aspx?StudyID=9800>

<sup>17</sup> <http://www.southampton.ac.uk/ctu/trialportfolio/listoftrials/remodlbtrialpage.page>

(DSRT).<sup>18</sup> In this approach, bone marrow cells from AML patients' biopsies are cultured *ex vivo* for three days before being exposed to 350 different drugs to determine which will be most effective. The results form the basis of the clinical decision as to which drug or combination of drugs to use; a process that only takes ten days from biopsy collection. The DSRT results are combined with genomic and molecular profiling and clinical information in a cancer drug sensitivity and molecular profile database. This further informs research into the key drivers and pathways for cancer, patient-specific treatment recommendations and patterns of response highlighting mechanisms of action, new drugs and biomarkers.

Professor Knowles also discussed a novel diagnostic approach used by clinicians in the US and Europe that consists of an advanced software program to perform extensive cancer biomarker analysis, both protein and DNA sequence from individual patient biopsies, and compares these profiles to responses in a large, ongoing five-year observational study and to the world literature on cancer biomarkers. This allows the prediction of which cancer therapies are more likely to be efficacious in individual patients and helps doctors to individualise cancer treatment.<sup>19</sup> Patient outcomes following treatment using this software are then tracked to understand impact and effectiveness. The use of this tool has been associated with dramatically increased length of survival in ovarian cancer and other terminal cancers as well as improved clinical decision-making.<sup>20</sup> According to Professor Knowles, this demonstrates the potential for real-time data analytics to improve patient outcomes by informing clinical decision-making and enabling drugs to be better targeted.

### **HIV**

Stratifying patient populations also provides an opportunity to more accurately weigh up the costs and benefits to an individual of a particular intervention. For example, a relatively rare but serious side effect of abacavir, a treatment for HIV, is increased risk of myocardial infarction. This was not identified in clinical trials but was observed after the drug launch, when an observational study revealed that this risk was highest in those patients already in the highest quintile of risk for cardiovascular disease.<sup>21</sup> Since the original clinical trials had excluded these patients, this side effect had not been detected. Another side effect of abacavir is an allergic skin reaction. Patients at risk of this hypersensitivity response can now be identified by screening for their HLA-B blood type, enabling the clinician to select an alternative treatment. A randomised trial in 2007 showed that the use of screening has eradicated this adverse reaction.<sup>22</sup>

<sup>18</sup> Pemovska T *et al* (2013) *Individualized systems medicine strategy to tailor treatments for patients with chemorefractory acute myeloid leukemia*, *Cancer Discovery* **3**(12), 1416-1429.

<sup>19</sup> The Caris Molecular Intelligence tool, <http://www.carismolecularintelligence.com/>

<sup>20</sup> <http://www.carislifesciences.com/news/caris-life-sciences-presents-ground-breaking-registry-data-demonstrating-caris-molecular-intelligence-provides-significant-improvement-in-survivorship-for-ovarian-cancer-patients/>

<sup>21</sup> D:A:D study group (2008) *Use of nucleoside reverse transcriptase inhibitors and risk of myocardial infarction in HIV-infected patients enrolled in the D:A:D study: a multi-cohort collaboration*, *The Lancet* **371**(9622), 1417-1426.

<sup>22</sup> Mallal S *et al* (2008) *HLA-B\*5701 screening for hypersensitivity to Abacavir*. *New England Journal of Medicine* **358**, 568-579.

**A cautionary note**

Professor Lundgren cautioned that while stratified approaches carried much promise, there remained a need to test whether the use of biomarkers to select therapies is effective. For example, measurement of procalcitonin levels can be used to test for uncontrolled infection in intensive care, but a RCT of this intervention appeared to show that its use to guide the intensity of antibiotic use did not affect patient outcomes (although it led to use of broader-spectrum antibiotics in the arm where clinicians were to use this biomarker to guide the use of antibiotic choice).<sup>23</sup> Evidence such as this could be used to improve clinical practice, for example by discontinuing routine blood tests if they have not been shown to be beneficial.

**The role of 'big data' in facilitating stratified approaches**

Underlying the advances in stratified medicine are efforts to realise the value of the data revolution, and it was widely felt that the many emerging sources of 'big data' had created an opportunity to transform medical science. However, in order to realise this opportunity, effective mechanisms for storing, linking and sharing data will need to be developed.

**From 'big data' to 'big health'**

Professor Stephen Holgate CBE FMedSci, MRC Clinical Professor of Immunopharmacology at the University of Southampton, highlighted the ambition to create a new taxonomy of disease through the development of an 'information commons', where large-scale data are combined and made available to researchers, and a 'knowledge network,' whereby the datasets are integrated with the evolving knowledge base of basic biology. Professor Holgate cited the National Institutes of Health (NIH) Pharmacogenomics Research Network, which enables phenotype and genotype data to be integrated with the aim of better understanding variation in treatment responses and translating this into stratified medicine.<sup>24</sup>

Professor Holgate noted that efforts have been made to address the challenges of forming such a system in Europe and recommendations on this were included in the European Science Foundation's recent report on 'Personalised medicine for the European citizen'.<sup>25</sup> In addition, the progress made in integrating basic and clinical research for the advance of stratified medicine by the MRC stratified medicine consortia was noted (see Appendix III).

Dr Nathalie Kayadjanian, Senior Scientific Officer at Science Europe, agreed that a more complete understanding of individual health could be gained by integrating different layers of data, including molecular 'omics datasets, clinical phenotype data, knowledge of the environment that a subject has been exposed to and citizen-contributed information

<sup>23</sup> Jensen J *et al* (2011) *Procalcitonin-guided interventions against infections to increase early appropriate antibiotics and improve survival in the intensive care unit: a randomized trial*, *Critical Care Medicine*, **39(9)**, 2048-2058

<sup>24</sup> <http://www.nigms.nih.gov/Research/SpecificAreas/PGRN/Pages/default.aspx>

<sup>25</sup> European Science Foundation (2012) *ESF Forward Look. Personalised medicine for the European citizen: towards more precise medicine for the diagnosis, treatment and prevention of disease (iPM)* [http://www.esf.org/uploads/media/Personalised\\_Medicine.pdf](http://www.esf.org/uploads/media/Personalised_Medicine.pdf)

about general health such as that provided by social networks. Dr Kayadjanian proposed that this 'Human Health Information System' will promote public health at a societal level as well as benefitting individual patients. In addition, it will provide a rich information base to further our understanding of the fundamental mechanisms of health and disease. Delegates suggested that the integration of socioeconomic data with these health data could also enable behavioural scientists to develop and test behavioural change interventions.

### **Potential models of data infrastructure**

In the 2013 report on stratified medicines, the Academy of Medical Sciences recognised several challenges concerning the development of adequate infrastructure to support the use of big health data, and recommended the development of standardised protocols for data collection, analysis and storage.<sup>26</sup> Several potential models for achieving this are currently under development.

### **Genomics England**

Professor Caulfield discussed how the 100,000 Genomes project had provided a potential model for the collection, linking and sharing of patient data. In addition to their use in patient management, the genomic data collected through the project are enriched with phenotypic information and pseudonymised for use in basic research. This phenotypic data is described using Human Phenotype Ontology, a standardised method which allows for global data integration without the need for re-formatting.<sup>27</sup>

Professor Caulfield explained that the patient data collected for the 100,000 Genomes project remains in a safe haven at a central repository. Amalgamated results that do not contain any patient-identifiable features are then distributed beyond a firewall for broader use. It was suggested that this project will leave behind a legacy of infrastructure and protocols for use by the global community in sharing health data and supporting the adoption of stratified medicine. This legacy will include next generation sequencing centres, an established sample pipeline, biorepository and large-scale data store that is usable by the NHS, as well as new diagnostic tests and therapeutics for patients.

### **Scotland**

Scotland has also made progress in the adoption of real-time data analytics in medicine, with infrastructure that harnesses individual patient data over a lifetime of interactions with the NHS and exposure to treatments. Professor Andrew Morris FRSE FMedSci, Director of the Farr Institute @ Scotland, presented several examples of how bioinformatics had been utilised to support the adoption of stratified approaches. These included:

- The **Emergency Care Summary (ECS)**: a clinically-led patient-focussed database of medications and adverse reactions. The use of this database had been shown to change patient management in 20% of cases; for example, by preventing adverse reactions, reducing care load and improving patient care.

<sup>26</sup> The Academy of Medical Sciences (2013) *Realising the potential of stratified medicine*. <https://www.acmedsci.ac.uk/viewFile/51e915f9f09fb.pdf>

<sup>27</sup> Köhler S et al (2014) *The Human Phenotype Ontology project: linking molecular biology and disease through phenotype data*, *Nucleic Acids Research*, **42**(D1), D966-974.

- The **National Picture Archiving and Communications System (PACS)**: a web-based image viewing database that is accessible in over 2000 wards across Scotland. Imaging records from 17 million studies are stored in a managed service, which can be accessed across all radiology departments. This system has been shown to reduce re-examination and re-imaging of patients by 10%, therefore reducing both costs and treatment delays.

Professor Morris highlighted how the Scottish healthcare sector was benefitting from the wealth of patient data available from its national patient database, ranging from optimising clinical processes to facilitating the identification of patients for potential participation in clinical trials. Enabling individuals to share their health record data for wider research use has also facilitated more robust evaluation of public health interventions and the sub-groups of the population most likely to benefit from these. For example, national data was used to monitor the impacts of the national smoking ban in Scotland, which included an 18% decrease in childhood asthma and a 17% decrease in acute coronary syndrome in adults.<sup>28</sup>

### **Denmark**

Professor Lundgren presented the benefits of the Danish National Health Service Register, a vast database containing data from birth to death for all Danish citizens. Researchers can capitalise on the wealth of data collected routinely to test decision-making and disease management within their local hospital. For instance, patient data collected at Rigshospitalet, a hospital in Copenhagen, is being used in the PERSIMUNE study to run real-time prospective studies to improve the management of infection control in immune-deficient patients (see page 8).<sup>29</sup>

---

<sup>28</sup> <http://www.ashscotland.org.uk/what-we-do/supply-information-about-tobacco-and-health/resources/national-evaluation-of-scotlands-smoke-free-legislation.aspx>

<sup>29</sup> <http://www.persimune.dk/Home/About>

## Next steps in the adoption of stratified medicines

---

Although stratified medicine is already delivering real benefits to patients, several barriers to widespread adoption across the health system remain. These include: patient adherence, access to health data, capitalising on the data revolution, organisation of healthcare services, education and training and assessing the value of stratified medicines. The nature of these challenges, and some of the potential solutions discussed during the meeting, are described below.

### **The role of patients and the public in driving adoption**

Professor Sir John Tooke PMedSci had initiated the day's proceedings by noting the important role that patients and the public would inevitably play in driving the adoption of stratified approaches and other types of medical innovation. Sir John argued that engaging patients, their families and the wider community in the shift towards stratified medicine – and 'P4' medicine more generally – will necessitate an evolution of the 'social contract' that exists between patients and those involved in medical innovation, in particular physicians, where patients are empowered to play a more proactive role in their healthcare.<sup>30</sup>

Sir John noted that understanding the public's perceptions of risk and value would be particularly critical to steering innovation and implementing stratified approaches, and that this would require ongoing dialogue and engagement.

#### ***Framing the technology: stratified, personalised or precision medicine?***

Participants agreed that meaningful public engagement would be vital if stratified approaches were to be widely adopted. However, a 2013 public dialogue exercise (initiated by Innovate UK and facilitated by the Sciencewise expert resource centre) revealed several important concerns, particularly regarding the vocabulary used to refer to this approach. According to the Sciencewise report 'Stratified medicine: a public dialogue':<sup>31</sup>

*'The first challenge to developing a more stratified healthcare system is having a clear, consistent definition to communicate with patients and the public about changes that are taking place. Participants in the dialogue often felt that the terminology being used was inaccessible and had negative connotations.'*

Meeting participants agreed that the term 'stratified' was potentially problematic and could be taken to imply a negative division of society, perhaps associated with ethnicity or socioeconomic status. Sciencewise concluded that the term 'personalised' may be better received. However, Professor Stephen Holgate CBE FMedSci, MRC Clinical Professor of Immunopharmacology at the University of Southampton, noted that the term 'personalised' was also potentially challenging, as it was loaded with meanings that differ

<sup>30</sup> Horne R *et al* (2015) *A new social contract for medical innovation*, *The Lancet*, **385(9974)**; 1153-1154

<sup>31</sup> Sciencewise (2014). *Stratified medicine: a public dialogue*. <http://www.sciencewise-erc.org.uk/cms/assets/Uploads/Stratified-medicine-a-public-dialogue-Final-report.pdf>

across healthcare systems; for example, in the US it pertains specifically to tailoring medicines according to companion diagnostic tools. A third option is 'precision' medicine, which is being increasingly used, particularly in the UK.<sup>32</sup> Delegates appeared to agree that the definition of stratified, personalised or precision medicine is still insecure, and that producing a clear and consistent definition will require sensitivity to differing perceptions of terminology in the medical arena and by the public. Care must also be taken not to frame stratified medicine as a 'new' technology, which could potentially carry with it connotations of the risks and uncertainties historically associated with other 'new' technologies such as genetic modification and cloning.

### ***Patient adherence and the rise of the expert patient***

It was noted that the rapid rate of technological change has led to a situation whereby medical professionals and the general public often gain access to information and medical research advances simultaneously. As a result, patients can have a great depth of understanding about their condition and potential treatments and the traditionally paternalistic relationship between patient and clinician – in which the patient only has access to information provided by the clinician – is rapidly evolving.

However, there was a widely felt concern that the channels through which patients and the public learn about medical advances are not sufficiently impartial or accurate, increasing the risk that decisions will be founded on poor information. This was seen as one of the potential drivers of poor patient adherence to treatment regimes. It has been estimated that 30-50% of patients taking medicines for chronic conditions do not take their medicines as prescribed, and wasted medicines are thought to cost the NHS in England around £300 million per year.<sup>33</sup> There was concern amongst delegates that this poor adherence may be worsened by the more complicated or pre-emptive therapies made possible by stratified medicine, and that there was a need to better understand the root causes of non-adherence in order to proactively tackle them.

### ***Access to health data***

As has already been noted, access to health data is essential to the development and implementation of stratified approaches. The recent public alarm caused by the Government's 'care.data' initiative is therefore a considerable cause for concern. Delegates recognised that public buy-in was key if broader data sharing practices were to be implemented across the NHS and beyond, and that 'care.data' had demonstrated the importance of effective public engagement and communication from the outset. However, it was noted that the public are generally willing to engage with new medical technologies, even when this requires personal data to be shared, as indicated by the rapid uptake of private genetic screening services such as 23&Me.<sup>34</sup>

Delegates also highlighted the potential tension between asking the public to share data for research purposes for the public good and the importance placed on intellectual property rights by commercial research organisations. It was suggested that this tension

<sup>32</sup> For example, by the Government's Precision Medicine Catapult Centre: <https://www.catapult.org.uk/precision-medicine-catapult>

<sup>33</sup> The Academy of Medical Sciences (2015) *Patient adherence to medicines* <http://www.acmedsci.ac.uk/download.php?f=file&i=31174>

<sup>34</sup> <https://www.23andme.com/en-gb/>

might soon come to the forefront of debates about access to data collected from the public via commercially developed 'apps' and digital devices.

***Potential ways forward for engaging patients and the public***

- Researchers, clinicians and others involved in the healthcare system should continue to engage with patients and the public about the opportunities and risks of stratified medicine. This should be framed as an evolving, rather than a 'new', approach to medicine, and care should be taken to ensure that the terminology used is both clear and meaningful to the audience.
- Efforts to improve the quality of information provided to patients about the risks and benefits of treatment should be ongoing, particularly where inaccurate or misleading information is easily available in the public domain.

## **Making the most of the data revolution**

It was felt that the UK is well placed to participate in the data revolution currently occurring in medicine. However, challenges remain in realising its full potential.

Dr Nathalie Kayadjanian, Senior Scientific Officer at Science Europe, outlined some of the difficulties associated with creating a shared 'Human Health Information System', which would integrate different types of data to create a whole that is more valuable than the sum of its parts. These challenges include problems of data integration, interpretation of combined datasets, and the need to create a 'data sharing ecosystem' which can allow for data sharing and circulation in a circular, iterative manner. Addressing how to integrate molecular pathology into patient records in a way that allows users to understand this information was also felt to be key. Solving these challenges will involve addressing issues with human resources and career structures, funding, data sharing, infrastructure and new organisational models. Dr Kayadjanian made reference to Science Europe's recent report, 'How to transform big data into better health', which highlighted several of these points.<sup>35</sup> The report also emphasised the need to include other disciplines such as social sciences and mathematics in this data sharing ecosystem, and to address the lack of incentives for sharing data in the current academic model.

Professor Andrew Morris agreed that several issues remain to be resolved before we will be able to easily utilise 'big data' in clinical practice. These include:

1. Technical challenges involving the management of extremely large datasets, such as those provided by the public via mobile apps. It was proposed that addressing this will require new methodologies to access, manipulate and visualise data, which would rely heavily on the involvement of computer scientists and mathematicians.

<sup>35</sup> Science Europe (2015) *How to Transform Big Data into Better Health: Envisioning a Health Big Data Ecosystem for Advancing Biomedical Research and Improving Health Outcomes in Europe*, [http://www.scienceeurope.org/uploads/PublicDocumentsAndSpeeches/SCsPublicDocs/Workshop\\_Report\\_MED\\_Big\\_Data\\_web.pdf](http://www.scienceeurope.org/uploads/PublicDocumentsAndSpeeches/SCsPublicDocs/Workshop_Report_MED_Big_Data_web.pdf)

It was noted that such interdisciplinarity is not well incentivised within the current academic system (see below).<sup>36</sup>

2. Challenges of scale i.e. how do we progress from small pilot studies to studies using data drawn from the whole UK population and beyond? Professor Morris noted that the Farr Institute – a virtual network of health informatics research centres – was contributing to this vision.
3. Issues of public trust. Professor Morris echoed other speakers and delegates in expressing concern about an apparent deficit in public trust and the need to reverse this in order to obtain a public mandate to access and share health data. Demonstrating that data curation issues have been resolved and that there is widespread agreement on how confidential patient information can be stored and shared securely was seen to be key to achieving this.

It was noted by delegates that although resolving these issues would be important for realising the potential of stratified medicine, the data revolution also has much wider implications, both within medicine and for society as a whole. A co-ordinated societal approach is therefore likely to be required.

### ***Big data and the need to partake in 'Team Science'***

Throughout the day, it was clear that 'Team Science' would be vital to the further development and uptake of stratified approaches. In particular, there was a sense that the relationship between mathematicians and computer scientists, and medical research scientists, needs to evolve from that of service providers to that of intellectual collaborators. The Biotechnology and Biological Sciences Research Council (BBSRC) flexible interchange programme (FLIP) aims to promote collaboration by fostering two-way partnerships between biologists and researchers in physics, engineering and IT.<sup>37</sup> Another proposed solution to increase the number of data scientists in medical research was to modify university estates to create multi-disciplinary centres with chemists, biologists, clinicians and mathematicians all working in the same building.

Delegates questioned how collaboration and interdisciplinary careers could be incentivised or rewarded in academia. It was suggested that the Research Excellence Framework could be used to better incentivise publications from collaborations and consortia, but this would rely on honest acknowledgement of team contributions from the submitting universities. It was observed that authorship is alphabetical in physics and mathematics and that team science is already achieved in genetics and clinical trials; these should be examples for the rest of medical academia to follow. It was also noted that the challenges and solutions for incentivising collaboration in academia were being addressed within the Academy of Medical Sciences' current working group project on 'Team Science'.<sup>38</sup>

<sup>36</sup> This is outlined in the Academy of Medical Sciences 'Team Science' discussion paper (2012): <http://www.acmedsci.ac.uk/download.php?f=file&i=13702>

<sup>37</sup> <http://www.bbsrc.ac.uk/business/people-information/flexible-interchange-programme/>

<sup>38</sup> The most recent 'Team Science' project update from the Academy (2015): <http://www.acmedsci.ac.uk/download.php?f=file&i=30834>

***Potential ways forward for big data and team science***

- Highlight existing examples of good practice in data access, integration and sharing, both to help build public trust and provide models for further roll-out.
- Bring clinical users together with data innovators to enable the development of technologies that are intuitive for the healthcare workforce to use.
- Identify ways to better incentivise cross-sector data sharing and interdisciplinary collaboration, particularly between the social sciences, mathematics, computer science and medicine.

**Organisation of healthcare services**

There was a sense amongst delegates that the NHS is too disparate to be able to consistently keep pace with the rate of technological innovation. It was proposed that increased use of regional nodes, which aggregate expertise and act as centres for specialist services such as pathology and genomics, might accelerate the uptake of innovative approaches such as stratified medicine. Professor Morris commented that such nodes should be connected both nationally and internationally and it was suggested that regional databases within them could be used to test treatment decisions and new technologies, and demonstrate the clinical impact of changes in policy and disease management. This evidence base could then inform nationwide roll-out of effective innovation. However, it was noted that introducing stratified approaches on a nodular basis will require nationwide monitoring to ensure that there is equity of access to high quality healthcare, irrespective of geography. The potential role of Academic Health Science Networks (AHSNs) as centres of knowledge exchange was also discussed.

It was observed that the focus of healthcare is shifting from a system based on organ specialisms to a more integrated approach which addresses the health of the individual as a whole. Whilst this adds strain to clinicians and requires more profound generalist training and scientific literacy, it was widely accepted to be better for the patient since it removes the need to attend multiple appointments with multiple specialists. Delegates felt that this shift towards patient-centric healthcare should be encouraged but would have significant repercussions for the way we train our healthcare providers.

***Potential ways forward for healthcare services***

- Continue to develop a nodular healthcare infrastructure to facilitate regional adoption of stratified medicine. These nodes should be connected nationally to ensure equity of access to healthcare innovations, and internationally to expedite wider adoption of stratified medicine.

**Education and training**

To fully facilitate the diffusion and uptake of stratified approaches, it was argued that both clinicians and researchers must have a robust understanding of the field and their role in

it. This will require both capacity building within the existing workforce and a new approach to the education of future generations.

### ***Educating the next generation***

A good understanding of genetics is arguably fundamental to the practice of stratified medicine. However, according to Professor Karen Temple, Professor of Medical Genetics at the University of Southampton, a 2013 review by the National Genetics and Genomics Education Centre reported significant disparity in the volume and content of genetics education in healthcare trainees' curricula.<sup>39</sup> Professor Temple expressed concern that education in this area is insufficient worldwide and that changing this will require a significant culture change in medical student education, from a focus on matching diagnoses and treatments to symptoms, to questioning why a patient is showing particular symptoms at a particular time. In essence, it was proposed that healthcare professionals should become more aware of the molecular pathology of disease.

It was felt that there was great potential to prepare future medical professionals to be adopters of innovation by addressing the undergraduate medicine curriculum. Professor Temple presented the example of the University of Southampton's clinical genomics programme as a model for how understanding in this area can be improved in future generations. She noted that medical undergraduates often arrive with limited experience of mathematics, statistics, ethics, the various 'omics and other related subjects. This was being tackled through this programme, however, Professor Temple highlighted that curriculum changes occur across a long timeframe: courses are designed five years in advance and so changes take time to appear in the classroom and even longer to appear in the clinic. Some delegates also questioned whether changing the curriculum would be sufficient. The professionals delivering the teaching will also need to be engaged and informed if any curriculum change is to be effective, but it was felt that there is a significant skills gap in the understanding of genomic medicine amongst medical lecturers.

Professor Temple proposed to address these issues by giving students the experience of analysing big data, with training and support from computer science and 'omics experts. This approach has been facilitated in Southampton by including online teaching materials on genomics in undergraduate medicine. A specialist ethics module has also been introduced, and it was felt that this was a key area for training since there are real issues in the clinic with respect to gaining patient consent for the use of personal information and the implications for family-wide medicine from genetic testing. Professor John Iredale FRSE FMedSci, Regius Professor of Medical Science at the University of Edinburgh, proposed that the Farr Institute could be involved in improving medical students' data science skills.

Questions were raised over the feasibility of modifying the medical curriculum to this extent, with some delegates feeling that the scope of the medical curriculum was already ambitious and unmanageable without seeking to include additional material. Others suggested that there is a need for fundamental evolution of current medical teaching, for

---

<sup>39</sup> NHS National Genetics Education and Development Centre (2013) *Genomics in healthcare education: a review of national curricula*, [http://www.geneticseducation.nhs.uk/downloads/1858\\_Genomics\\_in\\_healthcare\\_education.pdf](http://www.geneticseducation.nhs.uk/downloads/1858_Genomics_in_healthcare_education.pdf)

which a nationwide investigation into the stratified medicine-related content of all current medicine degree programmes might be helpful in the first instance.

### ***Training the existing workforce***

Professor Holgate suggested that addressing the gap between technology development and clinical adoption required the relevant professionals to be trained to use new technologies, from computer software to diagnostic tests.<sup>40,41</sup> Delegates considered there to be a lack of such capacity in the UK healthcare workforce, both in terms of ability to use specific technologies and the broader skills of manipulating and interpreting data. Additional skills are also important to adopting stratified approaches such as sample collection at a high standard. This requires the professional collecting the sample to be sympathetic to, and knowledgeable about, sample degradation and how to best to conserve sample fidelity from patient to processing.

It was highlighted that some clinical specialisms were already well educated in genomics, but that there were barriers to transforming that knowledge into clinical practice. It was felt that understanding and addressing these barriers would be critical for the success of improving education systems. It was noted that Health Education England is currently investigating how to augment personal development and training across all levels of health service infrastructure and set out recommendations for producing a more knowledgeable and effective workforce in its 2013 'Shape of training' report.<sup>42</sup>

### ***Potential ways forward for education and training***

- Review UK undergraduate medicine curricula in terms of quantitative skills teaching and content covering molecular pathology, genetics and the 'omics.
- Conduct further research to understand the training requirements for the current UK health workforce to become adept in the delivery of stratified approaches.

## **Assessing the value of stratified medicines**

### ***Pharmaceuticals***

Professor Holgate reiterated the notion that the 'blockbuster' drug no longer provides an appropriate model for how the pharmaceutical industry will operate in the future. The high cost and time needed for return on investment for most drugs – around \$1bn and 10-12 years – are particular causes for concern. Professor Holgate suggested that stratified medicines could offer a partial solution to this problem, as 'omic methods become cheaper, faster and more informative, and our ability to interpret and use the resultant data to develop treatments improves. He stated that industry has realised that many diseases share common biological pathways and that these common pathways can

<sup>40</sup> For evidence of this gap, see: Medical Research Council (2014) *Molecular Pathology review* <http://www.mrc.ac.uk/documents/pdf/mrc-molecular-pathology-review/>

<sup>41</sup> Department of Health (2011) *Innovation health and wealth: accelerating adoption and diffusion in the NHS*, [http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/prod\\_consum\\_dh/groups/dh\\_digitalassets/documents/digitalasset/dh\\_134597.pdf](http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_134597.pdf)

<sup>42</sup> Health Education England (2013) *Shape of training: Securing the future of excellent patient care* [http://www.shapeoftraining.co.uk/static/documents/content/Shape\\_of\\_training\\_FINAL\\_Report.pdf](http://www.shapeoftraining.co.uk/static/documents/content/Shape_of_training_FINAL_Report.pdf) 53977887.pdf

be targeted to design drugs that could be effective in multiple patient populations. This shift underlies the new focus on rare diseases: each of which represents a small patient market in isolation, but which together can make up a significant market when defined by a common pathway.

It was noted that while the increased uptake of stratified approaches has the potential to deliver significant savings to the healthcare system, this conflicts with a popular perception that because such approaches are innovative, they are inherently expensive. It was suggested that a case needs to be made to demonstrate the cost-effectiveness of such treatments to counteract this perception and encourage adoption by commissioners.

The current reimbursement system was identified as a significant challenge faced in the development of stratified medicines, as volume-based pricing models do not well reflect the differential value often delivered by targeted treatments. Professor Knowles suggested that further direction is needed from regulators, who should be clearer in detailing the requirements for new therapeutics and strict in adhering to these when considering whether to approve and/or reimburse a new drug. It was argued that this would incentivise further research into areas of unmet clinical need while discouraging investment in drugs of marginal value compared with existing treatments.

It was noted that non-responders within the large populations used for phase III clinical trials can mask the true effect of a new treatment in the subpopulation of responders. However, Professor Knowles argued that the lack of an effective reward mechanism from payers and regulators to support the investment in clinical research required to identify responders, does not incentivise companies to try to specifically identify such populations of responders. He proposed that the academic community should become more involved in identifying non-responder populations using big data to counter this lack of incentive elsewhere in the healthcare system.

The question of how best to value and incentivise the development of stratified medicines was identified as a significant research need: one delegate made the point that in attempting to deliver stratified medicines under current volume-based pricing and reimbursement models we were '*trying to implement 21<sup>st</sup> century healthcare using 20<sup>th</sup> century health economics*'. It was suggested that a roundtable meeting might usefully be convened by the Academy to identify gaps in the evidence base concerning the health economics of stratified approaches and the potential efficacy of alternative value-based pricing and reimbursement models.

### ***Diagnostics***

The Academy's 2013 report particularly highlighted the issues surrounding the development and use of the diagnostic tests that so often accompany stratified medicines. Dr Tito Bacarese-Hamilton, Chief Technology Officer at EKF Diagnostics, also focused on these issues in his presentation.

Dr Bacarese-Hamilton outlined the great potential for our improved understanding of molecular pathology to enable advances across the breadth of P4 medicine by:

- Contributing to pre-emptive and preventative medicine by identifying high-risk populations.
- Informing diagnosis.
- Enabling clinicians to select targeted therapies, often by acting as 'companion diagnostics' to particular stratified medicines.
- Advancing the long-term monitoring of disease progression and/or health status.

The barriers to adoption of molecular pathology in each of these applications differ, but they broadly include the high cost of test development and validation, compared with the relatively low price point of the final product, and the overwhelming burden of clinical evidence generation. It was suggested that addressing these barriers will require new models of collaboration between both pharmaceutical and diagnostic companies and their regulators.

It was noted that regulators and payers, as well as commercial developers, are concerned about the low price typically paid for diagnostics and it was felt that there was a need to more closely align price and value, as there is for pharmaceuticals. Under this model, the price of a diagnostic would not be defined by what the market will tolerate as is currently often the case, but by the quality, reliability and convenience of the test, and by the patient outcome to which it contributes.

#### ***Generating evidence to support appraisal and uptake***

During the discussion, delegates pointed out that a strong evidence base is needed to test the value of stratified approaches and to encourage uptake. It was particularly noted that the results of RCTs tended to be major drivers for guideline revisions, which are themselves important drivers of adoption. Since the precision required in stratified approaches often reaches the level of the individual patient, it was felt that trials needed to be designed in a way that allows identification of success rates and patient outcomes in small subgroups of the tested population. Sufficiently powered trials will therefore rely on a large base of subjects. Professor Morris highlighted that Scotland and Denmark were models for how extensive patient databases can be used to generate robust evidence across medium population sizes. The opportunities presented by the larger populations of the UK and Europe are potentially even greater.

In contrast, some delegates challenged society's reliance on large-scale clinical trials and saw this as a barrier to progress. Professor Knowles, for example, highlighted the considerable investment in phase IV (post-marketing authorisation) trials and postulated that this was due to the inappropriate use of RCTs in phase III. Participants also discussed the need to engage with regulators on the issue of accepting qualitative information on patient outcome as an acceptable output. It was suggested that patient reported outcome measures are better predictors of long term prognosis than many of the measures currently used and will become more prevalent as citizens contribute to data collection. Several delegates proposed a move towards alternative methodologies, such as observational studies, and data, such as qualitative information, to test the efficacy of decision rules and treatments.<sup>43</sup>

<sup>43</sup> The Academy of Medical Sciences launched a project in June 2015 on 'Methods of evaluating evidence' to explore 'How does society use evidence to judge the risks and benefits of medicines?':

Professor Djukanovic pointed out that the human element involved in molecular pathology, such as in sample handling and processing or in data interpretation, can affect the reliability and reproducibility of results; for example, as a result of batch effects and bias.<sup>44</sup> In presenting a new unbiased methodology for analysing complex clinical and molecular datasets, Professor Djukanovic highlighted the potential dangers of researcher-led data analysis, especially where particular genes and pathways have already been associated with a disease. In order to find truly novel mechanisms of disease, he proposed that data analysis be supervised by a naive entity, such as a computer algorithm. This approach has borne fruit in the fields of asthma and cancer, but its adoption demands multidisciplinary collaboration between clinicians, molecular scientists, mathematicians and computer scientists.

***Potential ways forward in generating evidence for appraisal and uptake***

- Identify gaps in the evidence base concerning the health economics of stratified approaches and the potential efficacy of alternative value-based pricing and reimbursement models.
- Collate a series of case studies that illustrate both the clinical and economic value of stratified approaches, in order to challenge preconceptions that such interventions are inevitably expensive.
- Continue to evaluate and evolve the methodologies used to generate evidence for safety assessment and health technology appraisal, particularly where patient populations make large RCTs impractical or impossible.
- Incentivise research identifying responders in clinical trials in order to increase granularity of results and avoid the loss of effective pharmaceuticals.

---

<http://www.acmedsci.ac.uk/policy/policy-projects/how-does-society-use-evidence-to-judge-the-risks-and-benefits-of-medicines/>

<sup>44</sup> The Academy of Medical Sciences held a symposium in April 2015 to explore the challenges and opportunities for improving biomedical research reproducibility and reliability in the UK, the report can be found here: <http://www.acmedsci.ac.uk/download.php?f=file&i=32558>

## Conclusion

---

This report attempts to summarise what was a wide-ranging discussion involving a diverse group of contributors. Bringing about further progress in implementing stratified approaches in healthcare settings will require engagement and action from many more.

The opportunities offered by stratified medicine were highlighted throughout the day, and it is clear that this potential is already being realised. However, progress is slow and many of challenges first recognised several years ago still remain. There was a sense from the room that leadership was needed to further accelerate the uptake of this potentially transformative approach, both within the NHS and internationally.

It was suggested that medical professionals should take greater responsibility for driving the adoption of stratified approaches. Commissioners can be encouraged to adopt new strategies once evidence of effectiveness has been generated, but the involvement of clinicians is essential in facilitating the necessary research and creating 'pull' for the resultant innovations. Clinicians also play a vital role in engaging with patients, helping to build trust and bring about the necessary evolution in attitudes that will ultimately provide a societal mandate for adoption.

The successful development and adoption of innovative technologies requires the input of clinical experts at the very earliest stages of development to ensure that the resulting products both fulfil a need and are capable of wide scale uptake; innovations will only be adopted if the product can be used effectively by the frontline professionals. Healthcare systems must also be organised in ways that support adoption. In addition, adoption of stratified medicine strategies requires clinicians to be adequately trained with a sufficient understanding of key technologies. The onus falls on educators to establish sufficient education and training for all levels of the profession.

There was a call for interested professionals to champion the cause across their networks in order to engage colleagues and peers. Specifically, it was noted that geographical regions currently demonstrating low levels of engagement must be targeted and convinced of the benefits offered by stratified approaches.

Finally, challenges posed by existing models for the pricing and reimbursement of stratified medicines – and the companion diagnostics that often accompany them – must be resolved if industry is to continue to lend its weight to the development of more targeted, effective and ultimately valuable products.

Several next steps towards achieving these broad aims were proposed over the course of the meeting and have been detailed in this report. In particular, a potential role for the Academy in convening a roundtable meeting to identify gaps in the evidence base concerning the health economics of stratified approaches and the potential efficacy of alternative pricing and reimbursement models was identified. Further dialogue between all the stakeholders will be crucial in ensuring a coordinated approach; the Academy, and the other organisations that provided support to this meeting, will continue to seek ways to support this process.

## Appendix I Programme

---

Tuesday 12 May 2015

**Heartbeat Education Centre, Southampton General Hospital**

<b>Symposium</b>	
09:30 – 10:00	<b>Registration</b>
<b>Introduction and welcome</b>	
10:00 – 10:15	<p><b>Introduction to the Academy of Medical Sciences' report 'Realising the potential of stratified medicine'</b></p> <p>Professor Sir John Tooke PMedSci, President of the Academy of Medical Sciences; Vice Provost (Health), Head of the School of Life &amp; Medical Sciences, University College London</p>
<b>The promise of stratified medicine</b>	
Chair: Professor Sir John Tooke PMedSci	
10:15 – 10:30	<p><b>Towards more precise medicine for the diagnosis, treatment and prevention of disease – UK and European perspectives</b></p> <p>Professor Stephen T Holgate CBE FMedSci, MRC Clinical Professor, Faculty of Medicine, University of Southampton</p>
10:30 – 10:45	<p><b>Leveraging Big Data to advance stratified medicine in Europe</b></p> <p>Dr Nathalie Kayadjanian, Senior Scientific Officer, Science Europe</p>
10:45 – 11:00	<p><b>The 100,000 Genomes Project and Genomics England</b></p> <p>Professor Mark Caulfield FMedSci, Co-director of the William Harvey Research Institute, Centre Lead for Clinical Pharmacology, Queen Mary University London</p>
11:00 – 11:30	<b>Q&amp;A</b>
11:30 – 11:45	<b>Tea &amp; coffee</b>
<b>Approaches to the stratification of human disease</b>	
Chair: Professor Jens Lundgren	
11:45 – 12:00	<p><b>Cancer as a model for targeted diagnosis and treatment</b></p> <p>Professor Peter Johnson FRCP FMedSci, Professor of Medical Oncology, University of Southampton and Chief Clinician, Cancer Research UK</p>
12:00 – 12:15	<p><b>Personalisation of medicine is essential for progress – how can we accelerate implementation for patients?</b></p> <p>Professor Jonathan KC Knowles, Former Head of Group Research and Member of the Executive Committee at Roche; Distinguished Professor in Personalised Health Care, Finnish Institute for Molecular Medicine, University of Helsinki; Visiting Professor, University of Oxford</p>
12:15 – 12:30	<p><b>The stratification of human disease across the lifecourse</b></p> <p>Professor Cyrus Cooper FMedSci, Director of MRC Lifecourse Epidemiology Unit, University of Southampton; Professor of Epidemiology, Institute of Musculoskeletal Science, University of Oxford</p>
12:30 – 13:00	<b>Q&amp;A</b>
13:00 – 14:00	<b>Lunch</b>
<b>Interdisciplinary approaches to stratified medicine</b>	
Chair: Professor Richard Trembath FMedSci	

14:00 – 14:15	<b>Application of informatics to study the epidemiological and molecular aetiological basis of chronic disease</b> Professor Andrew Morris FRSE FMedSci, Professor of Medicine, Director of the Usher Institute for Population Health Sciences & Informatics and Vice Principal - Data Science, University of Edinburgh; Director of the Scottish Farr institute for Scotland; Chief Scientist (Health) in Scotland
14:15 – 14:30	<b>Biomarker discovery through creating an 'information commons': the EU Innovative Medicines Initiative U-BIOPRED project</b> Professor Ratko Djukanovic, Professor of Respiratory Medicine and Director of the Southampton NIHR Respiratory Biomedical Research Unit
14:30 – 14:45	<b>Diagnostics and molecular pathology</b> Dr Tito Bacarese-Hamilton, Chief Technology Officer, EKF Diagnostics
14:45 – 15:15	<b>Q&amp;A</b>
15:15 – 15:30	<b>Tea &amp; coffee</b>
<b>The future of stratified healthcare</b> Chair: Professor John Iredale FRSE FMedSci	
15:30 – 15:45	<b>Uptake of personalised medicine by the healthcare provider</b> Professor Jens Lundgren, Leader of Danish National Research Foundation's Centre of Excellence for Personalised Medicine of Infectious Complications in Immune Deficiency 'PERSIMUNE', Department of Infectious Diseases, Rigshospitalet, University of Copenhagen, Denmark
15:45 – 16:00	<b>The need to incorporate stratified medicine into medical education</b> Professor I. Karen Temple, Professor of Medical Genetics, University of Southampton
16:00 – 16:15	<b>Q&amp;A</b>
16:15 – 16:30	<b>Concluding remarks</b> Professor John Iredale FRSE FMedSci (training) and Professor Richard Trembath FMedSci (practice)
16:30	<b>Close</b>

## Appendix II Symposium delegates

---

### Workshop delegates

**Dr Mohammad R Abdollahi**, University of Southampton  
**Ms Beth Allen**, Department of Health  
**Miss Gaia Andreoletti**, University of Southampton  
**Mr Meg Ashton-Kay**, University Hospital Southampton  
**Dr Tito Bacarese-Hamilton**, EKF Diagnostics  
**Professor Jonathan Barker**, King's College London  
**Professor Eleanor Barnes**, University of Oxford  
**Professor Henrique Barros**, Instituto de Saude Publica da Universidade do Porto  
**Miss Leesa Benson**, University Hospital Southampton  
**Ms Angela Blackmore**, University Hospital Southampton  
**Dr Louise Brown**, University College London  
**Dr Hilary Burton**, PHG Foundation  
**Dr Rachel Butler**, All Wales Genetics Laboratory  
**Professor Iain Cameron**, University of Southampton  
**Dr Helen Campbell**, University of Exeter  
**Professor Mark Caulfield FMedSci**, Queen Mary University of London  
**Dr Ying Cheong**, University of Southampton  
**Professor Phil Chowienczyk**, King's College London  
**Dr Tracy Coelho**, University of Southampton  
**Professor Cyrus Cooper FMedSci**, University of Southampton  
**Professor Andrew Cope**, King's College London  
**Professor Nick Cross**, University of Southampton  
**Dr Sophie Dale-Black**, Innovate UK  
**Professor Donna Davies**, University of Southampton  
**Dr Emanuele de Rinaldis**, King's College London  
**Dr Ratko Djukanovic**, Southampton General Hospital  
**Dr Jacek Donocik**, King's College London  
**Dr Lisa Douet**, University of Southampton  
**Dr Andrew Douglas**, University Hospital Southampton  
**Professor Diana Eccles**, University of Southampton  
**Professor David Edwards FMedSci**, King's College London  
**Professor Sarah Ennis**, University of Southampton  
**Dr Andreia Feijao**, Fundação para a Ciência e Tecnologia  
**Dr Yifang Gao**, University of Southampton  
**Mr Nigel Gaymond**, Personalised Healthcare Alliance  
**Professor Keith Godfrey**, University of Southampton  
**Professor Olga Golubnitschaja**, European Association for Predictive, Preventive & Personalised Medicine  
**Professor Annette Grüters**, Science Europe  
**Mr Simon Hadlington**, Science Europe  
**Hans Michael Haitchi**, University of Southampton  
**Miss Gill Hamblin**, North West Coast AHSN  
**Dr Shahid Hanif**, ABPI  
**Professor David Haslam**, National Institute for Health and Care Excellence

**Professor Andrew Hattersley FRS FMedSci**, University of Exeter  
**Dr Timothy Hinks**, University of Southampton  
**Professor Stephen Holgate CBE FMedSci**, University of Southampton  
**Professor John Holloway**, University of Southampton  
**Professor John Iredale FRSE FMedSci**, University of Edinburgh  
**Mrs Juby Jacob-Nara**, AstraZeneca  
**Mr Ben Johnson**, University Hospital Southampton  
**Professor Peter Johnson FMedSci**, Southampton General Hospital  
**Professor David Jones**, University of Newcastle  
**Mr Rakesh Kantaria**, AstraZeneca  
**Professor Richard Kaplan**, University College London  
**Dr Nathalie Kayadjanian**, Science Europe  
**Dr Alastair Kent OBE**, Genetic Alliance UK  
**Professor Jonathan Knowles**, Ecole Polytechnique Fédérale de Lausanne  
**Mr Marcin Knut**, University of Southampton  
**Dr Katherine Lachlan**, University Hospital Southampton  
**Professor Karen Lillycrop**, University of Southampton  
**Mr Joseph Lu**, Legal & General  
**Professor Anneke Lucassen**, University of Southampton  
**Professor Jens Lundgren**, University of Copenhagen  
**Dr Deborah Mackay**, University of Southampton  
**Dr Alan McNair**, Chief Scientist Office  
**Professor Andres Metspalu**, University of Tartu  
**Miss Kay Mitchell**, University Hospital Southampton  
**Professor Andrew Morris FRSE FMedSci**, University of Edinburgh  
**Mr Enrico Mossotto**, University of Southampton  
**Professor Frank Nestle FMedSci**, King's College London  
**Dr David Oppenheim**, NHS England  
**Professor Richard Oreffo**, University of Southampton  
**Dr Christopher Parker**, West Midlands AHSN  
**Dr Jonathan Pearce**, Medical Research Council  
**Mr Lee Pearce**, University Hospital Southampton  
**Mr Reuben Pengelly**, University of Southampton  
**Professor Hugh Perry**, University of Southampton  
**Professor Costantino Pitzalis**, Queen Mary University of London  
**Professor Robert Read**, University of Southampton  
**Dr Matthew Reed**, University College London  
**Dr Faisal I Rezwan**, University of Southampton  
**Dr Paul Robinson**, Merck Sharp & Dohme  
**Dr Jan-Paul Rosen**, Merck Serono  
**Dr Matthew Rose-Zerilli**, University of Southampton  
**Dr Rowena Sharpe**, Cancer Research UK  
**Dr Emily Shaw**, Cancer Research UK  
**Dr Jo Slater-Jefferies**, University of Southampton  
**Dr Jonathan Strefford**, University of Southampton  
**Professor I. Karen Temple**, University of Southampton  
**Sir John Tooke PMedSci**, University College London

**Professor Richard Trembath FMedSci**, Queen Mary University of London

**Dr Philip Turner**, University of Oxford

**Dr Mohib Uddin**, AstraZeneca

**Mrs Bronwen Vearncombe**, Wessex AHSN

**Dr Ian Walker**, Cancer Research UK

**Mr Andrew Webb**, EKF Diagnostics

**Dr Helen White**, University of Southampton

**Ms Doris-Ann Williams MBE**, British In Vitro Diagnostics Association

**Professor David Wilson**, University of Southampton

**Sir Kent Woods FMedSci**, European Medicines Agency

**Secretariat**

**Ms Victoria Charlton**, Academy of Medical Sciences

**Dr Claire Cope**, Academy of Medical Sciences

**Dr Mehwaesh Islam**, Academy of Medical Sciences

**Ms Naomi Penfold**, Academy of Medical Sciences

## Appendix III Summary of poster presentations

<b>University of Southampton</b>
<p><b>Real-time gene expression profiling to identify subtypes of diffuse large B-cell lymphoma (DLBL) for targeted therapy. The REMoDL-B study of the UK NCRI and SAKK lymphoma groups</b></p> <p><i>Andrew Davies, Sharon Barrans, Christoph Mamot, Matthew Care, Tom Maishman, Debbie Hamid, Andrew MacMillan, Paul Fields, Andrew Jack, Peter Johnson</i></p>
<p><b>Measuring information in the human genome</b></p> <p><i>Jacek Brodzki, Conor Smyth, Iva Špakulová, Ben MacArthur, Diana Eccles, Andrew Collins, Rosanna Upstill-Goddard</i></p>
<p><b>Epigenetic regulation of interleukin-8, an inflammatory chemokine, in osteoarthritis</b></p> <p><i>Atsushi Takahashi, María C. de Andrés, Ko Hashimoto, Eiji Etoj, Richard O. C. Oreffo</i></p>
<p><b>Identifying variants in next generation sequencing data from 61 paediatric Inflammatory Bowel Disease patients</b></p> <p><i>Gaia Andreoletti, Dr Jane Gibson, Dr Andy Collins, MD Mark Beattie &amp; Dr Sarah Ennis</i></p>
<p><b>Primary immunodeficiency caused by a novel compound heterozygote mutation in MTHFD1</b></p> <p><i>Reuben J. Pengelly, Ananth Ramakrishnan, Saul N. Faust, Anthony P. Williams &amp; Sarah Ennis</i></p>
<p><b>Application of RNA-Seq for gene fusion identification in leukaemia</b></p> <p><i>Marcin Knut, William Tapper, Sarah Ennis, Nicholas Cross</i></p>
<p><b>Analysis of thiopurine S-methyl transferase phenotype-genotype correlation in a single centre paediatric IBD cohort and identification of a novel TPMT variant</b></p> <p><i>Tracy Coelho, Gaia Andreoletti, Nadeem Afzal, Akshay Batra, Rachel Haggarty, Alex Lee, Yifang Gao, Anthony Williams, R.Mark Beattie, Sarah Ennis</i></p>
<p><b>A mathematical model to predict the clinical behaviour of oral cancer</b></p> <p><i>E Mossotto, K Moutasim, B MacArthur, S Ennis</i></p>
<p><b>Collagen mutations identified by targeted next generation sequencing are the most frequent mutations underlying Adult Focal Segmental Glomerulosclerosis</b></p> <p><i>C Gast, R Pengelly, G Venkat-Raman, S Ennis</i></p>
<p><b>Effects of Purified Eicosapentaenoic and Docosahexaenoic Acids in Nonalcoholic Fatty Liver Disease: Results From the WELCOME* Study</b></p> <p><i>Eleonora Scorletti, Lokpal Bhatia, Keith G. McCormick, Geraldine F. Clough, Kathryn Nash, Leanne Hodson, Helen E. Moyses, Philip C. Calder, and Christopher D. Byrne; on behalf of the WELCOME Study Investigators</i></p>
<p><b>Multidimensional endotypes of asthma identified by topological data analysis</b></p> <p><i>Timothy Hinks</i></p>
<p><b>National Platform for Molecular Diagnostics: Results of the Cancer Research UK</b></p>

<p><b>Stratified Medicine Programme</b></p> <p><i>Shaw E, Lindsay CR, Butler R, Gonzalez de Castro D, Griffiths M, Hanby AM, Hair J, Rae F, Rogan J, Morton D, Brenton J, Chester JD, Johnston SRD, Walker I, Johnson PWM.</i></p>
<p><b>Personalised medicine: lessons from the POSH study</b></p> <p><i>Diana Eccles, Ellen Copson, Tom Maishman, Ramsey Cutress, Lorraine Durcan, Sue Gerty, Will Tapper, Sajjad Rafiq, POSH Steering Group</i></p>
<p><b>Deep-sequencing reveals the molecular landscape of Splenic Marginal Zone Lymphoma: biological and clinical implications</b></p> <p><i>Matthew JJ Rose-Zerilli, Marina Parry, Viktor Ljungström, Jane Gibson, Jun Wang, Renata Walewska, Helen Parker, Anton Parker, Zadi Davis, Anne Gardiner, Neil McIver-Brown, Christina Kalpadakis, Aliko Xochelli, Achilles Anagnostopoulos, Claudia Fazi, David Gonzalez de Castro, Claire Dearden, Guy Pratt, Richard Rosenquist, Margaret Ashton-Key, Francesco Forconi, Andrew Collins, Paolo Ghia, Estella Matutes, Gerassimos Pangalis, Kostas Stamatopoulos, David Oscier, Jonathan C Strefford</i></p>
<p><b>Genome-wide methylation analysis of patients with imprinting disorders by single sample analysis: a prospective bioinformatic diagnostic tool</b></p> <p><i>Faisal I Rezwani, Louise E Docherty, Rebecca L Poole, Gabrielle A Lockett, S Hasan Arshad, John W Holloway, I Karen Temple and Deborah JG Mackay</i></p>

<b>MRC Consortia</b>	<b>Overview of aims</b>
<p><b>PSORT</b> <i>Professor Jonathan Barker, King's College London</i></p>	<p>The Psoriasis Stratification to Optimise Relevant Therapy consortium aims to use and develop clinical and scientific knowledge about psoriasis, and investigative tools, to develop tests that will support a personalised treatment approach.</p>
<p><b>STOP-HCV</b> <i>Professor Eleanor Barnes, University of Oxford</i></p>	<p>Using a clinical database and a bio-repository of blood samples from hepatitis-C patients to address how a large proportion of patients do not respond to direct antiviral therapy.</p>
<p><b>AIM-HY</b> <i>Professor Phil Chowienczvk, King's College London</i></p>	<p>Examining whether treatments for hypertension can be improved by addressing ethnic heritage to deliver a personalised treatment for high blood pressure from a single blood test.</p>
<p><b>RA-MAP</b> <i>Professor Andrew Cope, King's College London</i></p>	<p>Aiming to understand the factors involved in remission of rheumatoid arthritis and how to leverage these early enough to significantly impact clinical outcomes.</p>
<p><b>RASP-UK</b> <i>Professor Ratko Djukanovic, University of Southampton</i></p>	<p>Stratifying asthma patients through assessing treatment adherence using remote monitoring technologies and biological markers on the basis of different types of lung inflammation.</p>
<p><b>STRATA</b> <i>Dr Jacek Donocik, King's College London</i></p>	<p>Developing a method to predict which schizophrenia patients will respond to dopamine medicines and those who are likely to respond to new glutamate drugs.</p>

<p><b>MASTERMIND</b>  <i>Professor Andrew Hattersley,  University of Exeter</i></p>	<p>Establishing a platform for a stratified approach to the treatment of type 2 diabetes.</p>
<p><b>GAUCHERITE</b>  <i>Dr Derralyn Hughes,  University College London</i></p>	<p>Investigating patients with Gaucher's disease to stratify them on the 'nature' of their disease and allowing for selection of more targeted medicines.</p>
<p><b>UK-PBC</b>  <i>Professor David Jones,  University of Newcastle</i></p>	<p>Establishing a better understanding of patient responses to treatments, collaborating with industry to develop new drugs and designing a national protocol to streamline treatment for primary biliary cirrhosis across the UK.</p>
<p><b>S-CORT</b>  <i>Professor Richard Kaplan,  University College London</i></p>	<p>Investigating the genetic changes in metastatic colorectal cancer cells to better understand different patient responses to treatment. This will hopefully support the development of clinical tests for colorectal cancer patients to select the best treatment.</p>
<p><b>MATURA</b>  <i>Professor Costantino Pitzalis,  Queen Mary University of London</i></p>	<p>Focusing on rheumatoid arthritis, this consortium intends to identify biological and genetic markers that may predict patient response to anti-inflammatory drugs.</p>



Academy of Medical Sciences  
41 Portland Place  
London, W1B 1QH  
+44(0)20 3176 2150

[info@acmedsci.ac.uk](mailto:info@acmedsci.ac.uk)  
[www.acmedsci.ac.uk](http://www.acmedsci.ac.uk)

Registered Charity No. 1070618  
Registered Company No. 3520281