

Personalised psychiatry

Summary report of a FORUM meeting
held on 6 September 2017

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Executive summary

There is a rising demand for developing better ways to diagnose and treat mental health disorders. Despite general improvements in population health, approaches to mental health have remained static in recent years. Lack of progress in this field not only has a significant health and lifestyle cost for patients, families and wider society, but also places an increasing burden on the health and social care system. There is a significant opportunity to improve outcomes for mental health disorders by taking a more personalised approach, including targeting new and existing treatments more precisely to the patients most likely to benefit from them. Healthcare systems in the UK and internationally need to be prepared to capitalise on this potential for a new era of precision psychiatry.

The Academy convened a roundtable on 6 September 2017 to discuss the potential for a personalised approach to psychiatry, followed by the FORUM Annual Lecture which looked more broadly at integration across 'The mind-body interface'. This roundtable explored what could be done now to better personalise psychiatric treatment based on recent advances in scientific knowledge and current challenges to implementation, as well as what could be done

in the future. This included discussions around the infrastructure needed to prepare the healthcare system strategically to embrace a more personalised approach to mental health disorders.

Key messages from the meeting included:

- The importance of **better understanding the molecular and genetic basis of mental health conditions** and risk factors in order to develop more effective prevention, diagnosis and intervention strategies.
- Mental health is very complex, comprising a broad range of underlying risk factors. The **breadth of risk factors needs to be understood and adequately captured** as part of a comprehensive patient dataset, including social and environmental measures alongside key clinical, phenotypic and genetic data. There was a clear consensus on the **need to better characterise and target children and adolescents** based on an understanding of the influence of early life experience on mental health trajectories. This will require integration across health and wider social care services.
- The need to **integrate approaches to mental and physical health**, overcoming traditional clinical barriers and facilitating re-organisation of services to better understand the interactions across this interface.
- It is essential to address some of the challenges around **building a robust evidence base for mental health conditions**, including difficulties in patient recruitment to trials and the need for more consistent, standardised and objective measures (particularly for phenotypic information). In the future, it was proposed that all clinical trials could incorporate mental health measures as routine practice, and that further high-quality longitudinal studies specifically on mental health are also needed.
- A robust **data infrastructure for mental health is required** that captures the range of measures described above, and ensures that such data is collected routinely as part of healthcare service provision. This includes establishing capacity and capabilities amongst various healthcare professionals for collecting this data, and building on current local and regional initiatives that have already started to collate these data.
- A **wider culture change is key** to reducing stigmatisation around mental health and enacting change for how services are delivered across all levels of care. This can be facilitated, in part, through engagement with the public, patients and healthcare professionals around mental health and treatment, as well as interdisciplinary training for those healthcare professionals involved along the care pathway to reduce stigmatisation.
- **What could we do now in personalised psychiatry?** In particular, participants identified four areas where a personalised approach could be immediately trialled to demonstrate the benefits of adopting a more individually tailored approach to diagnosis, treatment and prevention of mental health disorders: characterising the inflammatory or auto-immune status of patients with treatment-resistant major depressive disorder or a first episode of psychosis; identification of patients with copy-number variations or other highly penetrant genetic risks for psychosis; prevention of mental health disorders in pregnancy and childbirth; and characterisation and prevention of risks for addictive disorders in young people.

Introduction

Embedding stratified medicine in the NHS

Professor Tim Kendall, National Clinical Director for Mental Health, NHS England, gave an overview of some of the initiatives aimed at embedding stratified medicine, and in particular genomic services, in the NHS. He emphasised the widespread recognition of the opportunities for better and more effective diagnosis, treatment and personalisation afforded by advances in genomics. The establishment of a new network of genetic testing laboratories and improved genomic medicine infrastructure alongside the legacy of the 100,000 Genomes Project will enable the UK to capitalise on the potential of stratified medicine.

More broadly, NHS England is looking to develop a comprehensive genomic testing strategy to incorporate genomics into routine care.¹ This will be facilitated, in part, by a joint commissioning model of integrated services for Clinical Commissioning Groups (CCGs), and a new informatics ecosystem to facilitate digitisation and more efficient use of data. In particular, Professor Kendall described some of the notable opportunities for utilising genomics to improve management of mental health conditions. These include: more precisely matching existing and new drugs to patients; developing a better understanding of stress vulnerability models and the likelihood of patient relapse; elucidating gene-environment interactions; and detailing the mechanisms underlying mental health such as the impact of epigenetics.

¹ NHS England (2017). *NHS England Board paper: creating a genomic medicine service to lay the foundations to deliver personalised interventions and treatments*. www.england.nhs.uk/wp-content/uploads/2017/03/board-paper-300317-item-6.pdf

The genetic basis of mental health

Professor Sir Michael Owen FMedSci FLSW, Director of the MRC Centre for Neuropsychiatric Genetics and Genomics, Cardiff University, highlighted that there is a significant genetic component to most psychiatric disorders – indeed, major mental illnesses are highly heritable. Research into the underlying genetics can inform how psychiatric disorders are treated, managed and classified. Sir Michael noted that three key aspects to the genetics of psychiatric disorders have emerged from recent genomic studies:

- 1. Complexity** – Psychiatric disorders are highly polygenic with multiple different genetic risk factors in each case.² There are no known single gene forms. This means that different individuals with the same disorder will carry different combinations of risk alleles and unaffected individuals will carry multiple risk alleles, and the consequences of carrying particular risk alleles depend upon the genetic background and exposure to environmental factors.
- 2. Pleiotropy** – Carrying the same risk allele can have more than one outcome, meaning that the same allele is associated with more than one psychiatric disorder. Thus it can be difficult to predict exactly how an individual's genetic risk may be clinically expressed in terms of disorder. For example, copy-number variants (CNVs: deletions or duplications of sections of the genome) that confer risk to schizophrenia also confer risk for autism and intellectual disability, amongst other disorders, and there is a substantial genetic overlap between schizophrenia and bipolar disorder.³
- 3. Convergence** – The pattern of genes implicated in psychiatric disorders is not random with the evidence to date supporting convergence on sets of genes involved with synaptic plasticity and epigenetic processes.^{4,5}

The implications of genomics for personalised psychiatry

The genetic complexity of psychiatric disorders means it is unlikely that genomic knowledge will be useful to sub-divide current psychiatric diagnoses into circumscribed disease sub-types. However, there is clear potential for genomic data to help stratify patients into those more or less likely to respond to specific treatments or to have a particular outcome trajectory, and in defining groups at relative higher or lower risk of developing a disorder in whom preventative measures could be prioritised. The utility of genomic data in a clinical setting is likely to be enhanced by its use in combination with clinical and biomarker information as well as information on environmental exposures. The pleiotropic nature of the underlying genetics means that patient strata and treatments may cross the boundaries between and beyond current standard psychiatric diagnostic categories, and current diagnostic systems will likely be insufficient for personalisation. The impact of many alleles on risk can be quantified using polygenic risk scores and it seems likely that these approaches will deliver value as components of care pathways to stratify patients and help predict outcomes and treatment response. Some rare alleles, particularly CNVs, are associated with high individual and familial risks as well as specific physical illnesses. These are increasingly

² Ripke S, et al. (2014). *Biological insights from 108 schizophrenia-associated genetic loci*. *Nature* **511(7510)**, 421-427.

³ Rees E, et al. (2016). *Analysis of Intellectual Disability Copy Number Variants for Association With Schizophrenia*. *JAMA Psychiatry* **73(9)**, 963-969.

⁴ Hall J, et al. (2015). *Genetic risk for schizophrenia: convergence on synaptic pathways involved in plasticity*. *Biol Psychiatry* **77(1)**, 52-58.

⁵ Singh T, et al. (2017). *The contribution of rare variants to risk of schizophrenia in individuals with and without intellectual disability*. *Nat Genet.* **49(8)**, 1167-1173.

used as part of the diagnostic process in intellectual disability and autism and there have been calls to introduce testing for these in schizophrenia.⁶ This would necessitate further support for management of co-morbidities and genetic counselling. To conclude, Sir Michael noted the rapid rate of progress in psychiatric genomics and called for larger data-rich studies, integrating genomics with large-scale clinical and biomarker data to build the evidence base required for a personalised approach to psychiatry.

The future of personalised psychiatry

Dr John Isaac, Senior Director for External Scientific Innovation, Neuroscience at Johnson & Johnson Innovation, emphasised that the challenge to implementing personalised psychiatry lies in the barriers to translation of research, such as converting genetic understanding into new interventions for psychiatric disorders. He highlighted the value of understanding the molecular basis of disease, for example, in ascertaining why the use of novel rapid-acting antidepressants in treatment-resistant depression can be effective in some patients and not others, and in predicting which depressed patients are least likely to respond to conventional antidepressants. In addition, current novel antidepressants can then be refined to develop more effective medicines and drive better personalisation. However, he described a series of key barriers to conducting drug discovery in mental health:

- A lack of detailed understanding of these disorders, which are heterogeneous and multifactorial, with complex symptoms and subjective diagnostic criteria.
- Difficulties in preclinical science with challenges in target validation, inadequate animal models and limited translational approaches.
- Challenges in clinical research, such as the notable length and cost of trials in this field when compared with other disease areas, which are often lower risk and cost. Patient populations for the trials are heterogeneous and placebo responses often very high, with a reliance on subjective rating scales for trial outcomes.
- Finally, to fully implement stratified – or precision – medicine, there is a need to better address underlying molecular mechanisms, develop new biomarkers and diagnostics, overcome difficulties in accessing human disease tissue and establish better infrastructure for objective measures.

Inflammation and mental health

Dr Isaac described the recent advances in understanding of the association between inflammation and psychiatric disorders. It is often observed that infection can lead to psychiatric symptoms such as depression and there is robust data suggesting that the immune system could be a fundamental component in depression. For example, studies have shown that IFN-alpha (a cytokine involved in inflammatory response) can induce major depression in humans that necessitates anti-depressant treatment.^{7,8} Moreover, there is evidence from re-analyses of existing clinical trial data that anti-cytokine antibodies can reduce the severity of comorbid depressive symptoms in patients with rheumatoid arthritis or other inflammatory disorders. Therefore industry is starting to explore whether patients with treatment-resistant major depressive disorder could be stratified by inflammatory biomarkers

⁶ Baker K, *et al.* (2014). *Chromosomal microarray analysis—a routine clinical genetic test for patients with schizophrenia*. *The Lancet Psychiatry* **1**(5), 329-331.

⁷ Bull S, *et al.* (2009). *Functional polymorphisms in the interleukin-6 and serotonin transporter genes, and depression and fatigue induced by interferon-alpha and ribavirin treatment*. *Mol Psychiatry* **14**(12), 1095-1104.

⁸ Musselman D, *et al.* (2001). *Paroxetine for the prevention of depression induced by high-dose interferon alfa*. *N Engl J Med*. **344**(13), 961-966.

for trials of anti-inflammatory drugs for anti-depressant efficacy.

Next steps for a personalised approach

Outlining the future for personalised psychiatry, Dr Isaac envisioned better diagnostics and patient stratification based on an understanding of biological mechanisms. Genomics and other biomarkers could allow for early prediction of treatment resistance and circumvention of ineffective interventions, and there is an opportunity to better integrate pharmacological and non-pharmacological treatments for a tailored approach to care. Ultimately, there may be an opportunity for prevention through building evidence on markers of risk. However, to achieve this vision he outlined a series of steps that need to be taken including further investment in the science and large-scale platforms for mental health research, perhaps similar to the Dementias Platform initiative.⁹ Key to this will be closer collaboration between preclinical and clinical science and across all stakeholders involved, including academia, the NHS and industry, as well as an overall evolution of clinical practice to engender belief that developing the research and knowledge base around psychiatric disorders is once again tractable.

⁹ www.dementiasplatform.uk/

Adopting a personalised approach to psychiatry

Participants identified the challenges to adopting a personalised approach to psychiatry and discussed next steps for enabling such an approach. They considered this in the context of what could be implemented now within the NHS, and the infrastructure and preparedness of the healthcare system necessary for future developments in the field. The discussions broadly explored three areas: what needs to be measured, including further risk factors and how these might be measured; the infrastructure needed to support a stratified approach including integration across the mental and physical health divide and data capabilities;

and how innovation can be driven in systems for mental health service provision.

What should we be measuring?

It was agreed that prevention and early intervention should be at the forefront of personalisation. There was widespread consensus on the importance of focusing on younger people whether for better understanding of the factors that influence mental health in early life or for exploring opportunities for intervention at these early stages. Mental health is a complex area comprising a broad range of underlying risk factors, and so participants advocated the need to consider all relevant key risk factors and to measure them systematically so that a comprehensive patient dataset is captured. It was envisioned that this might include genetics, clinical phenotypes and other markers, imaging and digital technologies, and social and environmental factors. The latter are not often traditionally considered as biomarkers for stratification but have a significant influence on mental health trajectories. It was noted that such a range of data is required to fully understand the disease and elucidate causality, which can in turn drive more effective drug discovery and development of novel therapies, more effective use of different treatments including psychological interventions (such as cognitive behavioural therapy - CBT) and improved service delivery.

A cautionary note was the need to recognise other key factors as part of the personalised psychiatry agenda such as gender or age differences. For example, gender may have an influence on effectiveness and optimum dosage of different medications, metabolism, adherence and side effects.¹⁰ This does not necessarily demand new therapies for men or women but simply more effective use of existing treatments.

Clinical risk factors

Prescription data was described as a useful tool for better understanding patient populations. Alongside recording of phenotypic information, there is an opportunity for better measuring inflammation in mental health, including in patients with physical conditions, and looking for prevention strategies for mental health problems in this group. For example, the frequent co-occurrence of back pain and depression could potentially be treated more holistically with anti-inflammatory agents in the future.

Prediction of mental health risk and early intervention for women around childbirth can have a significant impact on outcomes. This group is at high risk of suffering a mental health disorder and there is already an understanding of the risk factors involved. Therefore participants emphasised that personalised care in this group could be implemented now through large perinatal services in the NHS. This is particularly timely as healthcare professionals are undergoing new training to track certain factors around birth including predisposing disease markers, and so further aspects around mental health could be added to these measurements.

¹⁰ Sramek J, Murphy M & Cutler N (2016). *Sex differences in the psychopharmacological treatment of depression*. *Dialogues Clin Neurosci.* **18(4)**, 446-457.

Early life and environmental measures

A key message was the need to work more effectively across the social care and education system, particularly targeting children and adolescents, since these early stages of life can greatly influence trajectories for mental health. Mental health questionnaires have been trialled across primary and secondary schools, providing a valuable source of data on risk factors. Integrating these measures as routine practice into the education and social care system will be essential for prevention and early intervention strategies.

In addition, delegates described the need for more robust and extensive data collection on addiction (e.g. drugs or alcohol). The behavioural and lifestyle changes required to address aspects such as addiction, and the importance of ensuring that adolescents and younger people are adequately captured in data collection, will increasingly require integration of social care with the NHS, and so these measures need to be built across both the health and social care system.

Digital markers

There is an opportunity to better capitalise on digital capabilities to capture key risk factors, including digital biomarkers from health apps and wearables that record signals such as physical activity, circadian rhythms, speech and cognition. Questionnaires also provide a valuable source of data and can be easily administered in a variety of settings, building on the routine clinical and school questionnaires that are already used. For example, Google searches for mental health now bring up PHQ9 – a patient health questionnaire aimed at helping people to evaluate their mental health – in the search results.¹¹

Data sources such as apps and questionnaires can be accessed at scale and relatively low cost, providing a valuable resource to complement 'omics and imaging technologies. It was noted that existing genetically rich cohort data from the 100,000 Genomes Project could also be used to better understand clinical groups, genotypes and phenotypes in mental health.

Challenges to building an evidence base

A key barrier identified in consolidating the right measurements and data for a personalised approach was the very low number of patients with mental health conditions that are involved in UK cohorts. In addition, some mental health disorders are even further under-represented in these studies. For example, it can be highly difficult to recruit and retain patients with schizophrenia and so there is limited data on this group in existing repositories such as the UK Biobank. As schizophrenia is a very disabling disease where the advances in psychiatric genomics have been greatest, there is a strong argument for developing cohorts in this area. Delegates proposed that a mental health research data platform may be a valuable new initiative to catalyse the creation and consolidation of a large clinical database directly relevant to the special requirements of precision psychiatry.

In addition, it was noted that objective phenotyping can be difficult and the subjective, questionnaire-based measures that are often employed make it challenging to build a meaningful evidence base. Therefore there is a need to develop better methodologies for more objective phenotyping of cognitive, emotional and psychopathological aspects of the clinical presentation of mental health disorders.

¹¹ <https://patient.info/doctor/patient-health-questionnaire-phq-9>

What infrastructure is needed?

Integration of mental and physical health services

There remains an overarching need to overcome the barriers between mental and physical health services to improve treatment across this boundary, enhance understanding of the interaction between mental and physical health symptoms, and develop better prevention and early intervention strategies. Psychiatric disability is not well measured or addressed in patients with physical conditions, and *vice versa*; yet better integration is readily achievable. In addition to integration across clinical boundaries, primary, secondary and tertiary care should be better joined up with closer working between psychiatrists and GPs, rather than mental health being seen as a specialised service. There is a need for a more interdisciplinary approach across basic and translational research, clinical practice and mental health services, so that patients, psychiatrists and other clinicians are more involved in the research agenda.

Several exemplars of integration across mental and physical health were described, including at University College London Hospitals where psychiatric services are integrated into routine care for cardiovascular disease. Chronic heart disease is a useful 'real world' example of the importance of integration across the mental and physical boundary as it has been shown that health outcomes are much poorer for those patients who also have a mental health condition.¹² There may also be an opportunity to stratify these patients as cognitive behavioural therapy (CBT) and conventional anti-depressant drugs are also not as effective in these groups and so novel interventions, including anti-inflammatory drugs, may be more useful. Other examples of integration include a platform at King's College London where a questionnaire is used to identify depression and other markers that predict poor treatment response for different physical conditions, and pain management clinics where patients often receive both traditional psychiatric treatments as well as analgesics.

Data infrastructure

Infrastructure is required for the collection of robust, high-quality data on mental health across the care pathway, covering a range of data sources that can be linked to create a rich, comprehensive dataset. Such data collection would also help to incentivise renewed interest in the field. Participants underlined the need for longitudinal data with follow-up over a time span of 10-15 years. This has not yet been done on a national scale and was described as a significant knowledge gap. A recent report from the Research Councils also highlighted this gap where, despite the UK's global excellence in longitudinal studies, there is dearth of this kind of data for mental health research.¹³ Therefore there is a need for more high-quality longitudinal studies of mental health disorders, but participants cautioned that such studies can be very expensive and lengthy, and so more achievable measures for data collection may need to be considered initially such as the suggestions outlined below.

Participants recognised a broader opportunity in the future for routinely measuring and recording robust key data related to mental health in all cohorts across any disease area, particularly in the light of the challenges around recruitment of patients with mental health disorders to clinical trials. This also requires reliable, standardised measures for trials to be developed using learnings from initiatives such as the Dementias Platform UK and European Medical Information Framework. This approach to all cohorts offers an opportunity for

¹² Nielsen TJ, *et al.* (2013). *Mental health status and risk of new cardiovascular events or death in patients with myocardial infarction: a population-based cohort study.* *BMJ Open.* **3(8)**, e003045.

¹³ Research Councils (2017). *Widening cross-disciplinary research for mental health.*

www.rcuk.ac.uk/documents/documents/cross-disciplinary-mental-health-research-agenda-pdf/

immediate benefit at marginal cost with advantages for funders in the context of developing more effective interventions and a better understanding of mental health conditions. In addition, there is a strong rationale for integrating this with data from outside of the healthcare system to look at the entire life experience of patients. In the shorter-term, participants recognised a more realistic aim of better utilising the mental health-related data from existing cohorts, which are already beginning to incorporate measures such as cognition, age-related data and digital recording of phenotypes such as activity and relationships. In addition, a standard mental health questionnaire could be carried out yearly on all patients in primary care.

Building on current data infrastructure

Participants called for better data infrastructure for mental health, based on the widespread use of electronic health records (EHRs) across the secondary care system for mental health. For example, in September 2017, the South London and Maudsley NHS Trust had 2.75 million patient records detailing up to ten years of patient history, and the system was expanding to cover 14 NHS Trusts. The importance of applying learning from the Dementias Platform UK was asserted. This platform enables the use of existing studies to make data discoverable, interoperable and usable, but has not yet addressed the need for high-quality, reliable and standardised measures that can be used in large studies, which is essential in mental health. It was observed that coding for mental health in primary care systems and the differences in local commissioning at a CCG level, can pose a challenge to using system-wide EHR information on mental health, but that the three main GP IT systems could be used to generate some standard measures. Finally, whilst improving the wider dataset for mental health, participants discussed the value of developing a psychosis register in parallel to benefit research in this area of severe mental illness where patients can be difficult to reach.

Capabilities for data collection

Alongside establishing the right infrastructure for data storage, linking, analysis and sharing, capabilities for data collection must be established amongst the healthcare workforce. Healthcare professionals seeing patients with psychiatric disorders need to be trained and supported to record data in a consistent, standardised way. This will need to extend outside of the healthcare system to ensure that all necessary data resources can be integrated and linked.

Participants emphasised that primary care for mental health could focus more on 'self-care', with patients encouraged to personally manage their mental health and collect key data for their care through tools such as wearables, health monitoring and disease management. With the increase in self-produced information, a public health approach can encourage patients to take more control of their own data and feed this into primary care themselves to better support primary clinicians in such data collection. However, this requires acknowledgment and management of the inherent biases of this method of data collection and curation.

How can we drive adoption?

Participants debated how to create traction in the NHS for implementing change in mental health services at both scale and pace. It was agreed that a balance is needed between 'push' and 'pull' so that scientific advances push to increase stratification and use a more targeted approach to treatment, and the NHS is primed to pull through a more stratified approach into treatment so that the science can be implemented effectively across the NHS.

Culture change

Participants explored the need to affect a culture change around perceptions and approaches to mental health, noting that stigmatisation not only occurs in the public but also amongst healthcare professionals when considering different classifications of psychiatric disease. Part of this culture change may be instigated through developing a more rigorous approach to diagnosis and treatment planning, through a more personalised approach to patient assessment. Other steps to support this culture change include destigmatising diagnostic testing at the clinical stage to encourage more patients to seek a diagnosis, and engaging children at a younger age to talk about mental health before they may even need to interact with the care system.

It was proposed that incentives could be introduced to propagate change, potentially similar to the financial incentives in place for routinely recording cholesterol levels and treatment outcomes, or blood pressure, in the NHS. Incentives could drive, for example, completion of a yearly questionnaire on mental health for patients in primary care. In addition, the need to convince clinicians and time pressured frontline staff of the value of good quality data collection was emphasised. The assessment tools currently used are often deemed irrelevant and of little value. Participants suggested that this is compounded by an *'anti-research'* culture within much of mental health services and a move to 'protect' patients from data sharing, which is founded on a lack of understanding of the value of data to improve patient care. There is a huge opportunity to energise healthcare professionals around the value of data and research and destigmatising mental health disorders both amongst patients and healthcare professionals may help to tackle some of the challenges in patient recruitment to trials.

The Royal College of Psychiatrists is undertaking a reform of training processes for psychiatry to foster a better understanding of the neuroscientific basis of mental health disorders and the utility of research and high-quality data. It was observed that these changes should be facilitated across the breadth of medical specialities involved in mental health. The interdisciplinary nature of a personalised approach, which will bring together psychiatrists, neurologists, paediatricians and geneticists amongst others, will itself begin to embed a research-led approach in psychiatry.

Awareness and engagement

Raising awareness across the public and healthcare professions is key to driving a positive culture change and preparing the health and social care systems for more personalised management of mental health. The perceived burden on clinicians for patient-clinician interactions is already high and participants argued that this must be addressed in mental health. For example, a level of personalisation is already enabled in some areas of the country through collaborative prescribing, where a joint treatment decision is made between the psychiatrist and patient through patient empowerment. Awareness must also be raised amongst other stakeholders involved including those deciding the value of new interventions and patient pathways such as payers, who can ultimately steer adoption practices.

Public Health England is carrying out a public-outreach training programme in mental health to encourage the public to take a mental health training course around caring for themselves and others with mental health disorders, and is considering how this can be subsequently integrated into the NHS.¹⁴

¹⁴ <https://mhfaengland.org/>

Demonstrating value of a personalised approach

It was agreed that mental health is a key priority for policy-makers as it not only represents a major financial burden through poorly managed and undertreated conditions, but also has significant costs for patients, families and wider society in terms of health and other factors. Demonstration of the benefits of a personalised approach such as prevention or reduction of burden on the secondary care system will act as levers for change. It was noted that this is already taking place in some institutions such as at King's College London and the John Radcliffe hospital, which are embedding psychiatrists in secondary care services, and already indicate a resultant reduction in re-admission and shortened lengths of stay.^{15,16} However, affordability is an issue. The healthcare system addresses areas so reactively that the necessary finance is not easily available to pump-prime the system for prevention, and so requires a full understanding of high-risk patients and how they can be supported holistically. Participants agreed that such commissioning challenges and constrained budgets are a systemic issue, and so there is some value in a top-down approach to instigate change, and a strong argument for implementing aspects of this approach now.

Improving the quality of information available on the benefits of a personalised approach to psychiatry, including good quality data on health outcomes and cost-effectiveness, should help to build a strong rationale and economic case for implementation. The value of a pilot approach was discussed – referring to the history of cancer services, one participant noted that personalised cancer treatment initially focused on acute lymphoblastic leukaemia, and then application spread to other areas after this had demonstrated benefit. Therefore four 'early wins' – or areas that could be trialled already – were identified by participants within personalised psychiatry to build an evidence base around the advantages of this approach:

1. Inflammatory or auto-immune status of patients with mental health conditions such as treatment-resistant major depressive disorder or a first episode of psychosis.
2. Identification of patients with CNVs or other highly penetrant genetic risks for psychosis.
3. Prevention of mental health disorders in pregnancy and childbirth.
4. Characterisation and prevention of risks for addictive disorders in young people (e.g. drugs/alcohol addiction).

Policy levers for a national approach

Mental health data collection is already tractable in principle, but is a very lengthy process with huge challenges around digitisation and integration of records, which organisations do not have the capabilities or capacity to address. Therefore despite the importance of demonstrating the benefits of personalisation, participants also argued for the need to use policy and organisational levers to ensure that standardised data collection and a personalised approach to mental health services become routine, rather than exceptional.

¹⁵ www.kcl.ac.uk/ioppn/depts/pm/research/imparts/index.aspx

¹⁶ www.ouh.nhs.uk/psychologicalmedicine/services/default.aspx

Conclusion and next steps

From the discussions around current and future challenges to adopting a personalised approach to psychiatry in the NHS, participants suggested a series of potential next steps that should be considered to support such an approach. Next steps suggested by participants in the shorter-term included:

- Develop more robust, reliable (and objective) measures for mental health disorders, including new social and environmental factors that may influence mental health with a focus on influence and impact in early life.
- Incorporate agreed measures of mental health for participants in all clinical trials as routine practice, alongside better use of existing information about mental health from cohorts.
- Explore ways to strengthen the data infrastructure in mental health including more investment in longitudinal studies and capabilities for data collection and integration in mental health.
- Consider piloting a personalised approach to psychiatry in selected areas, demonstrating the benefit of such an approach and thereby facilitating wider personalisation in mental health. Three areas where participants proposed that this could already be done in are:
 - Inflammatory or auto-immune status of patients with mental health conditions such as treatment-resistant major depressive disorder or a first episode of psychosis (given advances in understanding of the mind body-interface).
 - Identification of patients with CNVs or other highly penetrant genetic risks for psychosis.
 - Prevention of mental health disorders in pregnancy and childbirth.

- Characterisation and prevention of risks for addictive disorders in young people (e.g. drugs/alcohol addiction).
- Continue driving better integration of mental and physical healthcare services and overcoming traditional clinical boundaries between GPs, secondary care and psychiatrists, building on exemplars taking place in different NHS Trusts.
- Reducing stigmatisation around mental health and raising awareness amongst the public and healthcare professionals of the opportunities for personalisation and the relevant training required.

Annex 1: Agenda

09.20 – 09.50	Registration and refreshments
09.50– 10.00	<p>Welcome</p> <p>Professor Ed Bullmore FMedSci (Chair), Vice President of ImmunoPsychiatry, GlaxoSmithKline, and Head of Department of Psychiatry, University of Cambridge</p>
10.00 – 10.15	<p>NHS England’s approach to personalisation in mental health</p> <p>Professor Tim Kendall, National Clinical Director for Mental Health, NHS England</p>
10.15 – 10.30	<p>The genetic basis for personalised psychiatry</p> <p>Professor Sir Michael Owen FMedSci FLSW, Professor of Psychological Medicine, Cardiff University</p>
10.30-10.45	<p>The future of personalised psychiatry: what will the system look like in the future and what is needed?</p> <p>Dr John Isaac, Senior Director, External Scientific Innovation, Neuroscience, Johnson & Johnson Innovation</p>
10.45 – 11.00	Tea and coffee
11.00-12.55	<p>Discussion: Challenges, opportunities and needs for adopting a personalised approach to psychiatry in the NHS</p> <p>The discussion should address:</p> <ul style="list-style-type: none"> • The current evidence base for personalised psychiatry – where are the current opportunities for a personalised approach to psychiatry (including genetic and physiological scientific advances)? • What will be the future developments in mental health research over the next 5-10 years? • How can the healthcare system prepare for such developments and what is the role of established and future infrastructure in supporting a personalised approach to psychiatry? • What are the future evidence ‘needs’ in psychiatry and mental health that need to be addressed? • What are the barriers to achieving this vision
13.45 – 14.00	<p>Key conclusions and next steps</p> <p>Professor Ed Bullmore FMedSci (Chair), Vice President of ImmunoPsychiatry, GlaxoSmithKline, and Head of Department of Psychiatry, University of Cambridge</p>
14.00	Close

Annex 2: Attendees List

Chair

Professor Ed Bullmore FMedSci, Head of Department of Psychiatry and Vice President, Immunopsychiatry, University of Cambridge and GlaxoSmithKline

Speakers

Dr John Isaac, Senior Director, External Scientific Innovation, Neuroscience, Johnson & Johnson Innovation

Professor Tim Kendall, National Clinical Director for Mental Health, NHS England

Professor Sir Michael Owen FMedSci FLSW, Director of the MRC Centre for Neuropsychiatric Genetics and Genomics, Cardiff University

Participants

Professor Kathryn Abel, Director of Women's Mental Health, Institute of Brain Behaviour & Mental Health, University of Manchester

Dr Marisa Casanovas Dias, Clinical Academic Mentorship Scheme Fellow, Cardiff University

Professor Jonathan Cavanagh, Professor of Psychiatry, University of Glasgow

Dr Gareth Cuttle, Project Manager - Gatsby/Wellcome Neuroscience Project, Royal College of Psychiatrists

Dr Mitesh Desai, Medical Lead, Neuroscience, Janssen

Professor John Geddes, Professor of Epidemiological Psychiatry and Director, NIHR Oxford Cognitive Health Clinical Research Facility, University of Oxford

Professor Matthew Hotopf FMedSci, Professor of General Hospital Psychiatry, King's College London

Professor Rob Howard, Professor of Old Age Psychiatry, University College London

Dr Henrietta Hughes, Medical Director for North Central and East London, NHS England

Professor Peter Jones FMedSci, Professor of Psychiatry, University of Cambridge

Ms Cynthia Joyce, Chief Executive, MQ: Transforming mental health through research

Professor Belinda Lennox, Associate Professor and Clinical Senior Lecturer, University of Oxford

Professor Anne Lingford-Hughes, Chair in Addiction Biology, Imperial College London

Professor Simon Lovestone FMedSci, Professor of Translational Neuroscience, University of Oxford

Dr Fiona Marshall FMedSci, Director and Chief Scientific Officer, Heptares Therapeutics

Professor Paul Matthews OBE FMedSci, Edmond and Lily Safra Chair and Head of Brain Sciences, Imperial College London

Ms Marsha McAdam, Service User Champion, Patient Information Forum

Professor Stuart Mercer, Chair in Primary Care Research (General Practice and Primary Care), University of Glasgow

Dr Declan Mulkeen, Director of Strategy, Medical Research Council

Mr James Peach, Precision Medicines Lead, Medicines Discovery Catapult

Dr Niels Plath, Vice President, Lundbeck

Professor Andrew Steptoe FMedSci, Director of the Institute of Epidemiology and Health Care and British Heart Foundation Professor of Psychology, University College London

Dr Karen Turner, Director of Mental Health, NHS England

Observers

Dr Rachael Panizzo, Programme Manager for Mental Health and Addiction, Medical Research Council

Ms Alex Pickard, Policy Manager, Medicines Diagnostics and Personalised Medicines Policy Unit, NHS England

Ms Alison Tingle, Research Liaison Officer & Research Development Lead, Department of Health

Dr Ursula Wells, Head of Research Liaison - Health Protection, Department of Health

Secretariat

Ms Liberty Dixon, FORUM Policy Manager, Academy of Medical Sciences

Dr Rachel Quinn, Director of Medical Sciences Policy, Academy of Medical Sciences

Mr James Squires, Policy Officer, Academy of Medical Sciences



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