



Strategy for Lifelong Mental Health Research

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CEO foreword



“Most of us at some point during our lives will be affected by mental illness, either personally or through family members or friends. The causes of mental disorders are complex and challenging, resulting from a combination of biological and psychological features and the impacts of the world around us, both social and environmental.

Our experiences in childhood can affect our mental wellbeing into and throughout our adult lives. The Medical Research Council has prioritised mental health and wellbeing for many years. We have supported excellent researchers who have made great contributions to our understanding of mental illness.

But the burden of mental illness is still all too prevalent so it is vital that we keep up our efforts and build on this progress, taking advantage of new scientific opportunities and tools, such as health data research, to help us create new and more effective interventions for mental disorders. This document, setting out our plans for the years ahead and the exciting research we will support, is just the start.”

Sir John Savill



MRC's Strategy for Lifelong Mental Health Research

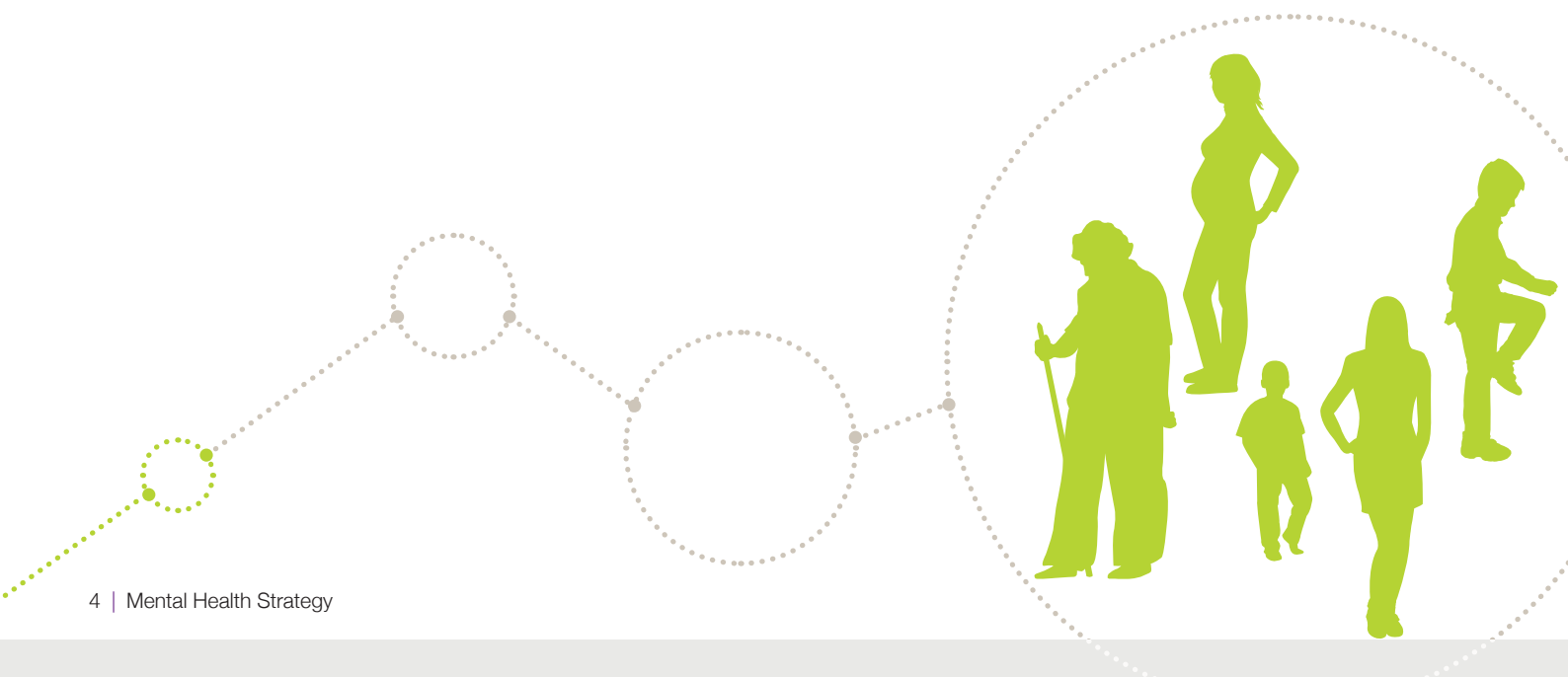
Executive Summary

Mental health issues, such as anxiety and depression, are estimated to affect approximately one in six people at any time in the UK. Mental illness can have a significant and long-term impact on the lives of individuals and their families. Depression and anxiety disorders are the third and ninth leading causes of global disability respectively. Mental disorders cost the UK economy an estimated £70-100 billion annually. By supporting world-class mental health research, the Medical Research Council is creating new opportunities to treat and prevent mental illness.

The UK is well-placed to be at the forefront of new discovery science for mental health. Building on the strengths of the UK research base, the MRC will:

- **Prioritise** mental health research, taking a holistic perspective from childhood throughout life.
- Support **discovery** science through: building capability as a prelude to new, flagship investments; promoting research that cuts across multiple disciplines such as biomedical, psychological, social, physical and digital sciences; elucidating mechanisms and validating new treatment targets.
- **Transform** mental health research by: taking stratified medicine approaches, ie identifying subgroups of individuals with distinct characteristics; making significant investments in global mental health to understand the causes and drivers of mental health; harnessing the data from population studies and the NHS; and by providing new opportunities for academic/industry engagement in mental health research.

To achieve our vision we will work in partnership with other Research Councils, Departments of Health across the four nations of the UK, research charities, industry and people with personal experience of mental illness.



How we will achieve our vision

We will continue to support mental health research through all our open competitions for research grants and fellowships. However, to further accelerate our understanding of mental illness and the development of new treatments, the MRC will:

Employ a lifelong perspective to mental health and illness with special emphasis on youth and adolescence because of the impact of early life on lifelong mental health.

- We will work with the child and adolescent research community to establish a research network, with a particular aim of supporting early-career academic clinical researchers.

Embrace a stratified medicine approach to create new ways of thinking about mental illness and encourage research looking across mind and body.

- Stratified medicine refines clinical phenotyping by identifying groups of people with shared characteristics within or across specific disorders – eg genetics, cognition, response to treatment etc – and by looking beyond standard diagnostic categories to find new treatments and better ways of using existing treatments. Recent genetic discoveries and the emerging promise of immunopsychiatry are already allowing us to work with subsets of individuals with distinct characteristics. **We will continue to endorse and support research that cuts across diagnostic categories.**
- Across all our research we will encourage careful consideration of the full set of coexisting disorders experienced by those with mental illness and the inter-relationships between mental and physical health.

Accelerate research and development to provide much-needed and better pharmaceutical and non-pharmaceutical therapies (including, but not exclusive to, psychological, behavioural, cognitive and digital) and early, preventative interventions for mental illness.

- A barrier to therapy development is that validated targets are not being developed quickly from discovery science effort. This could be accelerated by the development of validated cellular, animal, cognitive and behavioural models. Progress may be accelerated via a call for funding for seeding and consortium research for therapeutic target validation for mental health.

Speed up the progress of discovery through establishing a new resource for mental health research that will harness biological, clinical, environmental and social data from patients, cohorts and other relevant groups and engage cutting edge informatics technology and analytics expertise.

- We will work with health services and other funders to link research programmes and informatics technologies on a large scale. This will facilitate better use of information about mental health in: existing UK population studies; new studies with patients; people at risk of mental illness; and healthy volunteers.
- We will support researchers to engage with the newly established Health Data Research UK. This MRC-led national institute for health and biomedical informatics research will provide opportunities for lifelong mental health research and will be vital in the development of capacity and methodology for data science.

Develop a major new investment in global mental health. This will help us further understand the interactions between biology, environment, culture, cognition and experiences during childhood and adolescence that contribute to mental health disorders and directly address the growing global burden of mental illness.

- This investment, of up to £20m over five years in the first instance, will support a cohesive programme of research for the understanding of vulnerability and resilience, with the long-term aim of developing strategies for prevention of, and early interventions for, mental disorders.

Support research into strategies for the prevention of the occurrence or recurrence of mental health disorders.

- These strategies should be based on improved understanding of key aetiological influences, both protective and risk factors, that underpin the development of mental illness.

Work in partnership with key stakeholders to build capacity and support the next generation of mental health researchers in the UK and globally.

- Our Centres and Units – in mental health, psychology, genetics, epidemiology, global health and other areas – will continue to provide excellent opportunities for interdisciplinary research as we seek to bring new researchers into the field.

Seed the formation of a new UK flagship MRC investment in lifelong mental health and mental illness research.

- Underpinned by the development of a new research infrastructure for mental health research, which will link extensive cohort and NHS data with novel digital science and in-depth biomedical phenotyping, we will work with other stakeholders to enable UK mental health research. Development funding will be made available to catalyse this and to support progress towards additional major investment able to exploit this in the medium to longer term.



Introduction

The MRC recognises the personal and societal impact of poor mental health and has long placed mental health and wellbeing as a key strand of its research priorities. Mental health disorders are common; depression and anxiety disorders are the third and ninth leading causes of global disability respectively¹. The 2014 Adult Psychiatric Morbidity Survey estimated that one adult in six reported a diagnosable common mental disorder². According to the same survey, since 2000, rates of mental health disorder have increased in women (to one in five) and remained stable in men (one in eight). According to the Office for National Statistics, the suicide rate in 2015 was 10.9 deaths per 100,000 people in the UK population. This was a slight rise compared to 2014³. In 2015, the Office for National Statistics reported that one in eight children aged 10 to 15 in the UK reported symptoms of mental illness in 2011 to 2012⁴. Many mental disorders begin visibly or invisibly during childhood: work on the MRC-funded Dunedin cohort showed that 50% of mental illness started before the age of 15 and 75% by age 18⁵. Mental illness costs the UK economy an estimated £70-100 billion annually as a consequence of lost productivity, social benefits and health care⁶.

Having a long-term mental illness is likely to have repercussions for personal economic prosperity, quality of life and physical health. In addition, the high level of social inequality related to mental illness is notable; the prevalence of mental disorders was greater among children with at least one parent who had no educational qualifications (17%) compared with those who had a degree level qualification (4%) and in families with neither parent working (20%) compared with those in which both parents worked (8%)^{7, 8}.

Given the prevalence and impact of mental disorders, the MRC is committed to supporting research that will have a positive impact on the lives of those who are affected by, or at risk of, mental illness.

Mental health and co-morbidities

People with psychotic illnesses have a reduced life expectancy of 15–20 years compared to the general population⁹. This is a two to three fold excess mortality compared to the general population, half of which is caused by physical illness¹⁰. In 2012, the Kings Fund estimated that 46% of people with any mental illness also have a long-term physical health condition and 30% of people with a long-term condition also had a mental health condition¹¹.

Alongside co-occurrence of mental and physical ill health, there is considerable co-morbidity of substance abuse and mental illness. This co-morbidity with physical health conditions is a challenge for the health and social care services, particularly as individuals with mental disorders often have poorer outcomes, for example, in terms of cancer survival rates¹². However, the presence of co-morbidities is also a challenge

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1. GBD 2015 Disease and Injury Incidence and Prevalence Collaborators, Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015, 2016, *Lancet*, 388, 1545-1602.
 2. McManus S, Bebbington P, Jenkins R, Brugha T. (eds.) (2016) *Mental health and wellbeing in England: Adult Psychiatric Morbidity Survey 2014*. Leeds: NHS Digital
 3. Office for National Statistics (2016), *Statistical Bulletin: Suicides in the UK: 2015 registrations*. Newport: ONS
 4. Office for National Statistics (2015), *Insights into children's mental health and well-being*
 5. Kim-Cohen J. et al, (2003). Prior juvenile diagnoses in adults with mental disorder: Developmental follow-back of a prospective-longitudinal cohort. *Archives of General Psychiatry*, 60, 709-717
 6. OECD, (2014). *Mental health and work: United Kingdom*. OECD Publishing.
 7. Davies, SC (2014). *Annual report of the Chief Medical Officer 2013. Public Mental Health Priorities: Investing in the Evidence*. London: Department of Health.
 8. Green, H., et al (2005). *Mental health of children and young people in Great Britain, 2004*. Basingstoke: Palgrave Macmillan
 9. Nordentoft et al (2013). Excess Mortality, Causes of Death and Life Expectancy in 270,770 Patients with Recent Onset of Mental Disorders in Denmark, Finland and Sweden. *PLoS ONE*, 8(1); e55176
 10. Schumann et al, 2014, Stratified Medicine for mental disorders. *European Neuropsychopharmacology*, 24, 5-50
 11. Naylor et al, (2012). *Long-term conditions and mental health. The cost of co-morbidities*. London: The King's Fund
 12. Chang, C-K. et al. 'A Cohort study on mental disorders, stage of cancer at diagnosis and subsequent survival' published in *BMJ Open* doi:10.1136/bmjopen-2013-004295

for research. The MRC will encourage better and broader links between mental and physical health research. Co-morbidity is common; physical and mental health researchers should, where possible, avoid focussing on single outcome measures and consider utilising a broader range of both physical and mental health measures in population research and in more detailed mechanistic and treatment studies.

Mental health and stigma

There have been promising shifts in the public understanding of mental illness and a reduction in some of the stigma which has had such a negative impact on affected individuals and their families. Nonetheless, important work still needs to be done to reduce stigma and the MRC will work with stakeholders to investigate how best to reduce stigma and to promote positive mental health and wellbeing at a population level throughout the life course. By working towards parity of esteem between mental and physical health we can continue to reduce the stigma of mental illness.

Working in partnership

We work closely with other funders and with policy makers in this field. In 2016, an independent Mental Health Taskforce to the NHS in England published a report, “Five Year Forward View for Mental Health”, which contained a recommendation that the Department of Health published a report setting out a 10-year strategy for mental health research¹³. The MRC is a member of the steering committee for the report, which will be published in 2017. The strategy will align with the overarching priorities agreed by the Roadmap for Mental Health Research in Europe (ROAMER), which brought together a wide range of stakeholders to identify gaps and set priorities in mental health research in Europe¹⁴.

Together with other Research Councils we are working to identify areas for specific action where interdisciplinary research will have an impact on mental health, for example, in seeking to integrate biomedical, clinical and social research methodologies and data to generate new insights into the development and trajectory of mental illness. In addition, the MRC is a member of a national group of mental health research funders to take a coordinated overview of mental health research. We are also members of the International Alliance of Mental Health Research Funders, which brings together a number of organisations together to promote coordination, collaboration and help research funders achieve greater impact. The latter two groups include active participation by MQ: Transforming Mental Health, which is a relatively new UK-based charity dedicated to mental health research (www.mqmentalhealth.org). The formation of this charity, which is committed to “create a world where mental illness is understood, effectively treated, and ultimately prevented”, is a welcome addition to the mental health research landscape.

The public, service users and the voluntary sector are key stakeholders in mental health research and the MRC recognises the importance of public and patient engagement. Many of our researchers work with multiple stakeholders, eg patient groups and people with lived experience of mental illness, in order to better shape their research projects and the MRC provides support for these activities.

13. <https://www.england.nhs.uk/wp-content/uploads/2016/02/Mental-Health-Taskforce-FYFV-final.pdf>

14. Wykes et al. (2015) Mental health research priorities for Europe, *Lancet Psychiatry*, 2, 11, 1036-1042.

The MRC's mental health research portfolio

In 2010, the MRC published a comprehensive review of mental health research in the UK. Based on the UK's research strengths, two strategic ambitions for the UK were highlighted: **preventing mental disorder and disability**, and **accelerating research and development for effective treatments for mental illness**. We will continue to build on these two themes over the medium term by capitalising on recent scientific developments in the field.

To support our mental health strategy in recent years, the MRC's Neuroscience and Mental Health Board (NMHB) has run a number of initiatives. These have stimulated experimental medicine research in mental health and encouraged data sharing and the better use of cohort resources for mental health studies, see box 1. In addition, we have worked in partnership with the Medical Research Foundation to support an innovative national fellowship scheme for academic psychiatrists in addition to providing support for the under-researched areas of eating disorders, self-harm and intellectual disabilities.

Box 1 – examples of previous strategic funding

As part of our efforts to grow our portfolio in interdisciplinary and translational research in mental health, we have invested in areas such as experimental medicine. A £3m initiative to support experimental medicine research in mental health supported 13 studies ranging from behavioural interventions for anxiety, panic disorder or depression to pharmacological interventions for addiction, psychosis, anxiety or depression. In addition, we have supported work at King's College London that is using novel ligands for positron emission tomography (PET) to investigate changes in the brain that lead to psychotic disorders such as schizophrenia. Work led by The University of Manchester is using a range of state-of-the-art imaging techniques to measure the release and activity of chemicals in the brains of people with schizophrenia.

The data sharing initiative provided support for seven studies. One of these, linking data from the Born In Bradford cohort and primary care data, showed the existence of common mental disorder detection disparities for minority ethnic women in the maternal period¹⁵.

In partnership with the Medical Research Foundation, we funded the Intellectual Disability and Mental Health: Assessing the Genomic Impact on Neurodevelopment study (IMAGINE¹⁶), which works with the Farr Institute¹⁷, to create a resource for intellectual disabilities research. The investigators are collecting genomic information, primarily from children and young adults with pathogenic copy number variants and/or single nucleotide variants, which are thought to be of aetiological relevance. The resource will contain information on individuals' behaviour, mental health as well as genetic phenotype.

Alongside specific initiatives, we have supported world-class mental health research through our response mode funding mechanisms. Indeed, major progress has been made in a number of areas of mental health research thanks to MRC-funded researchers. For example, important advances in the field of psychiatric genetics and genomics have led to the identification of key genes involved in the development of multiple forms of mental illness¹⁸. In addition, we have a better understanding of the impact of childhood experiences on cognitive, mental and physical health outcomes in later life¹⁹.

15. Prady SL, et al. (2016) Evaluation of ethnic disparities in detection of depression and anxiety in primary care during the maternal period: combined analysis of routine and cohort data. *Br J Psychiatry*. 208(5):453-61

16. www.imagine-id.org

17. www.farrinstitute.org

18. Doherty, J.L. and Owen, M.J. (2014), Genomic insights into the overlap between psychiatric disorders: implications for research and clinical practice, *Genome Medicine*, 6(4): 29.

19. Arseneault L. (2017) The long-term impact of bullying victimization on mental health. *World Psychiatry*. 16(1):27-28.

New assessment, self-monitoring tools and treatments have been developed and new clinical trials are underway to evaluate novel interventions in mental illness with support from our translational research funding schemes. Since 2010 there has been over a ten-fold increase in our translational mental health funding. Spend on the development and evaluation of treatments and therapeutic interventions has risen from ~£0.5m per annum in 2010/11 to £5.5m per annum in 2015/16. We intend to develop new activities to build on the successful growth of our translational mental health research portfolio and maintain this upwards trajectory.

Details of our mental health funding portfolio are available on the MRC website²⁰. This shows an increase in our spend from £20.5m per annum in 2010/11 to £25.2m per annum in 2015/16; the portfolio over this time includes around 300 grants and fellowships. A new, detailed analysis of mental health research applications submitted to the MRC reveals that success rates are comparable to applications across our broader neuroscience portfolio. However, despite efforts to stimulate activity through various mental health-focused calls for proposals in the past few years, we have not seen this lead to an increase in the number of applications submitted to the boards and panels through regular funding routes. We still receive relatively low numbers of proposals, which could be indicative of insufficient capacity within the field.

How the MRC funds mental health research

The majority of the MRC's mental health research portfolio is funded through NMHB, either through response mode or bespoke calls, although other boards and panels also support the area. Our fellowship panels also support early career stage researchers from the PhD stage onwards, particularly at key career transitions. Research aimed at providing new, more effective treatments for mental illness is funded by the MRC through the Biomedical Catalyst: Developmental Pathway Funding Scheme (www.mrc.ac.uk/funding/science-areas/translation/biomedical-catalyst) and the Efficacy and Mechanism Evaluation scheme, which is administered by NIHR (www.nets.nihr.ac.uk/programmes/eme).

In addition to fellowships, projects or programme grant support, we support mental health research through our Centres, Units and Institutes. MRC Centres are partnerships with the host university that build on existing support from the MRC and other organisations to add value and help establish sustainable internationally recognised centres of excellence, while MRC Units and Institutes are longer term investments that pursue large-scale and interdependent programmes of research. As well as supporting cutting-edge research, these strategic investments provide a multidisciplinary training environment to support the growth of research capacity in this area. The MRC currently supports two Centres with a focus on mental health research: the MRC Centre for Neuropsychiatric Genetics and Genomics at Cardiff University (www.cardiff.ac.uk/mrc-centre-neuropsychiatric-genetics-genomics) and the MRC Centre for Neurodevelopmental Disorders at King's College London (<https://devneuro.org/cnodd/>). Several of the MRC's Units support programmes with direct relevance to mental health research include: the MRC Cognition and Brain Sciences Unit in Cambridge (www.mrc-cbu.cam.ac.uk); the MRC Integrative Epidemiology Unit at the University of Bristol (www.bristol.ac.uk/integrative-epidemiology); the MRC Unit for Lifelong Health and Ageing at University College London (www.ucl.ac.uk/iehc/research/accordion/mrciha); the MRC London Institute for Medical Sciences (csc.mrc.ac.uk); MRC/CSO Social & Public Health Sciences Unit in Glasgow (www.gla.ac.uk/researchinstitutes/healthwellbeing/research/mrccsosocialandpublichealthsciencesunit/); and the MRC/UVRI Uganda Research Unit on AIDS (www.mrcuganda.org).

20. <https://www.mrc.ac.uk/research/funded-research/>

MRC's strategic priorities for lifelong mental health research

Employing a lifelong perspective with a focus on children and young people

The MRC is dedicated to increasing our understanding of, and finding treatments for, mental illness at all stages of life. We support investigations into foetal programming (where events within the womb can lead to long-term effects in later life), the perinatal mental health of parents, childhood and adolescent development, and mental health and wellbeing throughout adulthood and in older age. Common adult mental health disorders such as depression and psychosis often emerge during adolescence; 50% of mental illness observed in adults is manifest by the age of fifteen and 75% by the age of eighteen⁵. Therefore, we are placing an emphasis on mental health research which focuses on children and young adults.

Childhood manifestations of mental disorder, such as conduct and emotional disorders, are more heterogeneous in phenotype than those presenting in adolescence and adulthood, but both are associated with biological, psychological and social factors. A 2004 Office for National Statistics survey determined that one in 10 UK children aged between five and 16 had a mental disorder. Despite this high incidence, we still understand little about childhood mental illness and how best to treat it.

As well as genetic and psychological risk factors, broader established associations for adult mental illness are early life experience of adversity including sexual, physical or emotional abuse, socio-economic adversity/poverty, household violence, substance misuse, mental illness or imprisonment; issues which may often be difficult to identify. Caregiver interactions are critical in early development; neglect is the most common form of child maltreatment²¹. Nonetheless, not all children who are exposed to adversity will develop mental health problems; these are important risk factors as opposed to definitive causal events²². Research is needed to better understand the mechanisms and dimensions that underlie vulnerability and resilience.

The benefits of early interventions

We need to better understand the early manifestations, resilience and the impact of the biological, social and environmental drivers of disorders if we are to deliver on ambitions in prevention and early intervention for mental health.

A number of psychosocial evidence-based interventions that target parent and child interactions in early life, or deliver classroom, or family-based curricula have been shown to reduce symptoms and adverse behaviour, including anxiety, depression, antisocial behaviour and aggression²³. Nevertheless, much more research needs to be carried out to develop new understandings and interventions that improve the lives of people living with mental illness. The MRC funded Pre-school Autism Communication Trial (PACT) trial has demonstrated efficacy of an early intervention to optimise parental interaction style to improve social-communication and repetitive symptom domains in the neurodevelopmental disorder autism^{24,25}.

21. Center on the Developing Child at Harvard University (2012). The Science of Neglect: The Persistent Absence of Responsive Care Disrupts the Developing Brain: Working Paper No. 12. www.developingchild.harvard.edu

22. Danese et al (2016), The origins of cognitive deficits in victimized children: Implications for neuroscientists and clinicians, *The American Journal of Psychiatry*, 31:10:2016

23. Greenberg, MT and Riggs, NR (2015), *Rutter's Child and Adolescent Psychiatry*, Sixth Edition

24. www.research.bmh.manchester.ac.uk/pact

25. Pickles et al (2016), Parent-mediated social communication therapy for young children with autism (PACT): long-term follow-up of a randomised controlled trial, *The Lancet*, Volume 388 , Issue 10059 , 2501 - 2509

Access to such interventions and services is critical. A longitudinal assessment of the association between service contact and depressive symptoms in a cohort of UK 14 year olds demonstrated a reduced likelihood of depressive symptoms by age seventeen in those children who had had contact with mental health services²⁶. This Wellcome- and NIHR-funded study highlighted the value of access to mental health services for the treatment of depression and the preventative value of these services.

In 2013, the Office for National Statistics determined that one in five young people over the age of 16 had shown symptoms of depression or anxiety. However, it is important to note that presenting with symptoms at the age of 16 does not necessarily equate to lifelong mental illness. It has been shown that of those adolescents with a single episode of disorder of less than six months in duration, just over half had no further disorder as a young adult²⁷. Other studies have suggested that the strongest predictor of young adult disorder was a longer duration of symptoms²⁸.

The patterns of occurrence and persistence of symptoms of mental health disorders present important opportunities for research in adolescents and young adults to better understand the mechanisms of disorder emergence, progression and recovery and recurrence, in order to reduce duration and prevent recurrence. In addition, a better understanding of high-risk individuals, with recurrent disorder, will be key to the development of more effective interventions and services. Therefore, MRC's ambition is to support researchers to develop and improve non-pharmaceutical and pharmaceutical interventions that treat and prevent mental illness at this key developmental stage.

Stratified medicine for mental health research

Stratified medicine is one of the MRC's strategic priorities to transform health research and innovation. Stratified medicine describes the identification of groups of people with specific, identifiable features, and looks beyond conventional diagnostic categories to find new treatments and better ways of using existing treatments. Stratification can be based on a number of factors, including: cognitive and psychological traits; genetics; environmental exposures such as adverse life experiences; behavioural symptoms; as well as response to pharmacological, psychological or combined treatments.

The power of genetics to stratify individuals with mental disorders

In some mental health disorders, heritability is high, for example, some studies have shown in schizophrenia it is approximately 80%²⁹. Recently a number of genes that predispose an individual to mental illness have been discovered (see box 2). The UK is world-leading in these efforts, with the MRC Centre for Neuropsychiatric Genetics and Genomics at the forefront of these activities.

The role of informatics in stratified medicine for mental illness

Linking data from richly phenotyped, population-based cohorts with care data as well as education, employment, social, environmental and justice data can help to identify groups of individuals for study or who may benefit from intervention. For example, digital science and informatics tools could help detect individuals with common or rare mental disorders and alongside this provide valuable contextual information into social or medical influences. This will provide novel insights into the manifestation of mental ill health or resilience to it and offer new routes for the stratification of study groups, epidemiological studies and subsequent research into mechanism.

26. Neufeld et al (2017), Reduction in adolescent depression after contact with mental health services: a longitudinal cohort study in the UK, *Lancet Psychiatry*, 10:01:2017

27. Patton et al (2014), The prognosis of common mental health disorders in adolescents: a 14-year prospective cohort study, *Lancet*, 383, 1404-1411.

28. Greenberg, MT and Riggs, NR (2015), *Rutter's Child and Adolescent Psychiatry*, Sixth Edition.

29. Sullivan et al (2003), Schizophrenia as a complex trait: evidence from a meta-analysis of twin studies. *Archives of General Psychiatry*. 60:1187-1192.

Box 2 – Stratification in mental disorders

Genetic discoveries – The identification of subgroups of individuals with distinct mechanisms of disorder, or particular responses to treatment, could provide useful insight into mental illness. Recent developments in the fields of psychiatric genetics and genomics have delivered exciting discoveries and revealed that several psychiatric and neurodevelopmental disorders share genetic features³⁰. For example, loss of function of the SETD1A gene has been shown to predispose individuals to developmental disorders including schizophrenia³¹. The SETD1A gene encodes a methyltransferase that is an epigenetic modifier of chromatin. This suggests a potential pathological mechanism for the cause of schizophrenia in some individuals. Other pathways implicated in the pathogenesis of schizophrenia are linked to plasticity. For example, enriched de novo mutations in genes encoding proteins belonging to postsynaptic densities at glutamatergic synapses have been found in people living with schizophrenia³². Increased understanding of biological mechanisms that underpin mental illness in subpopulations of individuals provides opportunities for the targeted development of new interventions.

Symptomatic stratification – The identification of subgroups of individuals with common behaviours, cognitive features or psychiatric symptoms could also lead to insights into personalised treatment for mental disorders. For example, although many children and young people exposed to trauma experience natural recovery, a minority develop post-traumatic stress disorder (PTSD). Research funded by the MRC in Cambridge aims to understand the evolution and early course of PTSD in young people exposed to trauma, investigating whether acute stress disorder and other acute symptoms might predict PTSD, other psychopathology, or distinct recovery trajectories³³. Further studies of stratification based on acute symptoms of experiencing trauma could help identify young people at risk of PTSD and provide routes for early intervention.

30. Singh et al. (2016) Rare loss-of-function variants in SETD1A are associated with schizophrenia and developmental disorders, *Nature Neuroscience* 19, 571–577

31. Singh et al. (2016) Rare loss-of-function variants in SETD1A are associated with schizophrenia and developmental disorders, *Nature Neuroscience* 19, 571–577

32. Hall et al. (2015), Genetic Risk for Schizophrenia: Convergence on Synaptic Pathways Involved in Plasticity, *Biological Psychiatry*, 1;77(1):52-8.

33. Meiser-Stedman R, McKinnon A, Dixon C, Boyle A, Smith P, Dalgleish T. Acute stress disorder and the transition to posttraumatic stress disorder in children and adolescents: Prevalence, course, prognosis, diagnostic suitability, and risk markers. *Depress Anxiety* 2017;00:1-8.



Research across clinical criteria – a dimensional approach for stratified medicine

The MRC's Neuroscience and Mental Health Board advocates an approach that works across clinical criteria and focuses on the role of complex behaviours and networks shared by different disorders. Mental wellbeing and mental illness depend on a multidimensional interplay of biological, social and environmental factors, which influence risk and resilience. This complexity means that mental illness is often challenging to diagnose and research. In addition, co-morbidity of physical and mental illness is common. Where possible, researchers should consider utilising a broader range of both physical and mental health outcome measures in population research and in more detailed mechanistic and treatment studies.

The MRC funds research related to all mental health disorders. However, one of the key barriers to success in developing new and effective treatments for mental health disorders is the lack of specificity in the diagnostic labels. Many disorders present with common features or behaviours, for example, impulsivity is common to ADHD, substance use disorders, bipolar disorder, borderline personality disorder and neurodegenerative diseases. In addition, mental disorders are often comorbid, and many will experience anxiety and depression in addition to other symptoms. Similarly, impairments in cognition are shared across disorders, eg impairments in executive functioning are seen in ADHD, autism spectrum disorder (ASD) and conduct disorder, whereas emotion is dysregulated in disorders such as depression, personality disorder, ADHD and ASD.

Studying the dimensions of a symptom/behaviour across different disorders is often the most appropriate approach. While symptoms may not directly reveal the underlying biology, psychology or predict how a condition will develop, they are important biomarkers for observing changes that occur during a mental illness. A focus on a dimension rather than a diagnostic label has the added advantage of facilitating translational research bridging the gap between model systems and people living with mental illness. A dimensional approach also lends itself to the exploration of the underpinning mechanisms for co-existing disorders. The generation of more precise and consistent datasets resulting from dimensional approaches will enhance the quality of quantitative, statistical and informatics science. More research is required to develop sensitive scales to measure dimensional symptoms, which are acceptable to regulatory bodies and that can be utilised to test new interventions.

The promise of neuroimaging for studying mental illness

The UK has a wealth of expertise in state-of-the-art neuroimaging such as functional and structural magnetic resonance imaging (MRI), magnetoencephalography (MEG), electroencephalography (EEG) and positron emission tomography (PET). Neuroimaging techniques can help us gain an understanding of the anatomy, connectivity and functioning of an individual's brain at rest and when undertaking a task, and how this might be perturbed as a result of mental illness. There are opportunities to understand more by combining approaches – known as multimodal imaging – and connecting this information with genetic, cognitive and/or clinical profiles.

The MRC has established a number of national imaging networks in MEG, combined PET/MRI, and high-field MRI that promote methods development, standardisation and knowledge exchange. These networks, together with the underpinning infrastructure, provide a powerful resource for future cohort and experimental medicine studies in mental health. This approach has already been shown to be successful; a MRC-funded, multi-centre study to investigate brain anatomy in autism – the UK Autism Imaging Multicentre Study (UK AIMS) – showed that people with autism have significant anatomical differences from people without autism and that those differences are related to severity of behaviour. The consortium became part of the large, international consortium of the *European Autism Interventions: A Multicentre Study for Developing New Medications*³⁴. This was part of the European Innovative Medicines Initiative, which is Europe's largest public-private partnership aiming to improve the drug development process by supporting a more efficient discovery and development pipeline for better and safer medicines for patients.

34. www.imi.europa.eu/content/eu-aims

The world's largest brain imaging study has just been commenced by UK Biobank³⁵. UK Biobank recruited 500,000 people aged between 40-69 years in 2006-2010 from across the UK. The imaging study will take a number of measures, including brain and heart images. These data can be combined with other information that has been collected from participants over a number of years and can be coupled with genetic, lifestyle and clinical information, thereby providing the potential to better understand factors influencing the most prevalent mental health disorders such as anxiety and depression.

Large scale brain mapping and imaging studies, such as the UK Biobank project and the human connectome project (www.humanconnectomeproject.org), will, in time, illuminate our understanding of the human brain. In addition, there is growing understanding of neural circuitry, ie how functional connections of neurons in the brain lead to behaviours. Informatics tools can be used to interrogate these data for mental health research in the future.

Developing new interventions

The development of new models, robust targets and clinically relevant end-points could draw the larger pharmaceutical companies back to the field of mental health. Since the publication of our previous mental health strategy in 2010, the pharmaceutical industry landscape has undergone a major shift. Many of the larger companies have stepped back from prioritising investments in mental health. In the meantime, other smaller companies maintain an active portfolio in mental health. If robust targets and clinically relevant end-points can be identified then it is envisaged that large-scale investment will return to the field. The MRC will support the UK academic community to work with industry partners.

The MRC will support activities to determine how best to capitalise on the recent discoveries in mental health research to foster an ethos of target identification and biomarker validation in the UK academic community. The field of immunopsychiatry (box 3) has already proven to be attractive to pharmaceutical research and development investment in mental health disorders. This is an area that provides opportunities to develop mechanistically-specific and peripherally-accessible biomarkers for drug development. In addition to immunopsychiatry, recent genetic discoveries present an opportunity to explore and broaden our mechanistic understanding of mental health disorders through a target identification and validation approach.

A critical next step in the functional analysis of newly identified risk genes is to undertake predictive modelling to prioritise the most tractable opportunities for therapeutic potential. The functional analysis of prioritised pathways and targets will require new multidisciplinary teams to develop relevant cellular, animal and behavioural models. Increased understanding of the complex functionality of these genes and the responses of the gene products to environmental influences could facilitate the development of new therapeutics and treatments. The development of new models could also enable a 'fast fail approach' where potential treatments could be screened to see if they are able to alter biomarkers and provide evidence of efficacy and tractability.

Recent developments in fields such as the ability to generate induced pluripotent stem cells (iPSC) from individuals with mental illness provide opportunities for both laboratory-based functional modelling and target validation screening in cells that are more representative of the underlying human biology. Similarly, gene-editing techniques also provide new opportunities to study key risk alleles in the human cellular context. Prior to the emergence of iPSC technology, the ability to study human neural cells was very limited. The potential impact of such approaches has been demonstrated by academics in the field of neurodegeneration research in particular, where progress has been rapid and has achieved notable engagement with the pharmaceutical industry. For example, the integration of networked stem cell programmes alongside well-characterised cohort populations has provided the backbone for the

35. www.ukbiobank.ac.uk

MRC Dementias Platform UK, which has attracted partnership from a number of large pharmaceutical companies and small medium-sized enterprises³⁶. The UK-led Innovative Medicines Initiative StemBANCC programme is another major European public private partnership seeking to exploit iPSC technology, with activity focussed in neurodegeneration but also in schizophrenia, bipolar disorder and autism³⁷.

In terms of target validation procedures for cognitive or behavioural measures, the underlying premise is the same as that for cellular or animal model systems. Once the cognitive or behavioural feature that is the target for intervention (which could cross diagnostic boundaries) has been determined, specific interventions (pharmaceutical or non-pharmaceutical such as cognitive or behavioural) can be tested. In addition to assaying changes in cognitive or behavioural measures of interest, basic biomarkers such as galvanic skin response, genetic variation etc, could also provide valuable insight into individuals' responses to the intervention. Indeed, such measures may help to stratify individuals into subgroups that are more likely to respond to a particular intervention.

Box 3 – Immunopsychiatry

New insights in subsets of individuals with different characteristics – from stratified medicine – can offer immediate opportunities for repurposing existing treatments. There is growing evidence of a link between inflammation and mental illness in at least a minority of those affected, for example:

- elevated interleukin-6 levels in nine year olds was predictive of the risk of depression and psychoses at age 18 in the ALSPAC cohort³⁸
- findings from a large-scale genome wide association study support a link between the immune system and schizophrenia³⁹
- many individuals with chronic inflammatory disorders have co-morbid depression⁷
- individuals with bipolar disorder have higher levels of C-reactive protein (increased levels of C-reactive protein in the blood is an indication of inflammation) particularly during periods of mania when they may be experiencing an increased inflammatory burden⁴⁰
- major depressive disorder is associated with replicable over-expression of genes involved in activation of the innate immune system by peripheral blood cells⁴¹

To maximise the potential of this emerging field, studies will need the full engagement of researchers with expertise in chronic systemic inflammation and/or immunology alongside mental health researchers.

The MRC has invested in an academic-industrial consortium for immunopsychiatry, led by the University of Cambridge, and has provided funding for a randomised double-blinded placebo-controlled trial of immunotherapy in patients with antibody-associated psychosis. The MRC Immunopsychiatry consortium brought together academic centres in Cambridge, Edinburgh, King's College London, Southampton and University College London as well as GSK and Janssen. Immunological mechanisms for mental health disorders are evidently attractive to industry and may provide a way forward to encourage the private sector to re-invest in the development of new medicines for immunologically stratified groups of people living with mental illness, including those who may also have physical health comorbidities.

36. www.dementiasplatform.uk/get-involved/partners/

37. www.stembancc.org

38. The MRC-funded Avon Longitudinal Study of Parents and Children recruited over 14,000 pregnant women and has followed them for over twenty years www.bris.ac.uk/alspac/

39. Schizophrenia Working Group of the Psychiatric Genomics Consortium (2014), Biological insights from 108 schizophrenia-associated genetic loci. *Nature*;511:421–427

40. Fernandes et al. (2016) C-reactive protein concentrations across the mood spectrum in bipolar disorder: a systematic review and meta-analysis, *Lancet Psychiatry* 3(12):1147-1156.

41. Leday et al (2017) Replicable and coupled changes in innate and adaptive immune gene expression in two case-control studies of blood microarrays in major depressive disorder. *Biological Psychiatry*, in press

The power of data and informatics: population and cohort studies

Studying groups of individuals with shared characteristics, known as cohorts, can help to elucidate the causes, risk factors and access to treatment for mental disorders in order to design better interventions. This has been done, for example, by using state of the art informatics techniques to link data specifically collected from cohorts with data from their patient records⁴². We will therefore seek to develop a resource that harnesses the richness of data from population and cohort studies and health-related records other relevant data sets to support academia and industry thereby accelerating the development of interventions for mental illness across the life course.

Given the success of the MRC Dementias Platform UK (www.dementiasplatform.uk/), which brings together experts with cutting edge technology, informatics and cohort resources to speed up progress in dementia research, there is a case for developing a similar integrated cohort-based resource for the study of mental illnesses. By integrating biological, clinical, epidemiological, social, economic, environmental and even educational data through state of the art technologies there is huge potential to harness the power of health, social and biomedical informatics to help understand the causes of mental disorders and the nature of resilience, and to develop new interventions or preventive strategies. It is essential that we secure public confidence in such a resource, particularly in relation to consent and the confidentiality of personal information. Therefore its development will require the engagement of cohort participants, patients and individuals with mental disorders throughout.

Informatics techniques could be productively applied, for example, to the emerging field of immunopsychiatry to better understand the associations between inflammation and mental health. In addition, data can be incorporated from wearable devices that monitor behaviour and feedback from the use of apps and websites thereby providing even richer, contextual information on individuals and the multifactorial influences on mental health and illness (see box 4). Additionally, informatics tools can provide a route to develop and validate objective outcome measures (eg wearable devices for patient reported outcome measures).

The UK has an excellent reputation for supporting world-class longitudinal population and cohort studies. In 2015/16, the MRC spent £12.2m supporting the core funding for twenty-two population cohorts, these resources are described in the cohort directory on our website (<https://www.mrc.ac.uk/research/facilities-and-resources-for-researchers/cohort-directory/>). This investment is in addition to support for specific disease- and disorder-based population groups. UK cohorts provide world-leading capability given the detailed and long term characterisation of the study participants, and the potential to integrate biological, psychological, clinical, environmental and social aspects underlying health and disease. Funded by the ESRC and the MRC, CLOSER (Cohort & Longitudinal Studies Enhancement Resources, www.closer.ac.uk), brings together eight UK studies in order to maximise their use, value and impact by stimulating interdisciplinary research, develop shared resources. The cohorts brought together by CLOSER provide important epidemiological, social, economic and environmental data to support mental health studies⁴³. Many UK cohort resources offer opportunities for research addressing the more common mental disorders, although to date these resources are not reported as part of our mental health research portfolio. For example, UK Biobank has successfully been utilised to study depression⁴⁴, and as mentioned previously provides a unique global resource that offers the potential to link brain imaging, genetic, clinical and lifestyle data to better understand the drivers of both mental health and illness in an ageing population.

42. Prady SL, et al. (2016) Variation and ethnic inequalities in treatment of common mental disorders before, during and after pregnancy: combined analysis of routine and research data in the Born in Bradford cohort. *BMC Psychiatry*. 16:99.

43. Evans-Lacko S, et al. (2017) Childhood bullying victimization is associated with use of mental health services over five decades: a longitudinal nationally representative cohort study. *Psychol Med*. 47(1):127-135

44. Smith et al (2013), Prevalence and Characteristics of Probable Major Depression and Bipolar Disorder within UK Biobank: Cross-Sectional Study of 172,751 Participants, *PLOS ONE* 8(11): e75362. doi: 10.1371/journal.pone.0075362

The MRC supports a number of cohorts of children and young adults that have been designed to study mental health, cognition and illness including the Avon Longitudinal Study of Parents and Children (www.bristol.ac.uk/alspac/), E-Risk Longitudinal Twin Study ([www.kcl.ac.uk/ioppn/depts/mrc/research/environmentalrisk\(e-risk\).aspx](http://www.kcl.ac.uk/ioppn/depts/mrc/research/environmentalrisk(e-risk).aspx)), Twins Early Development Study (www.teds.ac.uk/) and the Wirral Child Health and Development Study (<https://www.liverpool.ac.uk/psychology-health-and-society/research/first-steps/>). These resources have enabled the study of common disorders such as depression and anxiety as well as dimensional phenotypes that are related to less common disorders⁴⁵.

Within the next 12 months we will convene an expert group drawing on academic, industry, charity and service user communities to consider the case for and potential models for such a resource. This could provide opportunities for enhanced research studies of individuals and groups identified as being at-risk of mental illness, (eg looked-after children, adoption cohorts, children of parents with mental illness and children identified by the justice system), and help identify both risk and resilience factors and the relationship with other comorbidities. In addition to cohorts of children and adolescents, the resource would include well phenotyped adult cohorts thus providing the potential for a rich platform for understanding mental health aetiology, progression and response to intervention.

There is also a possibility to take a more strategic view of the UK's world-leading cohort resources to provide full coverage of the life-course. Targeted investment in key age groups that are under-represented, whether through new recruitment or new data sweeps in existing cohorts, might provide a cost effective route to linking existing resources thereby enhancing their research power.

Box 4 – Wearable devices and the internet

Recent technological advances in wearable devices and apps provide new opportunities to record activity and behaviour, enabling greater self-awareness of an individual's behaviour patterns. Remote monitoring, by researchers and clinicians, has the potential to bring new insight into mental health disorders, for example, recognising changes in behaviour can facilitate early detection and intervention and/or the refinement of therapies. Data collected from wearable devices and apps can also be linked to other data sets to enable research on a scale not previously possible. In partnership with the National Institutes of Health in the USA, the MRC has supported an international workshop on methods for the design, analysis, evaluation and implementation of digital interventions⁴⁶.

The MRC has a number of schemes to support the development of novel, translational mental health interventions, diagnostic tools and interventions and measures essential for mental health research, eg Developmental Pathway Funding Scheme, Confidence in Concept and the Methodology Panel.

The MRC has funded researchers at the University of Manchester to develop a mobile phone app called Clintouch (www.herc.ac.uk/research_project/clintouch) that provides individuals with psychosis the opportunity to monitor and manage their symptoms. The app asks users to respond to a series of questions, and alerts clinicians if responses indicate an increased risk of relapse. Building on the Clintouch software, the Actissist (research.bmh.manchester.ac.uk/actissist) mobile phone app, also developed at the University of Manchester, aims to prevent relapse of psychosis in people with schizophrenia through self-management of their symptoms with cognitive behavioural therapy (CBT). Actissist aims to facilitate early intervention in schizophrenia, as well as increase access to CBT.

45. Jones et al (2016), Phenotypic Manifestation of Genetic Risk for Schizophrenia During Adolescence in the General Population, *JAMA Psychiatry*, 73(3):221-8

46. Yardley et al, 2016, Theme: Digital Health: Leveraging New Technologies to Develop, Deploy, and Evaluate Behavior Change Interventions, *American Journal of Preventative Medicine*, 51, 5, 814-863.

Going global

MRC, often working with other funding partners, has a longstanding commitment to global health research and has made substantial contributions to the fight against infectious disease. However, the health needs of low and middle income countries (LMICs) are evolving and non-communicable diseases (NCDs) represent a major new health challenge (see box 5). In 2012, NCDs were responsible for 38 million deaths, ie 68% of all global deaths, a figure projected to rise to 52 million deaths by 2030⁴⁷. In 2010 the worldwide cost of mental disorders were estimated at \$2.5 trillion and in 2016 they were projected to rise to \$6 trillion annually by 2030⁴⁸. Therefore, the MRC plans to deliver a major new investment in global mental health to help us further understand the interactions between biology, environment, cognition and experiences during childhood and adolescence that could contribute to the development of mental illness.

Box 5 – mental health and sustainable development

Mental health and substance abuse are part of the United Nations' 2030 Agenda for Sustainable Development, which includes the commitment to the 'prevention and treatment of non-communicable diseases, including behavioural, developmental and neurological disorders, which constitute a major challenge for sustainable development'⁴⁹. Improving the mental health of the global population should be seen as a key outcome of sustainable development efforts; mental health is a lens to consider the real impact of broader sustainability efforts. Mental health is central to the achievement of the Sustainable Development Goals in health, education, gender equity, work, reducing inequalities and sustainable communities.

Creating a new investment in global mental health

Given the scale of need, global mental health science has to date, focussed on the implementation of interventions and design of health service delivery mechanisms. The MRC has funded this science through its joint global health trials, joint health systems research initiative and implementation research for adolescent health calls. In 2017 we launched a £2m call for the prevention and management of mental disorders as part of the Global Alliance for Chronic Diseases (www.gacd.org). However, there are further opportunities, drawing on the strengths of the UK research base, to understand how challenges to early brain development affect mental illness and cognition. Taking this research into a global context could provide a better understanding of the personal, social and economic impact of mental illness as a consequence of a range of external drivers/risk factors. These factors include: poor nutrition, infectious diseases, parasites, chronic inflammatory states, war, violence, migration, environmental determinants (air pollution, drought, flood, climate change, urbanisation), alcohol and substance abuse, parental and personal support interactions, and education or policy implementation. An improved understanding of how such challenges impact on mental health could inform the development of new interventions. Research on the global aetiology and epidemiology of mental health and illness should deliver new key insights that:

- directly address and influence the growing global burden of mental illness
- deliver fundamental insights into the epidemiology of mental illness, which are as relevant to high income countries as they are to low income countries, including presentation, prevalence and persistence of disorder and the scale of the resulting disability
- provide insight into the culturally-dependent and culturally-invariable components of mental illness
- deliver improvements to existing treatment approaches by increasing the understanding of their efficacy in different environments.

47. WHO, Global status report on noncommunicable diseases 2014

48. Trautmann, S., Rehm, J. and Wittchen, H.-U. (2016), The economic costs of mental disorders. EMBO reports, 17: 1245–1249.

49. United Nations, Transforming our World: The 2030 Agenda for Sustainable Development, 2015

Understanding the aetiology of healthy mental development and mental illness will require combined expertise from a number of fields in order to better understand the biological, social, cultural and environmental factors that influence mental and cognitive development both in the UK and in LMICs. Addressing these challenges will require: long-term commitment; a large, well-networked, multi-disciplinary team of researchers; foundation work; and the establishment of relevant methods and key baseline data. We will therefore create a new network of researchers from UK and LMIC centres of excellence in mental health research who will link with groups with expertise in child and cognitive development (including family and educational research). We anticipate that this will require a substantial financial commitment (of up to £20m) to support a large, multi-disciplinary team of researchers across a number of sites. We will continue to work with the other funders with an interest in this area to further consider how to take the area of global mental health research forward and in 2017 will hold a community building workshop to bring together researchers from a range of disciplines who are able to contribute to this initiative. We will also ensure that this new, major investment complements the global mental health funding being made available through the Wellcome Trust and National Institute for Health Research.

Prevention of mental illness

The MRC is leading the development of a new £40m-£50m UK Prevention Research Partnership, which will bring together a number of key UK funders. Its vision is the generation of new insights into sustainable and cost-effective ways of improving population health, and reducing health inequalities. This will be achieved via modifying common risk factors for non-communicable diseases and conditions, and addressing upstream and environmental determinants of the health of the public. The prevention of mental illness will be a key element of this investment. In addition to this partnership investment, the MRC will also support research that addresses the prevention of mental illness with a particular focus on early intervention through response mode-mechanisms.

Building capacity and support for the next generation of mental health researchers in the UK and for global mental health

In addition to training support via our Centres and Units, we will continue to work with the mental health research community and other funders to support the next generation of researchers in the field through workshops, networks and fellowships. This will be vital to support a new cadre of mental health researchers who will work to study aetiology across the lifecourse, develop new interventions and harness the power of informatics in the UK and/or LMIC settings. In addition to providing research training opportunities, we will develop a national research infrastructure that will provide a new flagship investment in mental health research in the UK and promote further opportunities and growth in the sector.

Mental health research capacity – workforce

It is often noted that the capacity of the UK mental health research workforce is sub-optimal. This could be one of the reasons for the relatively low numbers of applications submitted to the MRC in the field of mental health research. Increasing the workforce capacity is a gradual process and few significant changes have occurred in the past few years, although a number of funders are working towards this goal. We particularly welcome the work of the Royal College of Psychiatrists, the Wellcome Trust and Gatsby Foundation to develop a new neuroscience postgraduate core training curriculum for the UK⁵⁰. The MRC provides funding opportunities for individual researchers at key transition points in research careers (see box 6).

50. www.rcpsych.ac.uk/traininpsychiatry/corespecialtytraining/neuroscienceproject.aspx

The ambitions identified within our priority for lifelong mental health rely on the strengths of the child and adolescent mental health research community, which is relatively small and disparate. We will work with this community of clinical academic psychiatrists and psychologists to form a national research network with the aim of providing mentoring support and guidance for early career researchers.

The MRC Centres and Units with programmes in the field of mental health research will continue to be vital resources for the provision of training for clinical and non-clinical PhDs and post-doctoral researchers in the area. We currently support two centres with a focus on mental health research: the MRC Centre for Neuropsychiatric Genetics and Genomics at Cardiff University and the MRC Centre for Neurodevelopmental Disorders at King's College London. Over the course of their MRC-core funding, these two centres will have supported over 50 PhD posts in mental health research. These investments provide interdisciplinary environments to expose trainees to new skills, for example, mental health and developmental neurobiology, neuroimaging, genetics or bioinformatics. Centres and Units can also provide novel environments to attract expertise from aligned fields thereby creating new capability and capacity eg, by providing placements for clinical specialist trainees to provide them with research experience prior to the submission of an application for a PhD fellowship.

Box 6 – MRC training

Recent MRC reviews of clinical and non-clinical training across our remit have mapped career pathways and we have engaged in wider conversations on the shape of clinical training (www.mrc.ac.uk/skills-careers). The MRC continues to engage in the broad discussions on clinical training and we work with the Royal Colleges and societies to inspire and enable clinically-trained individuals to pursue an academic career. We have established a Clinical Training Research Fellowship (CRTF) in depression that is jointly funding by the Royal College of Psychiatrists and, working with the Medical Research Foundation, we have funded nine new CRTFs through the £2.2m Psychiatry: Scottish Training in Academic Research Programme (PsySTAR). In recognition of the need for extra capacity to support addiction research in the UK (particularly in academic psychiatry and clinical psychology), we fund the MRC Addiction Research Clinical (MARC) training programme. The programme aims to instil multidisciplinary approaches to training and relevant methodologies in addiction research, and to develop future leaders in the field (www.imperial.ac.uk/medicine/mrc-addiction-research-clinical-training/)

Our clinical training schemes are open to clinical psychologists, public health specialty trainees, allied health professionals and nurses as well as medics. For non-clinical careers we have simplified and increased the flexibility associated within our fellowship schemes, for example, by removing eligibility criteria based on years of post-doctoral experience. We have established clear expectations of the skills and experience that need to be demonstrated in order to secure a fellowship.



Building a new UK flagship investment in mental health research

In order to capitalise on recent developments in the field of mental health research, we recognise that new, focussed investment is needed to promote coordinated research efforts and help establish the next generation of research leaders. This would be in addition to the existing MRC Centres and individual Unit programmes that already provide valuable insight into mental illness. Therefore, we are committing to the establishment of a new national research platform for mental health (akin to MRC Dementias Platform UK) that will link the new opportunities in informatics research to cohorts and stratified medicine capabilities.

The newly formed Health Data Research UK, the MRC-led informatics institute, provides an ideal setting for research programmes and new analytical methodologies that will be able to link data to an integrated cohort-based resource in order to explore mental health and illness in new ways. In addition, such an infrastructure might help engage companies seeking novel approaches to investigate mental health and comorbidities in real world populations and in a way amenable to identifying well-defined population groups for future intervention studies. Such a platform will provide the basis for expanding capacity, partnerships and investment, and could pave the way for a new strategic MRC investment in mental health research in the longer term. Therefore, we will make available seed funding to support the necessary development of activities to potentiate the establishment of a major new strategic investment in mental health research in the medium to long term.

Conclusion

The MRC encourages high-quality applications for support into mental health and illness research. Awards will continue to be made according to scientific quality and importance to human health, from fundamental lab-based science to clinical trials. All our funding decisions will be based on supporting the very best science with potential for clinical impact.

Within this strategy we have identified areas with existing momentum where the MRC can stimulate key activities within the next five years. Through these actions we expect that there will be:

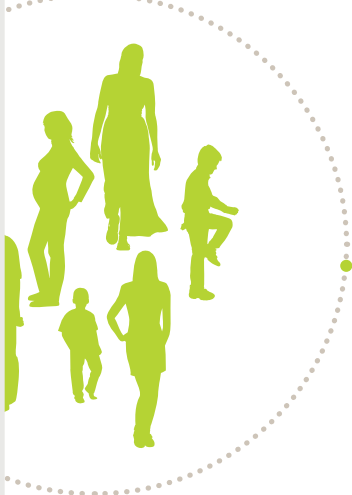
- enhanced understanding of the causes of mental illness
- improved linkage of biological mechanism with social and environmental drivers of mental health and illness
- routes to new interventions and preventative approaches
- better diagnosis and treatment development through stratified and precision medicine
- accelerated progress in the understanding of disorder mechanisms through better models and markers of disorder, and the use of big data and informatics
- increased understanding of the importance of co-morbidity between disorders and the complex interactions between physical and mental health
- enhanced capacity and capability of researchers.

We have a strong history of working in partnership and will continue to do so. We will seek partners for the activities articulated herein and participate in other appropriate strategic activities that emerge.

For more information about the MRC's work in mental health research and to meet some of our researchers, visit www.mrc.ac.uk/mentalhealth

To find out more about the MRC's Neurosciences and Mental Health Board, visit www.mrc.ac.uk/nmhb





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