MRC Medical Research Council

Review of Mental Health Research

Report of the Strategic Review Group 2010

A review undertaken by the MRC on behalf of OSCHR partners

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Annexes

1. Executive Summary

Poor mental health is common and disabling, affecting 16.7 million people in the UK at any one time and accounting for 15 per cent of all the disability due to disease. It is estimated to cost at least £77 billion annually in England alone and severe forms of mental illness are associated with social exclusion and deprivation. Mental health problems frequently start in childhood and persist throughout the life course, affecting people at crucial stages of life: in the home, during school and through working life into old age.

There are a number of challenges to research into mental illness and wellbeing, including unravelling the complexity of multiple genetic, social and environmental influences in a way that is able to inform effective, preventive, therapeutic and rehabilitative strategies. However, the progress of research into understanding the factors that contribute to mental illness has accelerated in recent years. This review has concluded that the UK is currently well-placed to be at the forefront of advances in our basic understanding of mental ill health; in developing new options for prevention, early detection and treatments; in assessing the effectiveness of treatment and preventive strategies and developing systematic guidelines for treatment and patient management; and in modelling the best ways to introduce new care options into health systems.

The UK's existing strengths include:

- research in the quantitative and molecular genetic, developmental, biological and social basis of mental illness;
- a very good track record of developing new psychological and social treatments, and new models of service provision;
- the unique potential for large-scale clinical studies provided by the strong UK base in population science, the NHS and the Mental Health Research Networks;
- the alliance of the Medical Research Council (MRC), National Institute for Health Research (NIHR) and devolved administrations in translating research to patient benefit and in building upon strategic developments brought in by the Office for Strategic Coordination of Health Research (OSCHR) partners in recent years.

Drawing on these strengths, we propose that the UK's strategic ambitions should be to:

1. prevent mental disorder and disability and promote wellbeing, based on better understanding of causes, risk levels and new approaches to early preventive interventions;
2. accelerate research and development aimed at providing new, more effective treatments for mental illness, and implement them more rapidly.

1.1 Purpose of review

The review was undertaken by the MRC to advise OSCHR and its funding partners on UK research opportunities and tractable priorities for improving mental health. The aim was to produce a strategic framework outlining investment opportunities in mental health research in the UK over the short to medium term (two to seven years), addressing the biological, psychosocial and public health needs.

1.2 Structure and remit of the review

The review was structured around four themes:

1. Severe mental illness (primarily psychosis);
2. Anxiety and depression (bipolar disorder was included in this theme);
3. Neurodevelopmental, learning and intellectual disabilities;
4. Pathways to mental wellbeing.

The review was guided by a Strategic Review Group chaired by Professor Christopher Kennard, and involving scientists with broad expertise across the spectrum of mental health research (membership at Annex A).

The review excluded explicit consideration of two topics with major impact on mental health, namely dementia and addiction/substance misuse. This decision was taken since the MRC had ongoing research initiatives in these areas, informed by an MRC strategic review of neurodegeneration and a major workshop and consultation on addiction and substance misuse, both undertaken in 2008.

1.3 Opportunities for UK mental health research

This report identifies research strengths that can be utilised to advance mental health research by embracing current scientific opportunities. It recommends that the major strategic aims over the short to medium term should be:

1.3.1 Promotion of preventive strategies

a. understanding the biological and social life-course determinants of mental illness and wellbeing, primarily by exploiting the UK's research strengths in genetics, neuropsychology, brain imaging and population sciences;

b. developing primary preventive strategies based on early detection of high risk states;

c. identifying the cognitive and neurobiological basis of wellbeing and healthy development;

d. promoting good mental health at key life stages particularly in childhood and adolescence.

1.3.2 Developing therapy

a. exploiting established UK strengths to increase innovation in mental health research, for example by:

   i) taking a cross-symptom approach: that is, understanding the psychological basis of aberrant processes such as inattention, impulsivity and aggression that may underpin maladaptive behaviour in different clinically-diagnosed psychiatric disorders;

   ii) exploiting new molecular genetic methods and UK expertise in developmental neuroscience;

b. identifying individuals at risk in order to target intervention by, for example, using stratified medicine to identify subgroups with common pathogenesis that may be specifically responsive to existing and new drug or psychological treatments;

c. developing new treatments by promoting experimental medicine and phase I clinical studies to rapidly detect the efficacy of novel therapeutics, for example, by encouraging collaboration between academia and industry in early drug development;

d. promoting recovery, including cognitive remediation and social rehabilitation;

e. evaluating whether improvements in management and service delivery can be made that benefit outcomes;

f. increasing the participation of patients, service users and carers in research design and in deciding optimal research outcomes.

The longer-term vision is to develop and evaluate ways of preventing the onset of mental illness through a better understanding of its biological and social causes. In the short-term we need to develop and improve existing treatments and target interventions based on an individual's vulnerability and resilience. Progress toward all these aims needs to be accelerated while a number of obstacles should be addressed, as outlined below.

1.4 Obstacles to progress

1.4.1 Capacity of UK mental health research

It is well established that, worldwide, the scale of mental health research is not proportionate to the burden of disease, which according to the World Health Organization accounts for over 15 per cent of the health burden in the developed world (see section 2.5). While research effort should reflect the likely potential for achievable benefit rather than simply the desirability of solving a problem, the evidence is that past investment in mental health has provided significant economic benefit[1] and that the current scientific potential for substantial advance is high.

Data supplied by major UK public funders (see Annex D) confirmed the disparity between disease burden and scale of research, which most probably reflects low research capacity coupled to the perception that the research questions in this field have been relatively intractable. Building enhanced research capacity to exploit the scientific opportunities highlighted within this review must be a primary goal of any investment strategy for mental health research.

1.4.2 Stigma

Stigma has pervasive effects. The most obvious include fear of the consequences of revealing mental illness to employers, friends and family, the perceived stigma attached to seeking treatment and unhelpful public and media portrayals of mental illness. Moreover, it may contribute to the lack of charitable donation for mental health research. Strategies to address stigma are therefore required, but there is an important role for improved research knowledge per se in reducing its impact.

1.4.3 Access to data

Some key areas for future research will be dependent on improved access to large numbers of patients, or samples and data, to overcome the inherent problems of multiple risk factors, overlapping phenotypes, small treatment effect size and co-morbidity. This is not yet well enough supported in the UK.

1 *Medical Research: What's it worth? Estimating the economic benefits from medical research in the UK* http://www.wellcome.ac.uk/About-us/Publications/Reports/Biomedical-science/WTX052113.htm

1.5 Recommended actions

The UK is better placed than most other countries to lead and accelerate the development and implementation of preventive approaches and of new treatments. Major opportunities would be provided through better integrating the excellent UK base in neuroscience, social science and mental health research with the potential of the NHS to conduct large-scale studies and for industry to develop novel therapies. When that has been progressed, the UK would be exceptionally well positioned to assess both the effectiveness of treatment and to determine the best ways of implementing evidence-based innovations into the healthcare system.

Our vision is for research productivity, capacity and funding to improve alongside each other. Short and medium term steps to drive improvements should be to:

a. strengthen research into population-based research through:
    i) the development of an NHS-based large-scale dataset and repository of biological and social factors for mental health research;
    ii) adding value to existing or planned cohorts;
b. promote experimental medicine and research into new treatments;
c. increase research capacity and innovation by:
    i) exploiting the key scientific opportunities in this field and expanding the foundations for new treatments and prevention through enhancing support for multidisciplinary research groups;
    ii) enhancing research training and increasing critical mass by adding incentive for research careers in mental health research and encouraging broader, structured training programmes across all relevant disciplines and careers;
d. working 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.

2. Introduction and background to the review

2.1 Purpose

The review was led by the Medical Research Council (MRC) to advise the major public funders and the Office for Strategic Coordination of Health Research (OSCHR) on research opportunities and tractable priorities for improving mental health. The focus was on recommending a strategic framework for investment in mental health research over the short to medium term (two to seven years).

2.2 Structure and remit of the review

The review was conducted by a Mental Health Strategy Steering Group chaired by Professor Christopher Kennard, chair of the MRC Neuroscience and Mental Health Board (NMHB). The Steering Group membership included scientists with broad expertise across the spectrum of mental health research (membership at Annex A). Additional members were co-opted as needed. The recommendations emanating from the Steering Group were informed by broad consultation through a series of workshops and an opinion survey.

The review was structured around four themes. As well as considering illness, the review considered wellness or wellbeing. The themes for this review were:

1. Severe mental illness (primarily psychosis);
2. Anxiety and depression (bipolar disorder was included in this theme);
3. Neurodevelopmental, learning and intellectual disabilities;
4. Pathways to mental wellbeing.

The review excluded dementia as the MRC had published a strategic review of neurodegeneration in 2008 and was currently implementing its recommendations. It also excluded addiction and substance misuse which, at the time of this review, was covered by an ongoing MRC-led strategic initiative between OSCHR partners and the Economic and Social Research Council (ESRC).

2.3 Process of the review

The review scoped the views of experts and opinion leaders in the field within the boundaries of the four themes listed above. Members of the Strategy Steering Group chaired workshops in each of the four areas, which were attended by academics, clinicians, and representatives of Government departments and charities working in the field of mental health. Workshop chairs summarised the outcomes by completing a structured template and circulating it to the workshop attendees for further comment. This provided the foundation for the final Sub-group reports, provided at Annex B.

In addition to the workshops, a questionnaire was circulated to canvass opinion from key research leaders and organisations. The outcomes of this consultation (see Annex C) informed the review and have been considered and incorporated into this report.

Analysis of the funding portfolios of major funding organisations of mental health research in the UK was also carried out (see Annex D).

2.4 Recent reviews of mental health

There have been a number of recent substantive reviews into mental health that were influential in producing a starting point for this review and for informing its recommendations. These included the Government's 2005 Foresight and 2008 Academy of Medical Sciences reports into brain science and addiction, and the 2009 Foresight report on mental capital and wellbeing. Further detail is provided at Annex E.

2.5 The burden of poor mental health

2.5.1 Prevalence of mental illness

Mental ill health is a major burden for individuals and health and social care services. Estimates suggest that more than one in four adult Europeans experience a mental health problem in any one year[2]. At least one in six people suffer from severe anxiety or depressive disorders at any one time[3] and the most frequent cause of death in young men is suicide[4]. The overall estimate of the prevalence of all mental disorders in the UK is that 16.7 million people suffer from a disorder each year[5].

2 EU Green Paper (2005) *Improving the mental health of the population: Towards a strategy on mental health in the European Union* section 3 and Annex 2

3 Sainsbury Centre for Mental Health (2003) *Policy paper 3 Economic and social costs of mental illness*, London SCMH.

4 Singleton et al (2001) *Psychiatric Morbidity among people living in private households in 2000*. London The Stationary Office Department of Health Safety First Five year report of the confidential inquiry into suicide and homicide by people with mental illness, London Department of Health 2001

5 Hans-Ulrich Wittchen and Frank Jacobi (2005) *Size and burden of mental disorders in Europe: a critical appraisal of 27 studies*, *European Neuropsychopharmacology*, Volume 15, Issue 4, August 2005, Pages 357-376

As with many other conditions there is a social gradient associated with mental health problems[6].

2.5.2 Economic costs

The costs of mental health on health and productivity throughout the world has long been underestimated. Data developed by the large-scale *Global Burden of Disease study*[7] conducted by the World Health Organization (WHO), the World Bank and Harvard University revealed that mental illness, including suicide, accounts for over 15 per cent of the burden of disease in established market economies.

This level of morbidity places a heavy burden on health and social services. For instance, general practitioners spend more than a third of their time on mental health issues[8]. The Sainsbury Centre for Mental Health estimated that the annual health, social and economic cost of mental ill health to England is £77 billion each year[9]. Mental ill health is also associated with considerable social exclusion and deprivation. A report from the Social Exclusion Unit on Mental Health showed that the loss of earnings is in the region of £23bn and state benefits account for another £9.5bn (*14th June 2004; Office of the Deputy Prime Minister*). A mental health problem is now also the most common reason for someone claiming Incapacity Benefit.

2.5.3 Childhood and adolescent mental health problems

Nearly 10 per cent of children aged five to 16 years have a clinically diagnosable mental health problem[10] and there is a high degree of persistence of these problems into adult life. Evidence already suggests that these problems have a serious impact on life chances[11] and life expectancy[12]. Poor childhood and adolescent mental health is associated with high economic cost in terms of service provision or social problems such as crime. The annual cost of autism to the UK is just under £28bn[13]. People with intellectual disabilities have particularly high rates of mental ill health and the costs of providing services to these special groups are half as much again as for all of the rest of the general population, with added health and economic consequences related to their family carers. It is estimated that 5 per cent of children have a conduct disorder in the UK and that these children go on to commit 30 per cent of crime, at a cost exceeding £22bn a year.

The long term consequences of childhood and adolescent mental health problems have been studied in the UK using three of the national birth cohorts[14]. This showed conduct problems in childhood were strongly associated with a wide range of adverse outcomes in adult life, including a higher likelihood of lacking educational qualifications, of experiencing chronic economic inactivity, and of criminality in early adulthood. Indeed a diagnosis of childhood conduct disorder is required for the adult diagnosis of antisocial personality disorder, a poorly understood disorder that is common in prison populations and associated with very considerable social and economic burden.

Psychopathy is another antisocial disorder which has its origins in childhood but it is much rarer than antisocial personality/conduct disorder. It is characterised by callous unemotional traits which may originate from a specific deficit in brain mechanisms of empathy. Studies in UK schoolchildren suggest it may be strongly heritable.

2.5.4 Scale of mental health research relative to the burden of disease

A subject raised by many participants in this review was how the scale of mental health research – measured though the scale of annual public and charitable funding – is low relative to the burden of disease. This has been highlighted in the UK Clinical Research Collaboration (UKCRC) Health Research Analysis[15] and in a report published in the British Medical Journal in 2006. The latter highlighted the difference between research funding and burden of disease (determined by disability-adjusted life years) and concluded that funding for mental health research, along with respiratory and gastrointestinal research, lags significantly behind other disorder-based research (Figure 1).

6 Asthana S et al, (2004) *The demographic and social class basis of inequality in self reported morbidity: an exploration using the Health Survey for England.* Epidemiology and Community Health, 58(4), pages 303-307 (http://eprints.soton.ac.uk/55396/)

7 WHO (2008) *The global burden of disease: 2004 update.* Accessed 30 December 2009 from http://www.who.int/healthinfo/global_burden_disease/GBD_report_2004update_part4.pdf

8 House of Lords April 2007 *"Improving the mental health of the population": Can the European Union help?* The Stationery Office

9 Sainsbury Centre for Mental Health (2003) *Policy paper 3 Economic and social costs of mental illness* London SCMH.

10 Green, H., McGinnity, A., Meltzer, H., Ford, T. & Goodman, R. (2005) *Mental health of children and young people in Great Britain, 2004.* Crown Copyright. Basingstoke, Hampshire: Palgrave Macmillan.

11 Fergusson, D., Horwood, L. & Ridder, E. (2005) *Show me the child at seven: the consequences of conduct problems in childhood for psychosocial functioning in adulthood. Journal of Child Psychologyand Psychiatry* 46: 837-849.

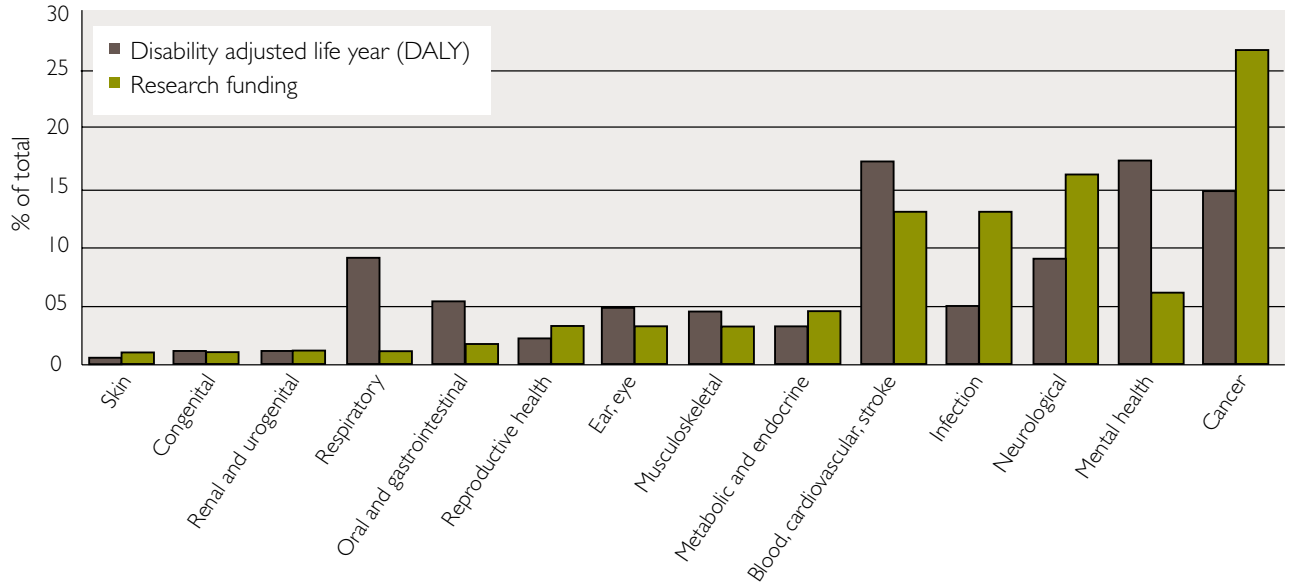
12 Jokela, M., Ferrie, J. & Kivimaki, M. (2009) *Childhood problem behaviours and death by midlife: the British National Child Development Study. Journal of the American Academy of Child and Adolescent Psychiatry* 48: 1-6.

13 The Economic Consequences of Autism in the UK report was commissioned by the Foundation for People with Learning Disabilities and funded by the Shirley Foundation. The research was carried out by Professor Martin Knapp, Renée Romeo and Jennifer Beecham of the King's College London, Institute of Psychiatry.

14 Sainsbury Centre for Mental Health (2009) *Childhood mental health and life chances in post-war Britain: Insights from three national birth cohort studies*: London SCMH.

15 http://www.ukcrc.org/researchcoordination/healthresearchanalysis/

Figure 1: Funding for UK research in 2004/05 by disease area and disability adjusted life year (DALY) (Kingdon D, 2006. BMJ, 332, p1510)



3. Analysis of funders' research portfolios

3.1 Total investment and capacity

Mental health research in the UK is funded by Government Departments, the research councils, charities and industry. The two major public funders of mental health research in the UK are the MRC and the NIHR, while two other OSCHR members, the Scottish Government (CSO) and the Welsh Assembly (WORD), have active programmes in this area. Analyses of the research portfolios of these organisations showed that OSCHR partners spent about 7 per cent (£91.5m) of their research budget on mental health research in 2007/08 (see Annex D1).

Both the NIHR and the MRC have a number of large strategic investments in mental health research. The MRC funds three centres in partnership with universities: in Cambridge, at the Institute of Psychiatry (IoP), Kings College London, and at Cardiff University. Two MRC units, in Cambridge and Glasgow, have long term programmes directed towards mental health research. The MRC also provides support to 30 UK-based population cohorts of which six focus on mental health (total investment value about £2.3m) and 14 programme grants for research on mental illness. OSCHR partners support Mental Health Research Networks and the NIHR provides support for clinical infrastructure, a Biomedical Research Centre at the IoP and a number of large-scale phase III clinical trials looking at the effectiveness of interventions to reduce mental illness in an NHS setting. The NIHR also supports 27 programme grants that have a mental health component – mental health has fared well in the short time that the NHIR programme scheme has been in existence and represented 26 per cent of this portfolio at the time of this review. Further detail of these investments is provided at Annex D3.

There is no major UK charity dedicated to funding research into mental illness, although the Wellcome Trust spends approximately 5 per cent of its total budget of £600m a year in this area.

3.2 Success rates in applications for funding of mental health research

MRC and NIHR research funding is for the most part allocated in 'response-mode', in open competition with applications across the full spectrum of biomedical research. A perception exists in the mental health research community that applications for studies addressing mental health may do less well through unintended biases in the peer review system, which may account for part of the relative underfunding of this area in relation to its burden of disease. To investigate this possibility, the award rates (by value and number) were measured for applications for mental health research to the MRC Neuroscience and Mental Health Board over a period of five years (15 board meetings). The success rate for mental health applications was not found to be significantly different to the award rate for all applications. This was also found to be true for the recent MRC schemes addressing translational gaps (eg biomarkers and methodology) and for MRC training fellowships schemes. In both of these cases the numbers of applications for mental health research were low, but the award rate was comparable to the award rates for all fields. The full analysis is provided at Annex D4.

3.3 Balance of portfolio

The analysis of the UKCRC Research Activities across the MRC and NIHR portfolios of mental health research indicated that grant support was strongest in the areas of underpinning and aetiological research and for research analysing the clinical effectiveness of interventions (Annex D2). Research into prevention had by far the lowest level of investment, though this is common for other disease areas, with the exception of cancer.

The titles of the project and programme grants awarded by the MRC and the NIHR indicated that research was being undertaken across the full spectrum of psychiatric disorders, but that there was an emphasis on severe depression and psychosis. There was less funding for research into anxiety, moderate or mild depression, bipolar disorder and adolescent mental health.

4. Strengths of UK research relevant to mental health

This chapter sets out the strengths in UK mental health research and related disciplines on which opportunities might be based. A few select examples are highlighted where the UK has made important contributions, though it should be recognised that there have been many other important contributions to mental health research from UK-based researchers over the past 10 years which have not been mentioned.

4.1 Genetics and Genomics

Genetics at the whole genome level increasingly involves a high level of international collaboration and the UK is internationally recognised as a leading contributor in this field. UK-based groups have made important contributions to understanding the genetic aetiology and risk in bipolar disorder, schizophrenia, depression and autism (see Major UK contributions example 1).

Mental illness is highly heritable, and recent research shows that psychiatric disorders are underpinned by a range of genetic effect sizes, allele frequencies and genetic mechanisms. For example, in schizophrenia it seems likely that common variants in numerous genes will individually account for a very small percentage of genetic risk, while collectively accounting for a substantial part of the genetic risk. Some of the strongly implicated genes are shared between several clinically diagnosed psychiatric disorders (for example, schizophrenia, bipolar disorder and autism), highlighting the need to seek the influence of genes across traditional diagnostic boundaries, and pointing to the involvement of common biological pathways.

Significant recent progress has been made in understanding the genetic basis of autism spectrum disorders. The international Autism Genome Project, supported by the MRC in partnership with Autism Speaks and the Irish Health Research Board, is among several studies that have shown that rare copy number variants (CNVs) affecting specific genes carry a high risk for rare sporadic cases of autism. Each variant may prove to be an infrequent cause of mental illness but they are often shared with a different clinically-diagnosed psychiatric disorder.

In the future, genetics will open up new possibilities for targeted treatment based on an individual's genetic 'make-up' and through identifying previously unknown molecular pathways to illness. Understanding the role of gene–environment interaction will also be important and may offer opportunities for prevention through highlighting environmental factors that moderate genetic vulnerabilities.

Epigenetics is increasingly seen as an important contributor to mental illness and may provide a mechanism through which environmental effects can be mediated. Epigenetic disruption is potentially reversible and is thus a potential target for pharmacological intervention (see Major UK contributions example 2). This field is new and there is some controversy about the prospects, but the UK has a strong presence in the basic biology in this area.

4.2 Developmental biology

Since many risk alleles identified for psychiatric disorders are known to exhibit an effect during development, the discipline of 'neurodevelopmental biology' has a potentially significant role to play in the understanding of the aetiology of mental illness. The UK has several internationally recognised research centres continuing to make important contributions to fundamental research on the mechanisms of development of the central nervous system. While this is a UK strength, it has not yet been fully exploited in the mental health area, although there have been a few exciting findings (see Major UK contributions example 2).

Major UK contributions (example 1):

UK-led molecular genetic studies in psychiatric illness

The DISC1 gene was originally identified in the UK (*Millar JK et al, 2000. Hum Mol Genet, 9(9), pp1415-1423*) in a Scottish family with multiple individuals affected by schizophrenia, bipolar disorder or unipolar disorder. DISC1 is now firmly established as an important risk factor in these diseases and is a focus of much international research activity.

The largest genome-wide association study (GWAS) of bipolar disorder came from a collaboration of genetics researchers led from the UK. The study, published in the journal Nature in 2007, supported the notion that many genetic variants each contribute a little to the risk of developing bipolar disorder (*Wellcome Trust Case Control Consortium, 2007. Nature, 477(7145), pp661-678*). Follow-up studies, published in Nature Genetics in 2008, identified specific gene variants influencing the risk of bipolar disorder (CACNA1C and ANK3) (*Ferreira MA et al. 2008. Nature Genet, 40(9)*, pp1056-1058) and schizophrenia (ZNF804A) (*O'Donovan MC et al, 2008. Nature Genet, 40(9), pp1053-1055*).

Major UK contributions (example 2):

Reversal of Neurological Defects in a Mouse Model of Rett Syndrome

Rett syndrome is a severe autism-like disorder caused by mosaic expression of mutated X-linked MECP2 in neurons. Using a mouse model, research based in the UK has shown striking phenotypic reversal of advanced neurological symptoms in both immature and mature adult animals (*Guy J et al, 2007. Science, 315(5815), pp. 1143–1147*). Mice born with the MECP2 gene inactivated developed disease symptoms such as breathing and mobility problems. When the gene was activated, the affected mice recovered and became indistinguishable from their healthy counterparts within a few weeks.

This raises the prospect that a severe brain disorder, that was thought to be incurable, could be reversed.

Major UK contributions (example 3):

The role of the brain in negative emotion processing in depression.

UK research has shown that abnormalities in emotional processing by the brain may underlie depressive disorder. Antidepressants reverse these changes and this effect occurs very quickly after taking them – before clinical improvement is observable. Emotional processing may therefore be useful as a sensitive way of detecting if a new drug is likely to be an effective antidepressant as well as providing an important clue into the understanding the causes of the disorder.

(*Sharot T et al, 2007. Nature, 450(7166), pp102-105*) and (*Leppanen JM, 2006. Curr Opin Psychiatry, 19(1), pp34-39*).

Applying UK expertise in neural plasticity during development may prove fruitful since changes in brain connectivity during development appear to be linked to certain disorders, for example, the period of brain overgrowth in autism. Neural plasticity is also clearly relevant to memory, which is lost or altered in some psychiatric syndromes and during normal cognitive decline.

New research opportunities also exist through the potential to use induced pluripotent stem cell technology to model the genetic processes underlying psychiatric disease. Skin biopsies could be used to derive neuronal cells from patients with mental illness, allowing the functional implication of genetic variation in humans to be studied more directly.

4.3 Neural systems and translational neurobiology

The phrase 'neural systems and translational neurobiology' is used here to describe research in animal models, often combined with neuropsychological and imaging studies in humans. This research identifies neural system functions relevant to psychiatric disorder that should inform on aetiology and provide clues to novel approaches to treatment. This research has high potential for better phenotyping and the development of clinically useful biomarkers which can be used in large scale genetic and epidemiological studies, experimental and stratified medicine and clinical trials. The UK has significant strength across this area of research (see Major UK contributions – example 3).

While animal models can never model mental health disorders in their entirety, they can provide exquisite insights into specific traits. Human experimental models can also facilitate back-translation to help understand the fundamental basis of pharmacological action and therefore improve drug targeting and efficacy. The translation to humans of psychological concepts developed in animals has been greatly facilitated by modern methods of in vivo imaging of regional brain function.

Leading UK neuroimaging centres have established the neuronal basis of cognitive processes such as memory and emotion. The UK has been at the forefront of using functional magnetic resonance imaging (fMRI) to visualise neural systems as they process cognitive and emotional inputs. This work is now being extended to help identify the anatomical correlates when such processes are disturbed in psychiatric disorders.

MRI studies in the UK have also been an important component of new insights in understanding the specifically human processes of social cognition and empathy – the ability to understand other people's intentions and to experience their emotions – which underpin normal social behaviour. Dysfunction in these systems may be key to the origins of the psychotic symptoms and social deficits of schizophrenia, to the development of autism and to antisocial behaviour and aggression in antisocial personality disorder and psychopathy.

Used in conjunction with structural imaging or fMRI, positron emission tomography (PET) can be very powerful in providing converging evidence to test key hypotheses. PET imaging, particularly with specific ligands, is a UK strength that is informing many aspects of biological psychiatry and addiction biology, such as the definition

of traits or endophenotypes. For example, the important evidence for specific increases in dopamine release in the caudate nucleus in early schizophrenia could not have been revealed by any other current technology.

4.4 Neuropsychology and psychological and behavioural therapies

Cognitive neuropsychology is strong in the UK. A number of significant contributions have been made to the cognitive assessment of brain-damaged and psychiatric patients, as well as the evaluation of drug effectiveness. The computerised CANTAB neuropsychological battery was originally developed in the UK and is now used worldwide for these purposes. An understanding of cognitive deficits and how they might be ameliorated also relies upon a fuller understanding of how such processes are mediated in normal subjects, which is the focus of significant investment in the UK.

Over the past three decades, scientists in the UK have developed and evaluated many of the now standard psychological therapies for mental health disorders. Most of these have been based on Cognitive Behavioural Therapy (CBT), originally developed in the US in the early 1950s, but now a UK research strength. CBT is the main psychological therapy used within the NHS because it has demonstrable efficacy in mental disorders and it has been thoroughly tested for its effectiveness in clinical trials. Tailored CBT approaches for both anxiety disorder and psychosis have been developed in the UK and are distinct from the therapy provided to those suffering from depression. The UK is also leading the development of CBT-based psychological interventions for use in persons with intellectual disabilities, who are not able to use interventions designed for more verbally sophisticated individuals.

4.5 Childhood mental health and neurodevelopmental disorders

Research into learning and intellectual disabilities, Attention Deficit Hyperactivity Disorder (ADHD) and conduct disorder is a UK strength in relative terms. While research activity is limited by the challenges in this area (see section 6.6) there are pockets of research strength in the UK and relatively little ongoing research worldwide. UK-based work includes the development and evaluation of clinical interventions for affective disorders, research into rare disorders such as Prader-Willi syndrome, prevalence work on mental ill health in adults with intellectual disabilities and treatment of aggressive behaviour. The MRC also supports work into the developmental pathways to aggression and conduct disorders.

Research into autism spectrum disorders has been encouraged by the MRC since 2001 and as a consequence there is some strength in an overall small portfolio (around £2m investment annually). This includes the first international molecular genetics studies of autism (the Autism Genome Project), research into the cognitive developmental psychology of autism and the establishment of one of the largest phase III clinical trials of parent-based therapy.

The UK's research capability in the problem behaviours and forensic needs of people with intellectual disabilities has developed in part through the provision of a specialist intellectual disabilities health service across the UK. This provides expertise in mental ill health and problem behaviours, particularly for adults. This does not exist anywhere else in the world.

4.6 Epidemiology

The UK has a unique and internationally renowned collection of cohorts, including birth cohorts spanning over 60 years. Longitudinal studies based on these studies in the UK have produced a series of important findings which include, for example, the risks of smoking in pregnancy, childhood asthma and the link with parental occupation, exposure to allergens, the origins and consequences of child poverty, the long term impacts of education and training and that there is a social gradient underlying predisposition to premature death and disease. The strength of UK population based studies is recognised worldwide and the UK has accumulated a wealth of rich and remarkable data resources which continue to be the foundation for innovative population based research on health, wellbeing and socioeconomics.

The UK continues to make a significant investment in high quality, long-term cohorts. The MRC investment alone amounts to around £14 million a year. The MRC funded a recent cohort initiative with OSCHR partners, and the ESRC also provides significant support in this area.

Evidence has already emerged identifying early predictors of mental ill health from UK-based research. This has come from cohorts set up to address specific questions in mental health, for example, the Twins Early Development Study (see Major UK contributions: example 4), the Dunedin Cohort in New Zealand and many others that were not set up specifically for mental health, for example, the 1946, 1958 and 1970 birth cohorts, the Avon Longitudinal Study of Parents and Children (ALSPAC) and Generation Scotland. The MRC and the NIHR Mental Health Research Network have established a registry of cohorts in the UK and around the world that collect data relevant to mental health research (http://www.mhrn.info/index/about/mrc-mhrn-cohorts-database.html).

Major UK contributions (example 4):

The Twins Early Development Study (TEDS)
https://www.teds.ac.uk/home_out.asp

TEDS focuses on the early development of the three common psychological problems in childhood: communication disorders including autism, mild mental impairment and behaviour problems. The TEDS twins were identified from birth records of twins born in the UK in 1994-96 and more than 15,000 pairs of twins have been enrolled. At seven and nine years, children are assessed for language and cognitive development and behaviour problems; teachers also assess behaviour problems as well as academic achievement. One set of findings is that the same genes largely contribute to both language and cognitive problems.

TEDS is used by many researchers and has been a platform for a wide range of published studies.

Population based and clinical mental health research in the UK has the unique advantage that the NHS is the single provider of health care. The general population coverage also means that there is little ascertainment bias. Nearly all patients with severe and enduring mental illness are in contact with secondary care services. This has facilitated the development of large electronic databases such as Psygrid and the related NeuroPsygrid which provide a health informatic resource containing phenotypic and treatment data for patients with psychosis (see Annex D).

4.7 Clinical Trials

Although there are obstacles to evidence-based practice in mental health as set out in section 6.4, the UK has strength in conducting the full range of clinical trials in psychiatric disorders from early evaluation of efficacy and mechanism to large-scale phase III trials with economic evaluation. The early phase work is increasingly leading to partnerships with industry where the methodological advances are recognised as providing a way of increasing the speed and efficiency with which new agents can be evaluated. The inclusion of evidence from clinical trials and other well designed studies into National Institute of Health and Clinical Excellence (NICE) guidelines and clinical and research governance, increasingly ensures that patients receive the best and increasingly standardised assessment, care, treatment and management.

Larger scale UK trials have provided definitive evidence on the comparative efficacy of existing therapies for bipolar disorder and schizophrenia which have informed global decisions on treatments. UK-led studies have also shown that individual placement and support helps people with severe mental illness gain open employment (see Major UK contributions – example 5).

The development of the Mental Health Research Network (MHRN) and Comprehensive Clinical Research Network (CCRN) has increased the capacity to conduct pragmatic trials in NHS settings. MHRN has the potential to help the UK improve access to patient populations so that the studies are better powered and provide outcomes that are generalisable to patients and service users.

In addition to MHRN and CCRN, Scotland and Wales have their own networks (SMHRN and CRC Cymru).

Major UK contributions (example 5):

UK-led Clinical trials

Conducting large scale clinical trials in mental health is a challenge, in part because of the difficulty of recruiting and retaining sufficient patients across multiple sites for the duration of a long-term study. Nevertheless, the UK had notable successes in delivering multi-site trials and two examples are shown below.

BALANCE

BALANCE was a UK-based international multicentre randomised controlled trial (RCT) following 330 patients for 24 months which showed that combination therapy with lithium plus valproate was clearly superior to valproate monotherapy in preventing relapse of bipolar disorder (*The Lancet online 23 December 2009*).

EQOLISE

EQOLISE was a UK-led RCT including 312 patients across six European centres. It showed that individual placement and support helps people with severe mental illness gain open employment (*Burns T et al, 2007. The Lancet, 370(9593), pp1146-1152*).

4.8 Health Services Research

The UK has considerable expertise in modelling improvements in health services and systems, research synthesis, creation of clinical guidelines for managing patients and the organisation of health care providers and purchasers. However, there are fewer researchers focusing on services for mental health. Nevertheless, the UK seems well placed to develop care models, test packages of treatments around new interventions and analyse treatment outcomes in this area.

The current focus of research in this area mostly relates to schizophrenia and relatively little has been done on care organisation and delivery for patients with mood and anxiety disorders.

Health Services Research for people with intellectual disabilities is led by work emanating from the UK. For example, research to understand support staff's reactions to aggressive people with intellectual disabilities has informed ways of helping staff build and sustain relationships with such challenging individuals and has led to developments in staff training.

5. Opportunities for UK mental health research

Insights into the neurobiology and social scientific basis of mental illness promise to lead to new evidence-driven approaches to prevention, detection and treatment of mental ill health. For example, there will be opportunities to develop and evaluate population-based approaches based on knowledge about the aetiology of poor mental health and how life-course factors affect mental illness. As new biological, cognitive and social markers of risk or early illness become available, the development of preventive strategies, applied at the time of earliest detection of high-risk mental state, becomes a feasible option. The UK could lead in this area by exploiting its unique patient care infrastructure.

Opportunities were identified by the review group as set out in the following section, although it should be noted that these often have relevance and complementarity across the various subsections in this chapter.

5.1 Preventive strategies

The ultimate objective for a public health strategy in this area has to be the prevention of mental ill health. However, on current knowledge this has to be a long-term aim. Nevertheless, distinct opportunities exist in the short term to accelerate research towards this goal as set out in the following sections.

5.1.1 Understanding the life-course determinants of mental illness and wellbeing

A population-based approach to the life-course determinants of mental illness is essential to understanding its aetiology and the factors that cause relapse and maintain chronic illness. Identifying and quantifying the lifetime effects of childhood and adolescent mental health problems is an important public health goal. Knowing the adverse environmental influences on brain and social development will help inform the development and testing of preventive strategies to reduce medical and social problems (such as violence, disorder, substance misuse and family breakdown). Early life adversity increases the risk of most adult disorders such as depression, antisocial disorders and to some extent the psychoses. More longitudinal work on childhood would plug gaps in our knowledge regarding how risk exerts its effects in early life and the differences in vulnerability between individuals during ageing.

Psychiatric disorders are both genetic and environmental in origin, often in equal measure. The heritability (degree of genetic influence) of serious mental illnesses such as bipolar disorder and schizophrenia can be high, for example up to 70 per cent for severe psychiatric disorders. However, in all cases of mental illness, genetic factors are likely to be influenced by an interplay of genetic and environmental factors as the brain develops. Identifying the full extent of these genetic and environmental influences and their interaction must proceed hand-in-hand if real progress is to be made. This in turn will require strong links to be established between the best social science and biological researchers working on this problem.

Large-scale datasets and banks or repositories, based on NHS patient contact, which include biological and social data, should be feasible. These would help resolve many of the questions currently unanswered because of the huge amounts of data needed to unravel the complexity of mental illness.

There is a clear opportunity to build on the current UK-based longitudinal cohorts, for example through data linkage and secondary analysis, and by including additional metrics such as measures of personality. These cohorts can be used to examine factors influencing mental illness and wellbeing across the whole life course, whether or not the cohorts were set up primarily to investigate mental illness. To reflect the importance of mental health, however, there needs to be effort to improve the measures of exposure and outcome in future 'sweeps' of longitudinal data.

Other scientific opportunities where a population-based approach would be valuable which overlap with the opportunities identified in other sections (for example, 5.2.4) include:

- identifying endophenotypes and new biomarkers of mental wellbeing, resilience and cognitive reserve;
- identifying endophenotypes and new biomarkers of illness;
- elucidating the different contributory effects of illness during co-morbidity, including establishing any causal relationship between them, for example, links between physical illness and poor mental health. Research on the physical health of people with mental illness suggests that the morbidity and the mortality from certain physical conditions is high in people with long-term mental illnesses. Therefore studies of the inter-relationships between mental and physical health are needed and would be important.

5.1.2 Primary preventive strategies based on early detection of high risk state

Primary prevention implies a capacity to identify subjects at risk and to change moderating factors which make illness more likely. There are known indicators of risk already. For example, there is good evidence that general cognitive ability declines with the onset of psychosis and that reductions in grey matter volume in the medial prefrontal cortex and the temporal cortex continues through transition to illness and the early years of psychosis. Both of these changes are predictive of later negative symptoms.

In relation to depression and anxiety, there is a good understanding of risk factors such as family history, neurotic temperament, early abuse and neglect which are moderated by alcohol, misuse of drugs and other lifestyle factors such as sleep disturbance and personal adversity (or life events). There is good epidemiological data to show the development of most first episodes of depression in the decade from 15-25 years of age. However, the foundations of this understanding were laid 30 years ago and little has yet been done to develop interventions based on this evidence base, which now merits very serious attention.

The effect sizes from current genome-wide association studies (GWAS) are too small for possession of genetic risk variants alone to have predictive value in individuals. However, this may change as complete sequencing of individual genomes becomes affordable and rapid, and as large-scale studies establish predictive relationships with outcome in combination with other risk factors.

5.1.3 Identifying the cognitive and neurobiological basis of wellbeing and health development

Mental wellbeing is generally regarded as more than the absence of mental illness, requiring the presence of positive attributes such as resilience, self-worth, empathy for others, normal emotion range and self-control. Wellbeing is an important concept since its promotion should enhance an individual's ability to learn, improve social skills and increase resilience to stress. Normal cognitive decline during ageing could potentially be reduced or delayed.

An important component of wellbeing is the ability to live and cooperate with other people. Social support is a powerful social determinant of resilience to adversity and affects the development of mental illness. Social skills develop through childhood and adolescence and depend on factors such as affection in childhood which conditions the development of specific psychological and neural processes underpinning empathy and emotional and behavioural regulation. Better understanding of these processes is needed to promote wellbeing and also to inform the development of more effective psychological methods for preventing and treating antisocial personality disorders.

Continued mental wellbeing appears to be related to the possession of cognitive resilience, a term used to describe an individual's resistance to impairment in cognitive processes such as memory, reasoning and attention. Such impairments can arise as a consequence of brain injury, psychiatric disorder, physical disease or the normal ageing process. A number of specific psychological characteristics have been associated with resilience and its biological basis is being investigated, for example, through brain imaging studies. Further underpinning research in this area, including studies of normative brain development and ageing, should be encouraged.

Cognitive training (also known as brain training or neurocognitive activation) has the potential to improve cognitive resilience throughout the life course into old age. There are opportunities to link academia, industry and healthcare providers in providing the technology and evidence to support such approaches, which might ultimately allow for population-level intervention.

In addition, the prospect of using 'cognitive enhancers' to specifically improve brain performance is attracting increasing attention. The potential for taking safe and effective drugs to improve mental functions, such as short-term memory or speed of thought, is increasingly considered to be realistic, raising the possibility of widespread use of cognitive enhancers. This in turn raises ethical issues which are discussed at length in a report by the Academy of Medical Sciences[16]. While debate has focused on recreational and performance uses of drugs, cognitive enhancement could offer new therapeutic approaches as well as provide effective maintenance of wellbeing in the UK's increasingly ageing population. Further research is needed to establish whether and how they could be used safely and ethically to this end.

5.1.4 Promoting good mental health at key life stages

Health promotion strategies, supported by national campaigns, have been widely implemented to prevent physical disease. However, expenditure on mental health promotion remains low. Many of the public health strategies that could be developed will need broad stakeholder participation. Promoting mental wellbeing in the workplace and in schools, providing educational and social care services for the elderly and persons with intellectual disabilities, and developing group-based parenting programmes could be addressed by OSCHR partners working with stakeholders. The role of OSCHR partners and the research councils could be to help in providing the evidence base for the effectiveness of interventions delivered in these different social contexts and life stages.

16 Academy of Medical Science report on Brain Sciences, Drugs and Addiction. http://www.acmedsci.ac.uk/p48prid47.html

The review highlighted three key life stages of which adolescence seems the most critical.

i) Childhood and adolescence

Childhood and adolescence are key stages in the development of mental illness. Adolescence is a key stage in relation to schizophrenia and depression, while earlier life is important for conduct problems and hyperactivity. Many childhood disorders persist into adulthood and they are associated with poor educational attainment and crime. For example, those with conduct disorders and Attention Deficit Hyperactivity Disorder (ADHD) are at high risk for a broad range of psychiatric disorders and for violent relationships likely to threaten the wellbeing of the next generation.

Educational programmes and parent training, which aim to help parents strengthen the relationship with their children, have shown some promise in addressing this issue and might offer the hope of improving behaviour and reducing later life problems such as theft and drug use. However, parenting programmes have yet to be shown to have lasting effects and much remains to be done to alter the long-term trajectories of antisocial children. Accordingly, further research is needed in this area.

ii) Working life

The importance of wellbeing and stress in the workplace has increasingly become a concern for employees, employers, professional bodies and Government. The factors affecting workplace mental health are discussed at length in the Foresight Project Mental Capital and Wellbeing Project. While the testing of the effectiveness of Cognitive Behavioural Therapy (CBT) in clinical trials is definitely a UK strength, it has not been fully explored as to which elements of this intervention may have a useful role in prevention of mental ill health in the workplace.

Preparing people for flexible problem-solving in the workplace through personalised learning and new technologies is also key to the promotion of mental wellbeing. The importance of the impact of unemployment on mental health needs to be explored.

iii) Later life

As people move into older age, evidence suggest that continued learning is important to protect against cognitive decline, and maintaining cognitive reserve and mental wellbeing into old age represents a significant goal. The National Institute for Health and Clinical Excellence (NICE) has published public health guidance on how occupational therapy and physical activity can improve the mental health of older people. The guidance focuses on how simple measures such as light exercise regimes can protect the mental wellbeing of older people in primary care and residential care. The guidance challenges some existing views that declining mental health is an inevitable part of the ageing process. Given the increasing ageing population, such pragmatic approaches should be explored further with rigorous evaluation of their effectiveness and the opportunities discussed in section 5.1.3. Increased research to understand and refine the active components of behavioural interventions in this setting should also be encouraged.

5.2 Developing therapy and promoting recovery

5.2.1 Exploiting established UK strengths to increase innovation in mental health research

The UK has strengths in genetics and genomics, developmental biology and the study of neural systems and translational neurobiology (sections 4.1 to 4.3). All these areas inform on new treatments but progress could be accelerated.

The UK is well placed to be a major player to exploit the increasing richness of genetic data given its combined strengths in neuroscience, genomics and clinical genetics. In the longer term there is the possibility of translating genetic information into an understanding of the biological underpinnings of disease and to construct pathways to see how the corresponding gene products are involved in the aetiology of mental illness. The use of genetic information as a diagnostic tool is also a possible but longer-term objective. In the short to medium term, a research priority will be to elucidate the complexity of how many genes of small effect could be further moderated by epigenetic and other biological, social and environmental factors. For example, how do genes influence the development and function of neural systems that mediate cognitive processes relevant to symptoms of mental illness in humans?

In the future, genetics will open up new possibilities for targeted treatment based on an individual's genetic 'make-up' and by identifying previously unknown molecular pathways to illness (pharmacogenomics). The UK will be well placed to exploit this, provided it combines the opportunities provided by genetic expertise in the UK and the regular patient contact afforded by the NHS. The creation of the UK Brain Banks Network, with the promise of more widely available

brain tissue from psychiatric patients and controls, should also provide a valuable resource for validating genetic findings in the human disease context.

One of the strengths of UK research underpinning mental health is the multidisciplinary interaction between the disciplines of cognitive psychology, neuroimaging, genetics and psychiatry. However, much more benefit could also arise through stronger interaction with experts in neurodevelopmental biology and neurophysiology. Many disorders have a strongly developmental component and there is substantial evidence that there are vulnerable periods in brain development which underlie predisposition to neuropsychiatric disorders that emerge later in life. Linking studies of brain and behavioural development would help understand how brain regions critical for mental disorders are associated with typical and atypical behavioural function.

The study of neural systems has shown that a cross-diagnostic, symptom-based approach is important. For example, animal models of critical traits of psychiatric disorders that cut across diagnostic categories are providing vital mechanistic clues. It would be beneficial to focus on symptoms such as aggression or impulsivity across diagnostic categories such as mania, ADHD and substance abuse; or to investigate specific cognitive functions (for example, impaired episodic memory) irrespective of disease diagnosis. The findings from genetic studies only serve to emphasise this point. Gene candidates arising from GWAS suggest that common biological correlates of mental illness cross diagnostic boundaries: for example, schizophrenia, autism, bipolar disorder and ADHD share overlapping risk genes.

5.2.2 Identifying individuals at risk to target intervention

UK strengths described in section 4 have high potential to inform the development of biomarkers for detection, screening and diagnosis of mental health disorders. The aim would be to detect individuals at risk and to intervene before the worst symptoms occur. This would not only ameliorate suffering but prevent the long-term cognitive damage that accompanies chronic mental illness.

Both molecular and cognitive biomarkers would be valuable. The latter represent the functional outcome of many interacting biochemical processes, so they have the potential to inform the development of entirely novel drug classes and drugs with complex pharmacology. Biomarkers would further facilitate the stratified medicine approach (described below and in the next section) which might transform clinical practice.

An understanding of the developmental trajectory of illnesses discussed at section 5.1.1 opens up the possibility of intervention to identify risk at the individual level (as opposed to at the population level as set out in section 5.1.4). Stratified medicine and personalised medicine are promising approaches[17] because patient subgroups and individual patients could be matched with therapies that are more likely to be effective and safe for them.

5.2.3 New treatments through investment in experimental medicine

The UK has the expertise, support networks and potential to access well-characterised patients to increase its capacity to carry out experimental medicine for new treatments. The major opportunities here are:

- research to underpin stratified medicine, based on novel approaches to phenotyping that exploits UK strengths in neurobiology, brain imaging and social science;
- methodological design – innovative experimental approaches to predicting drug efficacy which would help prioritise novel candidate compounds and lessen the risk to the huge investment required to carry out formal clinical trials;
- the development of combination therapies – cognitive and pharmaceutical – based on convergent neuroscience models.

One of the major opportunities is for greater partnership with industry to increase leverage. This would both increase the amount of research funding available and improve the speed of the development of new therapies. Several initiatives are striving to achieve this within the UK, and one model for linking academia and pharma interests is the approach developed by P1vital, a clinical research organisation that has established a consortia involving five pharma companies and five leading academic groupings to provide central nervous system (CNS) efficacy biomarkers in anxiety, depression, schizophrenia, cognitive disorders and obesity. The EU Innovative Medicines Initiative (IMI) also enables commercial clients to make more rapid and effective decisions in the Phase I and Phase II clinical development of drugs[18]. The recently established MRC initiative to increase capacity and academic-industrial linkage in PET imaging (see 7.4.3) should also provide support for experimental medicine studies in this area.

17 In stratified medicine, patients with a disorder are identified as belonging to a subgroup that is particularly responsive to a drug. In personalised medicine, matching is done at an individual level. In each case, biomarkers or genetics have the potential to identify the targeted groups or individuals.

18 The EU Innovative Medicines Initiative (IMI) should also facilitate the search for drugs for treating cognitive dysfunction in schizophrenia

5.2 4 Promoting recovery including cognitive remediation and social rehabilitation

Many of the positive symptoms[19] of severe mental illness can be controlled with current therapies, but negative symptoms[20] and general cognitive impairment are not so easily managed and it is usually these symptoms that are most predictive of poor social and occupational outcome. There is a pressing need to improve medical, social and occupational outcome following psychosis. UK studies have shown that treatments such as behavioural family therapy and supported employment schemes lessen relapse and improve social and occupational functioning, but these are not routinely provided in community mental health services. There is also an opportunity to develop combined pharmacological and cognitive remediation strategies to reverse impaired cognitive function and longer term damage. In both these cases, strategies are required to ensure full recovery, and research should focus on developing practical versions of therapies that can be effectively implemented in the NHS.

5.2.5 Evaluating whether improvements in management and service delivery can be made to benefit outcomes

There is an opportunity to develop science-based models of service delivery for people with mental illness. The greatest need is for those conditions with the highest prevalence (for example, unipolar and bipolar mood disorders, anxiety disorders), conditions associated with the highest economic costs (for example, autism and intellectual disability), and harder to reach individuals such as those in prison and the homeless. Another important area is the management of mental disease in the elderly.

Approved treatments often do not reach patients and there is little understanding of the training and dissemination issues required to improve this state of affairs. It is critically important to reduce the treatment gap especially for those suffering from common mental disorders. One opportunity will be to use innovative IT approaches based on the web and mobile phones, and to consider novel settings for making contact with sufferers, such as the workplace.

More health service research in the area of people with intellectual disabilities and autism would provide an opportunity to reduce the huge financial burden these conditions exact on care systems. Research is also needed to identify what interventions are effective and cost-effective in providing acceptable treatment and care to people in black and minority ethnic groups and, in the case of severe mental illness, to do this under conditions of least legal and physical restriction.

5.2.6 Increasing the participation of patients, service users and carers

The Mental Health Research Network (MHRN) has successfully set up user groups. While this review did not recommend any further initiatives in user participation, it was noted that there are circumstances where the involvement of users adds value to mental health research. For example, users can advise on more feasible experimental designs involving patients and suggest research outcomes, some which might be subjective, that more closely reflect the needs of patients. It was recommended that researchers and funders consult users more consistently on experimental design and outcomes to improve the real world value of research. It was noted that the Economic and Social Research Council (ESRC) was leading on a scheme to improve research into subjective wellbeing and that MRC was a co-funder of this initiative.

19 Positive symptoms generally involve, for example, hallucinations and delusions or observable patterns of behaviour that seem to others to be disorganised and bizarre. They are often associated with an acute, psychotic phase of mental illness.

20 Negative symptoms are major deficits in motivation and spontaneity that appear to be responsible for much of the chronic and long-term disability associated with severe mental disorder.

6. Obstacles to progress

6.1 Capacity and focus of current research

The analysis presented at Annex D highlighted two obstacles: the limited capability of the current UK mental health research community to deliver the scientific innovation recommended in this review, and the gaps in research in the areas of prevention and treatment development. These obstacles to progress have to be addressed in any investment strategy for mental health research. Given the relevant research strengths of the UK identified in this report, it seems highly feasible that a start can be made in addressing these obstacles.

6.2 Stigma

This was a significant issue during the review. Stigma has pervasive effects including the fear of sufferers of the consequences of revealing their illness to their general practitioners, employers, families and friends. While awareness of mental illness is increasing, research for the Time to Change[21] campaign revealed that 92 per cent of the British public believe admitting to having a mental illness would damage their career.

In Europe mental illness affects 27 per cent of people every year, yet 74 per cent of them receive no treatment, notably in anxiety and mood disorders, the areas of highest prevalence. Two factors which contribute towards this degree of neglect are the reluctance of many people to seek help because of their anticipation of stigma should they be diagnosed, and the reluctance of many people who have a diagnosis of mental illness to advocate for better mental health care for fear of shame and rejection on disclosing their condition. Many depressed people prefer a prescription for an antidepressant rather than referral to a psychiatrist – this is probably not meeting the needs of those with moderate and severe depression and results in unnecessary prescribing for those with mild depression. The value of any new therapies will be seriously diminished if too many people continue not to seek help for fear of prejudice and being stigmatised.

Stigma also impacts upon research capacity. First, clinical and social research studies are harder to deliver since research volunteers are more difficult to reach and retain, which in turn impacts upon the attractiveness of the area for students choosing the research area they want to study. This also provides an indirect negative effect upon funding for mental health research, since there is very little charitable donation for mental health research and currently no dedicated UK-based charity for funding mental health with anything like the funds available for research charities supporting physical disease.

There remains an overwhelming need for the research community to speak with one voice on the value of science and the pursuit of reliable knowledge in the area of mental health. If there is one single benefit that such knowledge brings, it is to reduce the stigmatisation that is felt so strongly by patients with mental illness and their carers.

6.3 Research challenges

6.3.1 The limitations of clinical diagnoses for research

Effective diagnosis is a particular challenge for common mental disorders. Scientists trying to develop treatments and preventive strategies have to deal with co-morbidity and heterogeneity. Clinical diagnoses are often 'broad-brush' and with even the most sophisticated techniques, there is overlap between normal and ill populations making diagnostic utility uncertain.

Furthermore, diagnostic categories may in fact represent the extremes of continuously distributed dimensions of liability in the population. A dimensional approach to mental disorders is likely to develop over time and may provide a richer description of disorder and facilitate the identification of the underlying cognitive and neural dysfunctions.

This review recommends that researchers and research funders look for preventive and treatment studies that make full use of the new opportunities to group ill health in new ways, based on biology, cognition, or clinical subtype – recognising that the treatments of the future will not necessarily reflect current diagnostic concepts based on the Diagnostic and Statistical Manual of Mental Disorders (DSM) IV and the soon to be issued DSM V.

6.3.2 The challenges of co-morbidity

Having a co-occurring disorder may worsen the symptoms of the first, leading to a poorer treatment response and a worse course of illness over time, with more impairment and greater social disability. Treatment adherence is a major challenge for those with co-occurring disorders that include mental illness and/or addiction. The challenges are exacerbated with age due to the emergence of further pathologies, cognitive impairments, increased incidence of treatment-related side effects and other physiological changes.

In addition to normal treatment challenges, there are also significant challenges in obtaining satisfactory treatment when mental and physical conditions co-occur. Access to health services can be difficult due

21 http://www.time-to-change.org.uk/

to the reluctance of different service sectors to take the lead if there is a co-occurring disorder. As a result, patients can fall between cracks and do not receive optimal treatment for either condition.

6.3.3 Measuring the causal contributions of the environment and social factors to aetiology

Many of the likely risk-increasing social and environmental elements are difficult to measure, for example, early family influences. It is therefore difficult to be specific and quantify which are the most important factors in the early origins of antisocial behaviour and aggression, for example, which limits our understanding of how such factors interact with genetic effects. Currently, studies that attempt to tease out such effects require very large cohorts and the research is logistically difficult and expensive.

6.3.4 Access to NHS patients, data and tissue

In many cases, solving unanswered research questions will depend on access to large numbers of patients because of the need to address multiple risk factors, overlapping phenotypes, small treatment effect sizes and co-morbidity. Where mental health databases have been set up to address this, they are under-resourced and limited by difficulties of access. There needs to be a drive to improve access to anonymised data from these resources and consideration of setting up new ones where it is feasible. There is no such resource for primary care mental health and rarely is there an identifier for intellectual disabilities or neurodevelopment disorders in most cohorts or datasets.

Access to psychiatric patients is limited by the way that NHS care is organised and the division of the life course in the specialties of psychiatry. There are also cultural aversions to perceived reductionist approaches among some psychiatric staff.

6.3.5 Disincentives and cultural issues

A strong theme emerging from the workshops and consultations underpinning this review has been the lengthy, time-consuming and onerous procedures required to initiate clinical research projects, especially those running across multiple sites. It was recognised that such procedures are there to protect patients and that the National Institute for Health Research (NIHR) is addressing this through the Integrated Research Application System (IRAS) and the Coordinated System for gaining NHS Permission (CSP)[22]. However, researchers still feel there is a problem and that the paperwork required is not always fit for purpose. The problems are heightened for experimental medicine if a study using a licensed drug or healthy volunteers is classified as a clinical trial by the Medicines and Healthcare products Regulatory Agency (MHRA), and also when the research is with people who do not have the decision-making capacity to consent to participation. Cumulatively, the time delays and increased research costs associated with navigating these issues present a significant hurdle for training clinical research academics.

Research governance bureaucracy and over-regulation can be energy sapping and make NHS Trusts risk-aversive to the point of disallowing any research by students, as well as limiting research involving nursing staff or social workers. This is compounded by many mental health teams still viewing research as an undesirable interference.

Another obstacle is the lack of integration between research and policy-making. Premature mandatory policy-making may lead to cost-ineffective treatments or service models being put into practice which undermine research activity.

6.4 Factors impeding the implementation of evidence-based practice

The MHRN has reported that in the Cochrane database only 5 per cent of clinical trials were catalogued under mental disorder. The trials often appeared underpowered and this predominance of small and often local studies prevents researchers and clinicians from drawing generalisable conclusions. As a result, the evidence base in mental health is in need of strengthening.

Although there has been more recent scientific effort expended in creating evidence on new treatments in relation to mental disorders, relatively little is known about the factors which impede the implementation of evidence-based practice. Another problem is that interventions developed in academic centres may not always be easily transferable to the 'real world' of the NHS.

The evidence gap is often filled with the best available evidence from studies performed overseas, usually in the US. The reliance of UK treatments on research evidence generated from international work is a weakness, since the treatments may not generalise due to cultural differences.

22 The NIHR Coordinated System for gaining NHS Permission (CSP) ensures all quality assurance and statutory requirements in respect of clinical research are met, through standardising and streamlining the process for gaining NHS Permission (in England). IRAS is the Integrated Research Application System for applying for the permissions and approvals for health and social care / community care research in the UK. IRAS captures the information needed for the relevant approvals from several review bodies including the Gene Therapy Advisory Committee (GTAC), the Medicines and Healthcare products Regulatory Agency (MHRA), NHS R&D offices and Research Ethics Committees

6.5 Research into adolescence and its clinical management

Adolescence is a critical stage in the development of mental wellbeing but there are obstacles to conducting research with adolescents, not just in performing clinical trials and health services research, but also in more basic aetiological research.

One obstacle is how services for the mentally ill are organised. Treatments for adolescent illness are often based on studies on adults and given the changes occurring in the brain during adolescence there is a significant risk that approaches effective in adults will not transfer to younger people. Examples of this include adolescent depression and schizophrenia, which is managed within the sub-specialty of general adult psychiatry, yet the antecedents of illness (the prodromal state) occur during adolescence.

The aetiological and maintaining factors for adolescent health are likely to differ from adults due to biological differences, co-morbidities, stigma, different social networks and life events. Therefore, it is not helpful, as is often the case in treatment and clinical management, to consider adolescents in a way that is as simple as viewing them as young adults.

6.6 Research into intellectual disabilities and neurodevelopmental disorders

A major obstacle in this important area for research is the exclusion from research of people with intellectual disabilities. Much child mental health research specifically excludes children with an IQ less than 70. Legislation – based on sound ethical considerations – nonetheless encourages researchers to exclude from general clinical trials and more basic studies adults who do not have the decision-making capacity to consent to research participation.

Mental health research with people with intellectual disabilities and neurodevelopmental disorders is expensive and labour intensive, and it requires input from specially trained staff. An additional obstacle is that there is rarely an identifier for intellectual disabilities or neurodevelopment disorders in most cohorts or datasets.

7. Strategy for delivering innovation and impact

This section sets out approaches for innovation that builds on the opportunities identified in section 5 while addressing some of the obstacles highlighted in section 6.

These recommendations are based on:

- the high burden and economic cost of mental illness;
- the strengths of UK research in social, molecular and systems biology underpinning research relevant to mental illness, as well as continuing strengths in epidemiology, clinical neuroscience and service-related research;
- the UK potential for large-scale clinical studies provided by the NHS and the tractability of research needing access to large amounts of patient data;
- the opportunity to exploit existing strategic schemes and the alliance of the MRC and NIHR in translating research to patient benefit;
- the need to redress the disproportional funding for mental health research compared to physical disease;
- the need to provide new treatments and the opportunity for collaboration with industry in experimental and stratified medicine;
- the opportunity to integrate social science in elucidating the role of the environment and 'macro-level' systems such as poverty and deprivation in determining illness, and maintaining – or even promoting – wellbeing at critical stages of the life course;
- the need to promote good mental health in the same way as we promote good physical health;
- the opportunity to reduce stigma through knowledge-led education about the causes and impacts of mental illness.

This review has concluded that the major strategic aims of a research strategy over the short to medium term should be as follows:

7.1 Developing resources for population science

Supportive infrastructure is available to the field and there is arguably unexplored potential to add to this in the area of mental health through, for example, the NIHR Research Capability programme, the MHRN, the new UK Brain Banks initiative and e-science resources such as Psygrid. There are further relatively easy opportunities to build on cohorts. Existing resources could be deployed more effectively, for example, by data linkage across cohorts.

7.1.1 The development of an NHS-based large-scale dataset and bank

This review has highlighted that improved access to patient data will be essential to help generate preventive and recovery strategies. A good example is the case of genetic risk variants where current findings only explain a small fraction of overall risk because studies have been too small. Large sample sizes are also necessary to understand how biological processes and genes interact with social factors such as urban birth, early adversity and substance misuse.

The solution recommended by the Review Group is the establishment of a large-scale dataset and repository or bank that would store patient data and records and demographic data alongside phenotypic measurements and DNA collected from saliva or blood which could be genotyped and linked anonymously to the phenotypic data.

Setting up these resources is not without challenges, such as the need to store data in an anonymised and secure electronic form and to standardise biological measures. However, there is precedent. It has already been shown that it is possible to separate clinical data from identifiers and to store it in an anonymised and secure electronic form (for example in the IoP, NIHR Biomedical Research Centre and SLAM database – see Annex D section 3.2.2). The PsyGrid[23] project has shown that such initiatives are feasible in terms of recruitment and collecting secure and confidential demographic and research information from several centres. It established clinical trial software with firewalls and data protection procedures to ensure confidentiality and security of patient data now available as freeware. Finally, another challenge would be to ensure that the accrual of a research bank was fully embedded in the core business of services.

23 It is important to note that different research questions may require very different scales of research. An NHS bank would be relevant to the need for thousands of gene-phenotype linkages but also to more detailed studies limited to samples in the hundreds (such as provided by Psygrid). Further work would be required to address the scope and scale of the suggested databank and how existing resource and schemes might be exploited or enhanced.

Such a resource would be most feasible in addressing the problems of severe mental disease where there is regular patient contact within secondary care[24]. However, it could also be a major boost for research on any disorders where there is regular patient contact, such as in intellectual disabilities and autism. Indeed, in this latter area the UK has unique opportunities for research that do not exist elsewhere, given that it is unique in having a specialist intellectual disabilities health service with specialist health professionals, and has the potential to assemble the necessary amount of phenotypic and genotypic data needed to undertake research into autism and intellectual disabilities.

Despite the apparently greater feasibility for a mental health database and tissue bank based on patients referred to secondary care, it is important to note that a major proportion of the morbidity of mental illness is due to mild to moderate depression where the patient contact point is often primary care. It will therefore be important to consider the greater use of primary care databases.

The review group was not aware of any country that has linked integrated routine care and research in this way and it could give the UK a competitive edge in the field. Furthermore, an e-science resource based on NHS contact would be free of ascertainment bias, as UK patients across the whole population come into contact with services through the NHS. Such a resource need not be established from scratch, and opportunities might be afforded to build on existing activities, for example, the Research Capability Programme.

In summary, an ambitious approach is needed to address the challenge of the need for very large numbers of carefully assessed subjects for research on complex psychiatric illnesses. This would also offer the potential to underpin efforts to develop stratified medicine approaches, to overcome co-morbidity and to make sense of the data being generated from genetic studies. The databank would be a valuable resource and should represent a major long-term target for funders and major research centres working together.

7.1.2 Cohorts

The heterogeneity and complex aetiology of psychiatric disease means that longitudinal studies and research based on human cohorts are key to addressing the strategic research questions identified in this review.

The UK possesses a relatively large number of cohorts, including several birth cohorts that can be used to examine factors influencing mental wellbeing across the whole life course. Evidence has already emerged identifying early predictors of mental health and continued follow-up of these cohorts and better linkage will allow us to test hypotheses across the lifespan.

A start has been made in 'aligning' some of the UK cohorts to study other research questions. For example, the HALCyon cohorts[25] programme includes nine cohorts of 30,000 individuals born between 1918 and 1958, and aged 50 years or older at the start of the programme. These cohorts have been chosen because they already have rich biosocial data and seven of the nine cohorts are life-course studies with data from childhood and adulthood. All the cohorts have data on adult physical or cognitive capability and are being studied together (as if a single resource) to predict those individuals who age well, and to understand the processes of ageing. This is a potential model for making the best of existing cohorts for understanding the processes underlying mental illness and wellbeing using the data rich cohorts available in the UK (and internationally), whether or not they were initially set up to study mental health. There are also opportunities to use both recent and established birth cohorts or international cohorts to study mental health in adolescence.

In general, this review finds no requirement for investment in major new cohorts. However, a major opportunity exists through the planned ESRC/MRC 2012 birth cohort and the Review Group considered it critical that this should include validated measures of wellbeing and mental health. Additionally, it was recognised that there are no existing cohorts that are able to answer research questions important for aetiology and later life consequences of adolescent mental illness, the links between intellectual disabilities and later life pathology, or for investigating the aetiology of personality disorders. Consideration should therefore be given to targeted investment in this area.

7.1.3 Promotion of good mental health as a public health strategy

Many of the recommendations in this review impact in the short to medium term on public health, in particular developing population science to study the aetiology of mental health to inform preventive strategies and improving therapeutic options.

The promotion of good mental health (in the same way that good physical health is promoted) is a largely unexplored area. It was, however, touched on by the Pathways to Mental Wellbeing Workshop held as part of this review. Conclusions from that workshop highlighted how it is essential to develop cognitive reserve by promoting mental as well as physical health from an early age. Delegates at that workshop raised the prospect of some behaviours (for example, exercise) having positive impacts on both mental and physical health. Targeted approaches to wellbeing are also developing a good evidence base, although further research in this area is required (see section 5.1.4).

24 Although the General Practice Research Database (GPRD) has been used to investigate the links between SSRIs and suicide.
25 http://www.halcyon.ac.uk/?q=cohorts

The Foresight Report and the recent New Horizons initiative[26] emphasise the benefits of wellbeing in terms of physical health and the importance of prevention through to effective treatment and recovery, educational attainment, employment and reduced crime. Developing strategies to promote good mental health would need to be supported by the broad stakeholder approach proposed by the New Horizons Initiative, which aims to promote services to improve whole population mental health.

7.2 Promoting experimental medicine for mental health and interdisciplinary collaboration

Experimental medicine for mental health and underpinning interdisciplinary collaboration is needed to accelerate the prospects of new treatments. There are very good opportunities to exploit the strengths of UK research in genetics, developmental biology and studies of neural systems, as well as the opportunity to collaborate with industry in stratified and experimental medicine approaches.

UK academia could help UK-based pharma find more innovative methodological approaches to smaller experimental medicine trials, help with identifying endophenotypes for drug targeting and help achieve the ambition of more personalised medicine by, for example, taking into account individual (eg genomic) differences in response. Another opportunity would be to combine the complementary forces of academia and industrial resources in developing combination therapies using both pharmacological and psychological approaches.

Encouraging multi-institution/private sector consortia or networks is one route for bringing together relevant expertise to tackle challenging research problems and leverage more resource for mental health research. Development of new preventive and treatment options from more basic clinical studies needs to be accelerated, though both non-profit and commercial routes. The new funding approaches developed by the MRC, NIHR and other OSCHR partners post-Cooksey provide opportunities which are being used by UK mental health researchers, though not yet on the scale needed. More ambitious developments need to be encouraged in this area to enhance preclinical-to-experimental medicine strategies through better exploitation of the strong systems and behavioural neuroscience already available in the UK.

Underpinning research might also be improved by a network or cluster approach. The involvement of developmental biologists, neurobiologists and functional geneticists should provide an opportunity to exploit disciplines relevant to mental health, to build capacity and increase innovation. In similar fashion, the involvement of social science in understanding disease causation, environmental interaction, continuity of care or treatment uptake is also vital.

7.3 Capacity building

Training and capacity building are pivotal issues for the future of mental health research. Award data indicates that the small numbers of research psychiatrists applying for clinical research training schemes are at least as competitive as applicants for fellowships in other specialties. This suggests that the quality of the research and potential of the candidates is very high but that there is a need to incentivise entry into a clinical academic career in mental health. This will mean working with partners in specialties and disciplines such as psychiatry, clinical psychology, mental health nursing and occupational therapy.

The review also highlighted the need for more 'translational neuroscientists', ie neuroscientists with a real interest in mental health issues (who would not necessarily be clinician neuroscientists) to bridge the gaps between the advances in fundamental molecular neurobiology (for example, in neurodevelopment and genetics) and behavioural neuroscience and psychopharmacology. It is important that basic scientists are effectively exposed to clinical issues and that clinician scientists spend some time in the best cutting-edge discovery research laboratories so that they are familiar with the opportunities and limitations of various experimental techniques. Research training is one way of addressing the gap between fundamental and clinical mental health research.

Increased use of summer schools helps attract trainees into mental health research, while consideration might also be given to dedicated schemes such as one-year 'entry-level' fellowships. However, this requires discussion with stakeholders to ensure that they are complementary (and not competitive) with other training schemes and, in the case of clinicians, that there is flexibility with professional training and recognition by the Medical Education and Training Board (METB) and local deaneries. More also needs to be done to ensure stronger support from NHS Mental Health Trusts to regard research and training as an essential component of good service delivery.

Finally, support should be considered wherever possible to help support the recruitment of research leaders in mental health from overseas to build up UK capacity, for example, through the MRC Strategic Appointments scheme or similar initiatives.

26 New Horizons: A shared vision for mental health – http://www.dh.gov.uk/en/Healthcare/Mentalhealth/index.htm

7.4 Links to other strategic initiatives

The Review Group recognised that there were many existing opportunities to build on strategic developments brought in by OSCHR partners in recent years to support the recommendations within this section.

7.4.1 Lifelong Health and Wellbeing (LLHW): a cross-council research programme

LLHW is a major cross-council, multi-funder initiative supporting multidisciplinary research addressing factors across the life course that influence healthy ageing and wellbeing in later life. Phase 1 of the LLHW initiative was funded by the Biotechnology and Biological Sciences Research Council (BBSRC), Engineering and Physical Sciences Research Council (EPSRC), Economic and Social Research Council (ESRC) and the MRC, and supported three new 'lifelong health and wellbeing' research centres (see Annex D). Under phase 2, one of the priority areas is mental capital, mental health and wellbeing, with a focus on interventions to retain cognitive functioning and exploiting the mental and social capital of older people for society. Clearly there is a possibility that recommendations from this review, especially those that have a healthy ageing life course theme, would be synergistic to this or future phases of LLHW which would merit further exploration.

7.4.2 UK brain tissue resources

The MRC is leading a UK Clinical Research Collaboration (UKCRC)-endorsed initiative to establish an independent and coordinated national network of existing UK brain tissue resources (banks). To address some of the research questions arising during this review, access to high quality brain tissue would be valuable for research into mental disorders, although the problems of collecting the requisite number of brains from psychiatric patients to sufficiently power future studies was recognised.

7.4.3 MRC-led PET initiative

PET imaging is set to provide a key translational technology in neuroscience and has good potential to provide payoffs in diagnosis, patient stratification and therapy. The MRC is committed to enabling PET-based research for the neurosciences within the UK and recognises that PET imaging techniques are of key importance to mental health research, as highlighted in section 4.3.

The MRC has already implemented a specialist postdoctoral training programme in PET neuroscience to train chemists and modellers in advanced methods. At the time of this review, discussions were underway between MRC, industry and MHRA representatives to better understand regulatory requirements and see if there might be scope for streamlining current approval processes to facilitate the development of PET capability in the UK.

7.4.4 MRC-led addiction initiative

At the time of the review, the MRC was leading an addiction strategy in partnership with the ESRC and members of OSCHR. This initiative aims to strengthen the translation of research into public health benefit in the area of addiction and substance misuse, which are often co-morbid with psychiatric illness. The pathways into addiction are not well understood and new interventions to treat or prevent addiction are urgently needed. Therefore, the investment strategy recommended here could be of added value to addiction and substance misuse research and vice versa. There would be obvious scientific opportunity for synergy between these initiatives, especially in terms of the interdisciplinary collaboration suggested at 7.2 and nurturing within the addiction cluster mechanism.

7.4.5 NIHR Research Capability Programme

This is a collaboration between the National Institute for Health Research (NIHR) and the NHS Connecting for Health Programme. The aim is to make the UK the preferred place to carry out research by building a nationwide health data and information platform that will enable health research to achieve its maximum potential. Scotland also has an established e-health programme. Clearly the aims of these programmes chime with the ambitions set out at 7.1.

7.5 Reducing stigma

This review has highlighted how stigma seems inextricably linked with mental illness. It is hoped that better understanding of the causes and aetiology of mental illness might make the public more likely to view mental illness as no different from physical illness. In turn, this will allow people to speak with less fear and ignorance about mental illness.

The effect of stigma in creating a 'treatment gap' is a major issue. Even in established market economies, far too many sufferers avoid seeking help for fear of being stigmatised. A recommendation from this report, therefore, is for more research examining the relationship between stigma or discrimination and help-seeking.

8. General conclusions and recommendations

Drawing on the strengths and opportunities identified during this review, we propose that the UK's strategic ambitions should be to:

1. prevent mental disorder and disability and promote wellbeing, based on better understanding of causes and risk levels, and new approaches to early preventive interventions;
2. accelerate research and development aimed at new, more effective treatments for mental illness and implement them more rapidly.

The investment strategy to meet these strategic ambitions is summarised below. The aims are to:

a. strengthen research into population-based research through:
   i) the development of an NHS-based large-scale dataset and repository of biological and social factors for mental health research;
   ii) adding value to existing or planned cohorts;
b. promote experimental medicine and research into new treatments;
c. increase research capacity and innovation by:
   i) exploiting the key scientific opportunities in this field and expand the foundations for new treatments and prevention through enhancing support for thematic multidisciplinary research groups;
   ii) enhancing research training and increasing critical mass by adding incentive for research careers in mental health research and encouraging broader, structured training programmes across all relevant disciplines and careers;
d. 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.

8.1 Short term to medium term research priorities

This review has identified strengths, weaknesses and opportunities in a way that builds to a number of compelling strategic objectives. In the short to medium term these are:

8.1.1 Strategic investments for population science

An immediate ambition would be to address the challenge of achieving the very large numbers of routinely assessed subjects required for research on psychiatric illness. A data bank or repository based on the unique resources of the NHS that tracked service use, treatment response and long-term outcomes in patients, and allowed linkage to information on symptoms and genetic and environmental factors, should be feasible using established electronic databases and would represent very good value for money. This could be used to address several scientific priorities, including the identification of at-risk individuals, understanding the trajectory of the disorder, factors affecting mental illness and wellbeing across the life course and the development of preventive strategies.

Another immediate ambition would be to look at the best way to fully exploit existing cohorts. The mental health review has focused on new approaches that might create opportunities for population studies based on existing cohorts by analysis across domains and imputation.

A new, targeted cohort might be justified for hypothesis-driven research on intellectual disabilities, neurodevelopment disorders or adolescent mental health.

The proposed strategic ambitions in this report around adolescent illness and wellbeing are highly relevant to public heath. Knowing the adverse environmental influences on brain and social development will help inform the development and testing of preventive strategies to reduce medical and social problems (such as violence, disorder and substance misuse) in later life. Early onset disorders and mental ill health and problem behaviours within the population of people with intellectual disabilities are of enormous health and social significance because they are associated with multiple health risks and social problems such as crime and parenting breakdown.

8.1.2 Early detection and developing new therapies and recovery strategies

It is important to develop new treatments for neuropsychiatric disorders. Treatment is likely to be more effective if treatment is early, hence the need for early detection. It is recommended that strong collaboration should be fostered between academia and industry that involves the leverage of expertise and resources. Such partnerships could promote the development of biomarkers and reduce risk in the development of drugs through experimental medicine.

Other valuable aims would be to develop stratified medicine approaches to drug targeting and develop combination therapies.

Promoting recovery after mental illness is another important objective where therapy may be at the drug or cognitive remediation level or through supported schemes that enable rehabilitation into working life and society. In the latter case, new collaborations are necessary between stakeholders and would require the input of social scientists.

8.1.3 Incentivising research training

It is clear that dialogue will need to be opened up with stakeholders to discuss means of increasing the flow of new blood into the field of mental health by adding incentive for research careers in mental health research and encouraging broader, structured training programmes across all relevant disciplines and careers.

8.1.4 Reducing stigma and promoting positive mental health

Stigma has pervasive effects, including its negative impact on people with mental illness seeking treatment, fear of the consequences of revealing illness to employers, and the lack of charitable donation for mental health research.

Reducing stigma is of paramount importance. Some progress is being made in altering public attitudes in this area, for example, a number of celebrities have recently highlighted their personal experience of mental illness and supported campaigns such as Mental Health Action Week[27]. Autism-specific charities have also done a lot to increase awareness about autism, and others such as SANE, RETHINK and the Mental Health Foundation have sought to highlight the negative impact of stigma more broadly. Further research into social attitudes and the effectiveness of current strategies to reduce stigma may be merited, though it seems likely that most long-term impact will be gained through improving and disseminating research knowledge about the causes and progression of mental illness per se.

There also seems to be much less focus on mental health in the promotion of best public health practice than there is for physical wellbeing. This review recommends that OSCHR partners explore with stakeholders how best to investigate the promotion of mental health at a population level at key stages of the life course.

8.2 Medium and longer terms aims and strategies

It is not premature to consider preventive strategies for mental illness. Preventive strategies targeted at individuals are likely to come first in those disorders that already have an identifiable high-risk state (for example, schizophrenia). Other approaches will follow as biomarkers are developed and the findings from genetics are implemented in the NHS. Diagnosis, prognosis and prediction of treatment response, at least partly informed by gene variants and gene expression, might be feasible.

In the medium term, the development of public health strategies needs to be informed by new knowledge from population sciences in the social and biological determinants of mental illness and wellbeing.

8.3 Closing remarks

This mental health research strategy for OSCHR partners should have clear benefits for public health in the medium term via the early detection and treatment of mental illness. This will improve mental capital and wellbeing and reduce the considerable morbidity and huge hidden economic cost of mental ill health. If there is one single benefit that such knowledge brings, it is to undermine the stigmatisation that is felt so strongly by patients with mental illness and their carers.

27 http://www.mentalhealth.org.uk/campaigns/mhaw/

Annex A

Mental Health Review Group Membership and Terms of Reference

1. Membership

Capacity	Name	Institution/role
Chair	Professor Christopher Kennard*	University of Oxford
Member	Professor Anna Cooper	University of Glasgow
Member	Professor Nick Craddock**	University of Cardiff
Member	Professor William Deakin	University of Manchester
Member	Professor John Geddes*	University of Oxford
Member	Professor Guy Goodwin	University of Oxford
Member	Professor Jonathan Hill	University of Manchester
Member	Professor René Kahn*	Utrecht University, The Netherlands
Member	Professor Peter McGuffin	Institute of Psychiatry, Kings College London
Member	Professor Barbara Sahakian*	University of Cambridge
Member	Ms Marjorie Wallace	SANE
Member	Professor Til Wykes	Institute of Psychiatry, Kings College London
Observer	Ms Joy Todd	ESRC
Observer	Dr Glenn Wells	NIHR
MRC Office	Dr Robin Buckle	Head Neuroscience and Mental Health Board
MRC Office	Dr Gavin Malloch	Programme Manager for addiction and mental health
MRC Office	Dr Leanne Rivers	Project Manager

* Members of the MRC Neuroscience and Mental Health Board
** Academic Chair of the Royal College of Psychiatrists

2. Terms of Reference

i) To consider the strengths and weaknesses of the portfolios of mental health research of the MRC and other OSCHR members in the light of other UK and international activity;

ii) To advise the MRC and other OSCHR members on future research opportunities and tractable priorities for improving mental health;

iii) To recommend a strategy for investment in mental health research over the short to medium term (two to seven years), addressing the biological, psychosocial and public health needs;

iv) To advise on future capacity building needs;

v) To consider ways of reducing the stigma attached to mental ill health and raising the profile of the mental health needs of the population and the consequent need for research.

Annex B

Mental Health Review Subgroup Reports

The review was structured around four themes. For each theme a workshop scoped the views of experts and opinion leaders in that filed.

The themes for this review were:

1. Severe mental illness (primarily psychosis);
2. Anxiety and depression (bipolar disorder was included in this theme);
3. Neurodevelopmental, learning and intellectual disabilities;
4. Pathways to mental wellbeing.

Templates of the workshop findings were drafted by the meeting chairs to circulate to the attendees in order to clarify the workshop outcomes. These outcomes were then written up into a final report.

Reports can be found below. The templates of the workshop findings will be available on the MRC website at the time of publication of this report.

B1.

Subgroup title	Severe mental illness (primarily psychosis)
Workshop Chair	Professor William Deakin
Workshop date	21 July 2009

Most people with severe and enduring mental illness (SMI) suffer from psychotic symptoms including disorganised thinking, hearing voices or delusional beliefs. The most prevalent diagnoses are schizophrenia and severe bipolar disorder. The SMI strategy group focused primarily on schizophrenia research. The enduring health needs in SMI arise mainly from the tendency of psychosis to recur and from secondary disabilities that result in impaired quality of life and poor social and occupational functioning. Poor quality of life occurs despite adequate medical control of psychotic symptoms and its origins are poorly understood. 80 per cent of patients with schizophrenia are unemployed and the associated costs are a substantial. In 2005 the estimated overall cost of schizophrenia to society was £6.7 million a year. SMI is associated with greater medical morbidity and mortality: symptoms are less often recognised, have less effective treatment and respond less well to treatment. Clearly medical, psychological and social treatments are unsatisfactory.

Developing and implementing better treatments are of the highest priority for patients, carers, researchers and society.

The strategy working party identified three areas in which UK clinical research has been prominent in advancing scientific understanding of causation that have realistic translational implications for the development of better treatments:

- New genetic mechanisms of vulnerability;
- Transition from risk to psychosis in early adulthood and the possibility of primary prevention;
- Prevention of disability and promotion of recovery.

New genetic mechanisms of vulnerability

Recent advances and future opportunities

Modern genotyping methods permit the whole genome to be covered in increasing detail for association with illness. Current microchips have markers for a million base-pair sites across the genome but quite soon it will be possible to sequence complete individual genomes rapidly and economically. Genome-wide association studies (GWAS) are becoming the norm. Recent meta-analyses of GWAS indicate that common variants in hundreds of genes, individually accounting for less than 1 per cent of the genetic risk for schizophrenia, are likely to collectively account for at least 30 per cent of the genetic risk. Some of the most strongly implicated genes influence the expression of other genes (ZNF804A, TCF4), are genes in the major histocompatability complex (MHC) and one is a synaptic protein (NRGN). Rare copy number variants (CNVs) affecting specific genes have recently been discovered that carry a high risk for rare cases of psychosis which are often severe and associated with learning disability or autism-like syndromes. They may prove to be an infrequent cause of schizophrenia but understanding the molecular consequences may suggest novel candidate genetic pathways to psychosis.

Genetic abnormalities so far identified only explain a small fraction of overall risk because studies have been too small. Detecting statistical significance for small effects of common variants or association with rare variants will require very large sample sizes of tens of thousands. Furthermore, large sample sizes are necessary to understand how genes interact with each other (GxG interaction) and with environmental factors (GxE interaction) such as urban birth, early adversity and substance misuse. Identifying genotypic effects requires

basic and consistent information about phenotype – at the least, consistent diagnostic criteria for schizophrenia and the systematic recording of symptoms, since many genetic effects will not respect traditional diagnostic boundaries. Relating genotype to basic information about environmental risk factors and about outcome will allow the identification of functional subtypes of psychosis.

Strategic response: NHS Psychosis Research Bank

Psychosis research needs to become much more integrated into routine clinical care and involve users, carers and clinical staff. Routine longitudinal clinical assessment and treatment is carried out in the NHS and is part of Good Clinical Practise. It is possible to separate such data from identifiers and to store it in an anonymised and secure electronic form (cf South London and Maudsley NHS Foundation Trust (SLAM)). DNA is simple to collect from saliva or blood. DNA samples can be sent through the post for the genotypic data to be linked anonymously to demographics and clinical phenotypic data. Attention will need to be given to how the clinical data is ascertained and recorded, what reliance is placed on novel capture methods such as text mining, web–based interviews and self-ratings, and the use of NHS information systems. Annual health and treatment checks are recommended practice for all patients with SMI and these could be a vehicle for systematic collection of phenotypic data. They could be extended to include self-administered web-based tests of cognitive performance and self-ratings of social and occupational functioning.

Objective of the NHS Psychosis Research Bank: to identify new multigene patterns, multigene-environment interactions and multigene-treatment interactions associated with disorder and with functional outcome based on sample sizes of thousands.

Better treatment from better understanding

Genetic epidemiology holds the promise of personalised medicine in psychiatry. We will be better able to predict risk of psychosis and who will respond best to which kind of medical or psychosocial treatment to prevent onset and mitigate disability. It will be essential to work out how genotypes translate risk at a molecular level and at the neural systems level (brain imaging, cognition). The former will provide molecular targets for development of entirely novel drugs; the latter will suggest biomarkers to detect drug action on brain systems relevant to symptom formation and thus to select or reject drugs for clinical development based on likely efficacy. As with some cancers, it is possible that treatments for schizophrenia may be effective only in those with a particular molecular pathogenesis which is targeted by a specific drug action.

UK expertise in experimental medicine needs better integration and encouragement to develop, validate and use molecular and neural system biomarkers for disorder and the evaluation of novel drug treatments.

Transition from risk to psychosis in early adulthood and the possibility of primary prevention

Recent advances and future opportunities

It is increasingly understood that risk of psychosis is continuously distributed in the general population and this is implicit in the evidence for polygenic inheritance. First episodes of psychosis occur in 30-40 per cent of those who have at-risk mental states (ARMS) who are, in turn, a subset of a larger group with early prodromal symptoms. Isolated psychotic experiences are common in the general population. Characterisation of the clinical, neural systems and molecular basis of risk traits in general and at-risk populations has the benefit of being free of the confounds of illness and drug treatment.

There is good evidence that general cognitive ability declines with the onset of psychosis and that reductions in grey matter volume from the medial prefrontal cortex and the temporal cortex continue through transition and the early years of psychosis. Both of these changes are predictive of later negative symptoms but almost nothing is known about their underlying GxE, biochemical or neuropathological changes. The Edinburgh high-risk study suggests that possession of common variants in some candidate genes predicts which at-risk individuals progress to psychosis. If the processes were better understood, preventive therapies could be devised and evaluated. One obstacle to research is the lack of understanding of how cognitive neural systems normally develop from adolescence to adulthood – the peak at-risk period for the prodrome of psychosis.

What are the limits of normal development in different systems? What are the effects of drug and alcohol misuse? How and when does psychosis deviate from the normal pattern and in which neural systems? What are the benefits of healthy diet, sports, social networks? Are there identifiable patterns of resilience to risk factors for psychosis?

The UK has developed unique experience in nationwide recruitment and assessment of patients with prodromal and early psychosis. The PsyGrid project recruited over 900 first-episode patients and collected secure and confidential demographic and research information from eight UK centres. NeuroPsyGrid showed that national multi-scanner MRI studies are feasible - an increased recruitment rate far outweighs the increased sample size required to deal with extra variance from using different scanners. The NHS has implemented Early Psychosis Intervention Services to reach and treat people distressed or seeking help for prodromal symptoms. The multicentre EDIE clinical trial is evaluating the effectiveness of cognitive therapy to prevent transition to psychosis in people with ARMS.

Responses to a call for studies of causation and treatment and in early psychosis could help to identify research demand for an enabling infrastructure that finds and recruits cases and controls and carries out clinical assessments.

Strategic response: UK Young Healthy Brains Study

The UK has the neuroscientific expertise and infrastructure to identify normative ranges for healthy brain maturation and the environmental and constitutional factors that promote and threaten it. Psychological symptoms come and go in adolescence. Psychosis-like experiences and mood shifts are surprisingly prevalent. Some may be prodromal harbingers of illness onset, others the normal expression of brain maturation. The neural systems that underpin human social behaviour, for example the moral emotions guilt, shame, pride, empathy, are increasingly known and aberrant functioning is implicated in antisocial behaviour, depression and psychosis. If the normal limits were quantitatively described, deviations in individuals could be spotted early and their prognostic significance read out to professionals to identify preventive strategies and the promotion of health. The measures would include assessment of personality, cognition and behaviour and measures of brain structure and function gathered across the UK in regional centres. Careful power estimates for the size of the normative population would be required to determine what degree of deviation could be detected in individuals. Such data is being gathered for children and adults but is missing for the key years of vulnerability to adult disorder from 15 to 30 years.

Prevention of disability and promotion of recovery

Recent advances and future opportunities

There is a pressing need to improve the social and occupational outcome of psychosis. This is poor despite control of positive symptoms with current therapies. Negative symptoms, general cognitive impairment, duration of untreated psychosis and number of relapses are predictive of poor social and occupational outcome but most of the variance is unexplained and this may be related to inadequate measures of functional outcome and poor understanding of mechanisms.

The development of novel psychological and pharmacological treatments to reverse impaired cognitive function in schizophrenia has been the focus of much interest from clinical psychology community and from industry. UK studies have shown that benefits in cognitive performance from remediation therapy translate into better social and occupational functioning. However, the gains lessen when the treatment stops. Based on insights from the neural organisation of the cortex, industry has identified a number of molecular targets for drugs to enhance cognition. The targets include modulation of glutamate, gamma-aminobutyric acid (GABA) and acetylcholine. Such treatments could consolidate the gains achieved by cognitive remediation.

Trials to investigate combined cognitive treatments are very much to be encouraged.

UK studies have shown that treatments such as behavioural family therapy and supported employment schemes lessen relapse and improve social and occupational functioning but they are not routine in community care.

Research is needed to develop practical versions of psychosocial and family therapies that can be integrated into routine multidisciplinary care.

B2.

Subgroup title	Anxiety and depression (including bipolar disorder)
Workshop Chair	Professor John Geddes
Workshop date	17 June 2009

UK strengths and opportunities in the field of mood disorders

Neurobiology with integration of neuroimaging, psychopharmacology, neuropsychology and genetics

Integrated neurobiology promises to lead to better phenotyping of mood disorders and the development of clinically useful biomarkers which can be used in large-scale genetic and epidemiological studies and clinical trials. For example, negative bias in emotional processing has been shown to be associated with depressive disorder. Antidepressant medication increases positive emotional processing before having an effect on mood: these changes are associated with neural modulation in limbic and prefrontal circuitry (1). These insights into the neurobiology of depression can lead to new science-driven pharmacological and psychological interventions as well as sensitive and efficient methods of early phase evaluation of new approaches to prevention, detection, screening and diagnosis, and development of personalised treatments for people with mood disorders. The development of simple, computer-based neuropsychological measures of underlying neurobiology means that it is feasible to use them in large-scale observational and experimental epidemiology.

Development and early-phase evaluation of novel psychological therapies

Over the past three decades, scientists in the UK have developed and evaluated many of the now standard psychological therapies for anxiety and eating disorders. Most of these have been based on cognitive behaviour therapy (CBT). Now, using insights from experimental psychopathology, new treatments are being developed in the UK for a wide range of disorders including mood disorders (depressive and bipolar disorders), post-traumatic disorder and anxiety disorders.

Clinical trials

The UK has major strength in conducting the full range of clinical trials in mood disorders from early evaluation of efficacy and mechanism (phase Ib) issuing sophisticated experimental medicine to large-scale phase IV trials with economic evaluation. The early phase work in particular is increasingly leading to partnerships with industry where the methodological advances are recognised as providing a way of increasing the speed and efficiency with which new agents can be evaluated. An example is the development of measures of emotional processing as an early indicator of antidepressant therapeutic effect (1). Larger-scale UK trials have provided definitive evidence on the comparative efficacy of existing therapies for bipolar disorder, such as BALANCE (2) and the MRC-funded trial of CBT (3). The development of the UK Clinical Research Network (UKCRN) has increased the capacity to conduct pragmatic trials in real-world NHS settings.

Epidemiology

The UK has a strong track record of conducting large-scale cohort studies and these data sources have been secondarily exploited to investigate risk factors for mood disorder. The General Practice Research Database (GPRD) is a unique resource for pharmaco-epidemiology and has been used to investigate the links between selective serotonin reuptake inhibitors (SSRIs) and suicidality.

Opportunities

The current UK research strengths in mood disorders fit squarely with the international recognition of the need for a new, science driven, translational research developing new treatments from phase I-III: the objective is to develop personalised treatments for patients. In particular, the strengths in experimental medicine and clinical trials fit with both the Cooksey recommendations and Best Research for Best Health.

Challenges faced by UK research into mood disorders

Capacity and funding

In mental health research in general, there is a well-documented problem in recruitment and retention combined with limited training opportunities and capacity. Research into mental illness is poorly funded compared to other illness areas and, within mental health, there is less research funding in mood disorders than in schizophrenia/psychosis. Heath services research tends to focus on schizophrenia and there are few interdisciplinary meetings between researchers in the field of mood disorders. For example, there has been little innovation or research into organisation of care for patients with mood or anxiety disorders in the NHS. Furthermore, there appears to be very limited applied research in anxiety disorders, especially in primary care.

Relationship with policy-makers

There needs to be greater integration between research and policy-making and adequate investment in research and development prior to nationwide implementation. Premature mandatory policy-making may lead to cost-ineffective treatments or service models being put into practice: not only does this undermine and disincentivise research activity, but it leads to the inefficient and wasteful use of scarce resources. Moreover, it fails to deliver the best health gains for patients.

Integration between the MRC and NIHR

To maximise the scientific outputs from research funding, there needs to be better integration between MRC and NIHR funding. Mental health was only represented by the Institute of Psychiatry in NIHR Biomedical Research Centres – it is important that it is fully considered and included in Department of Health and NHS initiatives.

Partnership with industry

Greater partnership with industry would improve clinical care by increasing the amount of research funding available and by improving the speed of development of implementation of new treatments.

Population-based and preventive approaches

In keeping with their importance and prevalence, there could be more research into population-based preventive approaches to mood disorders. Existing work on UK cohorts can be 'squeezed out' by the better funding available for physical illness. If mental health research is an MRC priority this should be reflected in the balance of exposure and outcome measure in the UK cohorts.

Research priorities

Short-term

- Expand current investment in experimental approaches to mental disorders;
- Standardise neuropsychological/neuroimaging measures for phenotyping;
- Further development of biomarkers;
- Expand UK capacity for phase Ib (early indication of efficacy) clinical trials of both drug and psychological therapies;
- Standardisation of mental health clinical trial methods including assessment of outcomes and methods of economic evaluation;
- Maximise use of current data via secondary analysis of existing datasets from cohorts and clinical trials.

Medium and longer terms aims and strategies

- Develop innovative and science-based psychological and pharmacological treatments and models of service delivery for people with mood disorders. These should more accurately meet the specific needs of people with mood and anxiety disorders, should be robustly based on discovery science findings developed through experimental/translational medicine, and should be rigorously evaluated to ensure they are effective, cost-effective, implementable in routine practice and acceptable to patients. This will also need greater strategic partnership with industry to allow earlier two-way access to novel agents.
- Research into anxiety and mood disorders needs to take account of age because there appears to be heterogeneity in terms of both aetiology and treatment response across the life course. In general, there needs to be more research focused on childhood/adolescence/early adulthood where the trajectory of the illness is still early enough to allow reliable identification of risk factors. At this time studies are less confounded by development of co-morbidity, secondary disability and effects of treatment.
- Development and evaluation of population-based approaches early in the life course to prevent depression and anxiety – this will need strategic partnership with educators.

Strategic partnerships

Interdisciplinary collaboration between psychologists, geneticists, imaging scientists, psychiatrists, epidemiologists and economists is beginning to prove fruitful. Further understanding could be achieved by integrating social and population sciences with these disciplines – the Foresight review is an exemplar of what is possible. Meetings to bring interested people from all these disciplines could be very fruitful.

Greater integration with service providers is needed to better understand the context within which treatments are delivered and thus improve the feasibility of implementation of research results.

Stigma

Stigma is important in this field. There are many current initiatives and funding by mental health charities. The MRC/OSCHR would be better to tackle stigma through generation of new knowledge, which would lead to a better public understanding and acceptance.

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B3.

Subgroup title	Neurodevelopmental, learning and intellectual disabilities
Workshop Chair	Professor Peter McGuffin
Workshop date	14 July 2009

Context

The recent tragic suicide/mercy killing of Fiona and Frankie Pilkington follows a long list of high-profile hate crimes against persons with intellectual disabilities, including murder, torture, rape and other abuse, demonstrating that there is still stigma attached to intellectual disabilities, and public ignorance[1]. However, considerable advances have been made in the UK to improve the lives of persons with intellectual disabilities and neurodevelopmental disorders. Following a series of scandals in the long-stay intellectual disabilities hospitals regarding abusive and degrading practices, there has been increasing recognition of the importance of human rights, the emergence of the concepts of social role valorisation, and a UK policy focus on social justice, inclusion and reducing inequalities. Key government white papers[2-7] led to the closure of the long-stay hospitals, and have established the principals of supporting persons with even the most complex needs in the community, and emphasise the importance of inclusion. Legislation also supports these endeavours, such as the Disability Discrimination Act, 1995, 2005, and the Disability Equality Duty, whereby public sector workers have to consider the impact of their work on disabled people and take action to tackle disability inequality.

It is thought that 2.5 per cent of the population's adults and 3.5 per cent of children have intellectual disabilities, though this figure may be rising due to increasing life expectancy (increasing at a higher velocity than for the general population)[8] and birth rate (older age of parents, very low birth-weight babies, maternal alcohol use, and a lower than previously expected uptake of termination of Down syndrome pregnancies, with changing public attitudes to disabled persons)[9]. Intellectual disabilities due to congenital rubella, syphilis, hypothyroidism and phenylketonuria are now rare in children and young persons following the successful translation of research findings into policy and practice.

Disease burden and health disparities

Persons with intellectual disabilities have much higher levels of mental ill health and problem behaviours than the general population, with a point prevalence rate of 40-50 per cent[10]. Problem behaviours occur in 22 per cent, the standardised incidence rate for schizophrenia is 10, and for mania is 40[11]. Over the age of 65 years, 20 per cent have acquired dementia[12]. Depression is more enduring than for the general population, and schizophrenia more severe[13]. 14 per cent of childhood mental ill health is experienced by children with intellectual disabilities[14]. Mental ill health occurs within the context of multiple comorbidities and therefore polypharmacy (eg 25 per cent also have epilepsy and 50 per cent have gastro-oesophageal reflux disorder[15]). Some of this mental health disparity is genetically determined. For example, 50 per cent of persons with Down syndrome over the age of 50 have acquired dementia in Alzheimer disease[16] and almost everyone with Prader-Willi syndrome due to uniparental disomy will acquire affective psychosis by the age of 30[17]. However, there is a growing awareness of the interaction of environmental factors with genetics in the aetiology and maintenance of mental ill health/problem behaviours[18], and a recognition that some of the mental health disparity is due to substantial health inequalities which should be addressed[19-21].

Mental ill health and problem behaviours within this population is a burden at the individual, family and societal level. This includes a cost burden: the annual expenditure on specialist services provision for persons with intellectual disabilities is 50 per cent of the equivalent amount for mental ill health in the general population, despite being only 2.5 per cent of the adult population[3,22]. Mental ill-health/problem behaviour is a major contributor to these costs.

Inequalities and challenges

'Good clinical practice' requires that persons who do not have decision-making capacity to consent to participate in trials of medicinal products are excluded from them. The countries of the UK have introduced capacity legislation that adds an additional layer of processes that must be followed in research with adults who cannot consent, and in Scotland, excludes some of the population. Research with this population takes longer to do and requires geographical dispersion, so is more expensive. It is not therefore surprising that persons with intellectual disabilities are routinely excluded from research, unless it is specifically focused on them. Even when not explicitly excluded, de facto exclusion occurs (eg the UK birth cohorts have not included appropriate measures that can be completed by persons with moderate to profound intellectual disabilities, and fail to retain even persons with mild intellectual disabilities over time; the mental health research networks are not aligned with the services and supports used by persons with intellectual disabilities and neurodevelopmental disorders). Moreover, it is not possible to extrapolate research findings from the general population and assume they apply equally for persons with intellectual disabilities. This is because aetiological and maintaining factors differ (eg behavioural phenotypes, co-morbidities, double stigma, social and environmental supports, different social networks, chronic stress, low income, mental capital and self-esteem, exclusion, abuse, multiple life events, cognition and learning), different interventions are necessary (eg social and environmental interventions, interventions for problem behaviours,

alternatives/modifications to talking therapies due to limited verbal communication skills and understanding), health and social care services and support are delivered and organised differently and policy priorities differ due to the different pattern of disease (eg employment, healthy working lives and tackling the health consequences of material deprivation, smoking and alcohol use are high priority for the general population, but of little relevance to persons with intellectual disabilities who typically do not have paid employment, few of whom consume alcohol or smoke, and who do not experience deprivation in the same way as the general population).

The UK's research expenditure on mental ill health and problem behaviours of persons with intellectual disabilities is tiny compared to that spent on mental ill health experienced by the general population[23] – which is also small compared to that on other areas such cardiovascular disease and cancer. Hence, development of new technologies and public health interventions preferentially advantage the general population, so widening the inequalities experienced by the population with intellectual disabilities and neurodevelopmental disorders, contrary to stated government policy aims.

Strengths and weaknesses

Intellectual disabilities and neurodevelopmental research is better funded in the USA, following President J.F. Kennedy's enlightened initiative in 1961, that every state should have a University Affiliated Programme in this area (now termed Centres of Excellence in Developmental Disorders), and the continued interest and support from the Kennedy family over subsequent decades, particularly the late Eunice Shriver Kennedy. However, despite the slim UK funding base, the UK is the world-leader in mental health research for persons with intellectual disabilities, with USA research focused in other areas such as education, family supports, ageing and cognition in autism. The Netherlands is also productive in health research for persons with intellectual disabilities, but focused on general health, ageing and sensory impairments. Australia has a small investment in research for persons with developmental disorders, with primary care research on general health screening, Rett syndrome and epidemiology of mental ill health in children with intellectual disabilities. Spain has expertise in policy and service delivery within the Spanish system. Elsewhere, research is patchy and lacks focus.

The UK's research strengths in mental health, problem behaviours and forensic needs of persons with intellectual disabilities have developed in part through a particular set of opportunities unique to the UK, ie the provision of a specialist intellectual disabilities health service across the UK providing expertise in mental ill health and problem behaviours, particularly for adults. This does not exist anywhere else in the world. Additionally, in parts of the UK there has been NHS investment in academic positions and while these were largely established to provide a leadership role, they have complemented the slim funding for research from the UK's higher education councils. The funding base has resulted in posts across all four countries and most regions, and sustainable critical mass in Scotland, Wales, and parts of England, rather than a concentration of academia in one or two institutions. While this has disadvantages, it is also a strength, given that study recruitment is typically, necessarily, across regions, and UK-networking is vital to the success of research in this area – especially so in the absence of a dedicated mental health research network for this population.

People with intellectual disabilities are the most complex and heterogeneous group with very considerable needs, and much health service research can usefully address issues for the whole group. For rare neurodevelopmental disorders, collectively the demand such persons make on resources, the lifelong nature of the disability and the considerable achievements over the last 30 years demonstrate the need for research investment. Just as we would invest in interventions for rare cancers, so we should invest in interventions for neurodevelopmental disorders. Such research primarily must be to benefit this population, but can also lead to understanding neurodevelopmental processes and provides windows into the biology of behaviour and its environmental interactions. Examples include how the link between Down syndrome and dementia led to the identification of the APP gene on chromosome 21, and motivational and environmental interaction in Angelman syndrome.

The UK has a range of medical disciplines engaged in intellectual disabilities and neurodevelopmental research which is also a unique opportunity (eg psychiatry, public health, genetics, medical physics, paediatrics, primary care), and benefits from interdisciplinary research with collaborations including clinical psychology, basic neuroscience, social scientists bringing a diverse range of skills such as ethics, geography, developmental psychology, health economics.

Priority needs

The immediate priority needs are for capacity building through studentships and fellowships; project funding calls for research in these areas to redress the current underspend and stimulate research activity; and augmentation of network/cluster infrastructure to improve relevance for people with intellectual disabilities/ neurodevelopmental disorders and children.

Medium to longer term priorities include further capacity building; trials of interventions for mental ill health and problem behaviours in this population, and to reduce existing health inequalities, based on the UK health and social care systems; more longitudinal research, to examine gene and environmental transactions that contribute to mental ill health faced by people with intellectual disabilities/neurodevelopmental

disorders, taking a developmental perspective to incorporate work examining how we can build resilience and reduce vulnerability to mental ill health (especially important in light of changing patterns of social care); and funds for prospective collaborations, for prospective study of the earliest processes.

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B4.

Subgroup title	Pathways to mental wellbeing
Workshop Chair	Professor Barbara Sahakian
Workshop date	10 July 2009

A lifespan approach is taken in the analysis in this report. Nonetheless, there are five particular areas of focus: childhood and adolescent development, learning through life, wellbeing at work, mental health, and making the most of cognitive resources in older age.

Early deprivation and poverty are key factors in future mental health problems. Interventions are needed to counteract the effects of these factors. It is essential to develop cognitive reserve by promoting mental as well as physical health from an early age. It is also important to stress that some behaviours (for example exercise) have positive impacts on both mental and physical health and these behaviours should be promoted accordingly.

Early development is critical with both early good rearing and education associated with lifelong wellbeing. Also, cognitive problems experienced by the child can lead to poor self-esteem, behavioural problems in school and disengagement from learning. A proportion of adult mental health problems are preventable through successful early intervention in childhood. It is important to capitalise on UK strengths of neuroscience and neuroimaging to focus on areas such as wellbeing, resilience and vulnerability.

Another key developmental stage is adolescence, where adolescents go through significant emotional, hormonal and behavioural adjustment, and are particularly prone to risk-taking behaviour, such as drug and alcohol use. As the brain is still developing, substance misuse can have a particular impact on mental capital at this stage, with long-term consequences on forms of cognition. Cognitive training in young people is important: for example, in teaching self-regulatory behaviour in adolescents to reduce many problems associated with impulsivity in this age group.

In adulthood, important factors that promote cognitive reserve and mental wellbeing will ensure people are effective, productive and have a good quality of life. The early detection of depression and its effective treatment, as well as preparing people for flexible problem-solving in the workplace through personalised learning and new technologies, are key to the promotion of mental wellbeing. In addition, the work-life balance is important in ensuring that individuals maintain creativity and productivity for the economy and society.

As people move into older age, they should continue to learn in order to protect against cognitive decline, maintaining cognitive reserve and mental wellbeing into old age represents a significant focus. A key target for neurocognitive activation is to keep the hippocampal network intact in later life. The importance of technologies for learning and social networking is emphasised as is the contribution older people have to give to society in terms of their ability to continue in paid and unpaid work. Positive, mentally-engaging work promotes mental capital and wellbeing.

A theme running through all stages is the importance of early detection and early treatment, as well as the need for new treatments for neuropsychiatric disorders, such as depression and Alzheimer's disease. For example, neural, genetic and especially cognitive biomarkers can play an important part in early identification of these disorders. This would enable some disorders to be prevented, while others could be treated effectively before they develop a chronic, relapsing or progressive course. Furthermore, new insights into underlying mechanisms, coupled with the use of more selective cohorts in clinical trials, is shown to be essential for the development of effective drugs in Alzheimer's disease, including those to enhance cognition or for neuro-protection.

Strong links exist and should be fostered between academia and industry to allow valuable collaborations to facilitate drug development and evaluation. As we move into the 21st century, it is important to change direction in novel treatment development, including pharmacological and non-pharmacologic ones to a cross-diagnostic, symptom-based approach which will be more appropriate in the field of mental wellbeing. For example, it would be valuable to focus on symptoms, such as impulsivity, across diagnostic categories (such as mania, attention deficit hyperactivity disorder (ADHD) and substance abuse) or specific cognitive functions (eg impaired episodic memory) irrespective of disease diagnosis. To illustrate this, a treatment which reduces impulsive behaviour may do so whether a person has a diagnosis of ADHD or substance abuse. Similarly, a treatment for episodic memory problems may prove useful for improving cognition and functional outcome in both mild Alzheimer's disease and first episode schizophrenia. These industrial partnerships could promote the development of biomarkers and neurocognitive training research, as well as novel drug development. Novel drug development benefits from a translational medicine approach which is a UK strength. In addition, these partnerships could promote the development of pharmacogenomics and personalised medicine in relation to mental wellbeing.

Learning difficulties and neuropsychiatric disorders require urgent action for the health and wealth of the UK. For example, learning difficulties such as dyslexia affect up to 10 per cent of children, reducing the probability of achieving good grades. This in turn has knock-on effects for behavioural problems, social exclusion, crime and reduced education prospects. Common mental health problems, such as depression, are widespread, with 16 per cent of adults in Britain affected at any one time. Indeed, the World Health Organization reported that depression

is the leading global cause of years lived with disability. The annual costs from mental ill health in England alone are about £36 billion for economic costs, rising to £77bn when wider impacts are included, such as reduction in quality of life. Measures to improve mental health would therefore yield benefits well in excess of costs. These costs will be rising with the age profile of the population and the increase in life expectancy as the costs of dementia grow. For example, over the next 30 years, the number of people with dementia in the UK could double to 1.4 million, and costs to the UK economy could treble to more than £50bn. Although these data for the prevalence and costs of neuropsychiatric disorders are presented for the UK, they reflect the circumstances for many developed countries around the world. Therefore, we need to act now to change the future trajectory of these escalating blows to mental capital and wellbeing. In order to ensure an economically competitive and flourishing society in the 21st century, what can we do? Some recommendations utilising a neuroscience approach have already been discussed above, such as the use of biomarkers for early detection of neuropsychiatric disorders. Others include resilience and cognitive reserve and investigating the use of neurocognitive activation (or cognitive training), for training impulse control in children with ADHD or substance abuse problems and training episodic memory in people with amnestic mild cognitive impairment (aMCI). Other recommendations involve a social science approach, such as addressing the problems of stigma faced by older people and people with mental health problems.

To promote mental wellbeing, multidisciplinary collaborations involving public and population health, statistics, social sciences and education research, as well as biomedical science are needed. Ethics and neuroethics are also important areas, with established UK strength, which could make an important contribution to interdisciplinary research. In addition, it is key that cost-benefit analyses, using world leading UK health economists, are applied to the interventions and their outcomes.

A UK strength are current birth cohorts that can be used to examine factors influencing mental wellbeing across the life course. Evidence has already emerged identifying early predictors of mental health and continued follow-up of these cohorts will allow us to develop models across the lifespan. A key new birth cohort needs establishment which starts from an early prenatal time point (12 week booking-in appointment) and critically includes key, validated measures of wellbeing and mental health.

The approaches detailed above should allow us to identify endophenotypes and core biomarkers of mental wellbeing, resilience and cognitive reserve and to better understand the neural impacts of poverty and to develop approaches and interventions to counteract the effects of poverty.

Finally, public engagement in science is important for many reasons, but it is particularly important where lifestyle choices are likely to impact on cognitive reserve, resilience and mental wellbeing. Therefore, there is a need to develop a strategy for engaging the public in constructive discussion of these issues and for training young scientists in these communication skills.

Specific recommendations, together with UK strengths and weaknesses in this area, are detailed in the MRC Pathways to Mental Wellbeing Template.

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Annex C
Review Consultation

The MRC consulted a wide range of individuals, groups and organisations to increase the opportunity for potential stakeholders to present views and evidence.

Method of wider consultation

This consultation was based on the questions addressed and the themes that emerged at the four Subgroup workshops (Annex B), and participants were asked to respond to 14 questions (see Appendix 1) that covered four key cross-cutting issues of the review:

a. opportunities for UK mental health research based on current strengths and weaknesses;
b. research infrastructure and personnel;
c. engaging stakeholders;
d. specific, thematic priorities.

The consultation was distributed to 130 individuals, groups and organisations. The MRC received 28 responses from a variety of stakeholders (see table 1). The views drawn from these responses are summarised below and have informed the review and fed into the recommendations described in the final report.

Method of consultation analysis

Responses to each of the questions posed were listed and grouped into themes. In the summary below, the series of letters in brackets corresponds to the type of stakeholder that made the comments (see stakeholder key at table 1). The frequency of each letter indicates the number of respondents making similar comments under each question.

It should be noted that this questionnaire was not designed for quantitative analysis. Therefore, where a point is raised by a stakeholder, it should not be assumed that other stakeholders would not have agreed with this point. For example, six different stakeholders highlighted that mental health research is underfunded compared with the burden and other disorders. However, this makes no statement about whether the other 22 stakeholders would have agreed or not with this statement.

In the interests of confidentiality, issues raised in consultation responses have been categorised by the type of stakeholder that raised them, rather than identifying individuals.

Table 1. List of the 'types' of stakeholder that submitted a response to the consultation. The code corresponds with the codes following each point in the summary.

Type of stakeholder	Code
Individuals from academia	a
Individuals from NHS organisations	b
MHRN	c
MRC-funded scientists or MRC Centre leaders	d
NIHR grantholders	e
Public organisations from overseas	f
Private organisations – associations/industry	g
Private organisations – associations/NHS/university	h
Private organisations – charity	i
Public organisations from the UK	j

Summary of consultation responses

a. Opportunities for UK mental health research based on current strengths and weaknesses

Question 1: What weaknesses in UK research into mental illness and wellbeing are apparent and in which areas could the UK make an impact with some targeted investment?

- Mental health is underfunded with respect to
  - Burden (g, i, d, g, g, i)
  - Other disorders (g, i, d, g, g, i)
  - Underpinning biological research, animal models, model systems etc. UKCRC heading is v broad so looks well funded (g, d)
  - Translational research (g, d)
  - Long-term prospective studies (g, d)
  - Clinical resources (g, g)
- Gap between health service research and underpinning biological research, resulting in weak translation of basic science to clinical applications (g, d, g, c)
- Little known about early determinants of MH disorders (g, g, a)
- Despite specific calls in 'translational research' few applications have successfully acquired funding (g, d, g)
- No research or 'biomedical' culture in psychiatric medicine (and in NHS in general) (routinely collect data with 'opt out' system) (g, g, h)
- Need targeted investment into MH and wellbeing, playing to UK strengths. Especially interventions (i, g)
- NICE guidelines need evaluating (j, b)
- Need to bring wellbeing into mental health services to look at promoting wellbeing within MH disorders (d, d)
- Evidence about the effectiveness of community level interventions in preventing mental health problems (a, j)
- Lack of interdisciplinary research, esp. between biomedical and social scientists (j, d)

Question 2: Related to the above, what are the research opportunities in the light of other UK and international activity? What strengths should the UK play to, and what should we avoid doing?

- Strengths in brain imaging, genetics, epidemiology – could improve infrastructure/international collaborations (i, d, i, i, g, g)
- NHS (and routine datasets) is great strength (g, d, g, a, h)
- The UK has opportunities to lead in intervention research – including in non-drug interventions (c, g, a, a)
- Clinical psychopharmacology is strength. However, we are in danger of losing UK expertise because of cuts in industry, academic training posts, etc (g, d, d)
- Wellbeing is an emerging and important field (d, j, a, j)
- Clinical research infrastructure (NHS, MHRN) is strength – has substantial investment and should help clinical trials research, characterisation of endophenotypes, linked to DNA genotypes, neuropsychological measures, imaging, social measures etc (g, j)
- Preclinical psychopharmacology is strength. Can provide a crucial underpinning to clinical research in terms of hypothesis-testing and development as well as understanding mechanisms underlying clinical observations (g, d)
- The MRC needs to avoid emphasis on single techniques (eg clinical genetics, imaging); an approach which has proved less fruitful than when the most appropriate techniques are combined to address the burning scientific questions (g, d)
- Cognitive psychology is strength. Need to explore physiological and neurophysiological mechanisms underlying cognitive strengths and weaknesses (i, g)
- Cohorts are strength. Many can be linked to health and social datasets. May provide opportunity to link with international cohorts (f, d)
- Capacity building key. Risk losing 'critical mass'. Especially in certain areas – applied health research, forensic research (j, h)

Question 3: What are the immediate and tractable priorities for investigation that would make an impact using existing resources (say £3-5m) in the short term (next 2 years)?

- Cognition in mental health disorders (and cognitive enhancement) (g, d, g)
- Enhance the optimal use of currently available treatments (g, d)
- In-depth total population epidemiological studies of the very early weeks and months of life – perhaps linked to the 2012 National Birth Cohort Study could make a rapid impact using existing resources (g, a)
- Modelling of the potential costs and benefits of initiatives such as mental wellbeing programmes for patients and accreditation schemes, multi-centre clinical audit and 360 assessments schemes for clinicians (a, e)
- New interventions, including non-drug treatments (Well conceived and executed, small scale studies leading to large scale) (a, c)
- Investigation into mental health of children and young people (g, d)

Question 4: What should be the medium and longer-term aims of a mental health strategy that would improve public health for which additional investment would need to be sought at a level of, say £10m, over the next 2-7 years?

- More drug studies – development, delivery, evaluation (g, d, g, a)
- Understanding of MH - including the underlying disease processes and the impact of treatments on integrated neuronal function, to reduce stigma and increase uptake of services (g, d, h)
- Strategies to reduce stigma are crucial to improving public health (i, h)
- A programme of research to build understanding of early life trajectory, aetiology and interventions (g, a)

b. Research infrastructure and personnel

Question 5: How best could we exploit current cohorts to examine factors influencing mental health and wellbeing? Are any new cohorts needed and if so, for what purpose?

- Exploit national and international bio-bank data (g)
- New large prospective cohort for defined mental disorders and family (g, d)
- Link cohorts: with networked collaboration and with primary care, combining cohort data (d, g)
- New cohort: Patients with schizophrenia (including research into perinatal factors and high risk of CV) (d, g)
- Look at gene x environment (d, a)
- Make cohorts accessible to researchers outside of planning consortia (g, a)

Question 6: What are the opportunities and barriers to access to biological resources (eg genetics, bioinformatics or biological samples), clinical networks, imaging etc?

- Barrier: Bureaucracy and over-regulation of research (g, a, a)
- Barrier: Gaining informed consent (i, d)
- Opportunity: Standardise genetic data collection (f, d)
- Barrier: Researchers not always generous in sharing data/facilities (f, d)
- Opportunity: Exploit cohorts (such as BASIS and ALSPAC) for translational research and make more accessible (i, g)

Question 7: How can information technology and e-resources be harnessed for the promotion of research into mental health and wellbeing?

- Improved access to anonymised data from health databases is needed (g, d)

Question 8: What are the priorities in building capacity and providing research training for personnel in mental health?

- More fellowships – including attractive financially worthwhile fellowships for all stages of career progression (g, i, i, d)
- Research training should be part of training for psychiatrists, nurses, psychologists, AHP etc (i, g, h)
- Protected time for clinical academics and other clinical staff who are often overloaded with NHS work (d, b, h)
- Improve infrastructure to support capacity building, eg centres of expertise and clinical trials units to focus on mental illness (c, h)
- Provide a good clear career pathway (i, i)
- Support both clinical and non-clinical researchers (g, d)
- A high attrition between PhD (or MD) and independent researcher is not helped by shortage of fellowship funding (g, d)
- Bridge gap between academics/basic research and clinicians to make transition easier and foster collaboration (a, d)
- Make use of clinical material (g, d)

c. Engaging stakeholders

Question 9: How could users best be engaged in the design of studies?

- Existing SU research groups are invaluable resource. Many members who are educated in research and have the lived experience of mental illness influence priorities and define research questions (h, f, i, j)
- Create groups of users with particular interest in and knowledge of research. Users can receive targeted training. They can participate in study design, steering groups, and in the research itself (g, d, i)
- Train and encourage academics to engage with users (h, i, j)
- SUs should only be involved at levels appropriate to their expertise. Users are not always the most qualified to determine quality of study design (g, a)
- Researchers to hold focus group meetings for stakeholders for their perspective on value, prioritisation, design, and implementation of research (i, h)

Question 10: Do you have any views on how the MRC could develop stronger links between academia and industry to facilitate drug development and evaluation?

- Mechanisms for dealing with issues of intellectual property, data sharing and open publication would need to be addressed (g, d, h)
- The negative view of the public and regulatory authorities to 'big pharma' needs to be addressed and reduced (g, g, h)
- Support funding programmes and joint posts between universities and industry – and/or secondments (g, d, g)
- The development of models to identify and exclude novel pharmacology early in investigation (g, d)
- Targeted support for industrial collaborations would be valuable (g, d)
- CASE awards provide collaboration at PhD level. Collaboration at Fellowship or project grant level is not favoured (g, d)
- Drug development should not be considered in the context of mental wellbeing (a, d)

Question 11: What role could interdisciplinary research play in the longer-term strategy in delivering public health needs (ie within biomedical research and within population and social science)?

- Interdisciplinary research is vital part of a short and the long term strategy to meet public health and mental health needs (g, i, d, g, d, a, h)
- A top-down/bottom-up approach could work best in translational research (ie clinical research informs animal studies and vice versa) (g, d)

Question 12: Consider how the MRC and OSCHR partners might develop a joint strategy with stakeholders to reduce stigma and raise the profile of the health needs of those affected by mental health issues.

- Working with Time to Change campaign could be explored (i, b)
- Educational initiatives are important, perhaps at school level (d, b)
- Moves to overcome the stigmatising regarding the risk mentally ill patients pose to the public (a j)

d. Specific, thematic priorities

Question 13: Are there any specific areas of UK mental health research that are underfunded?

- Mental wellbeing research in general (d, g, f, a)
- Prevention and intervention research (i, d, g)
- Severe or chronic MI (h, f, h)
- Eating disorders – including co-morbidities with learning difficulties (h, g, h)
- Understanding co-morbid conditions (mental and physical) (i, g, f)
- Consistent evaluation of therapies – pharmacological and non-pharmacological (g, a)
- Children and adolescents; wellbeing, substance misuse, self harm, suicide prevention (g, h)
- Forensic mental health (i, j)
- Infant mental health (g, a)
- Intellectual disabilities (i, a)
- Bipolar disorder and personality disorder – given the size of the problem (f, d)
- Dementia – and emotional co-morbidities (i, g)
- Inter-individual variability – why and how do individuals vary in respect to vulnerability and resilience, efficacy of treatment, prognosis etc (g, d)
- Cognition in MH disorders – cognitive deficits are apparent in both psychotic and mood disorders and impact quality of life (g, d)
- Suicide research (i, i)

Appendix 1 Consultation document

Introduction

The Medical Research Council (MRC) has been given the role to lead on mental health as a public health theme on behalf of the Office of Strategic Coordination of Health Research. As part of this, the MRC is now developing a research strategy for mental health across the biological, medical and health research sectors. Key drivers behind the exercise are the significant burden of mental health on care systems and society and the increasing priority of mental health for a number of key policy leaders. The review will consider future research opportunities and tractable priorities for investigation. It will recommend a strategy for investment over both the short to medium term.

In order to deliver a strategic framework for mental health research and a potential bid to the next Treasury spending review, a Strategic Group (membership and Terms of Reference at Annex A) was set up. This group agreed to divide mental health into four themes (see below) to be overseen by Sub-groups. As part of their work, each Sub-group held a workshop with an invited group of experts. Each Sub-group then summarised the workshop outcomes by answering a series of generic questions.

Themes for mental health review

- Severe mental illness (primarily psychosis);
- Anxiety and depression (bipolar disorder was included in this theme);
- Neurodevelopmental, learning and intellectual disabilities;
- Pathways to mental wellbeing.

The Review Consultation

The MRC wishes to further consult a wide range of individuals, groups and organisations to increase the opportunity for potential stakeholders to present views and evidence. This consultation is based on the questions addressed and the themes that emerged at the four Sub-group workshops. The views drawn from this further consultation will inform the ongoing work of the review and feed into the recommendations to be reported in December 2009. Responses to the consultation will be considered alongside further discussion by the Strategic Group.

Consultation Process

A series of questions are set out below that cover the key cross-cutting issues of the review. We would welcome your views on any or all of the questions. We suggest you give your response as a series of bullet points in order to facilitate analysis of the responses. Please send in your comments by **19th September 2009**.

Confidentiality

Please note that any information you provide may have to be disclosed in accordance with the Freedom of Information Act (2000) and the Data Protection Act (1998). Where any respondent wishes their response to remain anonymous this will be considered by the review team. Any individual's names and personal contact details will be removed.

Mental Health and Wellbeing: Consultation Questions.

The questions below are grouped around four cross-cutting issues:

a. Opportunities for UK mental health research based on current strengths and weaknesses;

b. Research Infrastructure and personnel;

c. Engaging stakeholders;

d. Specific, thematic priorities.

a. Opportunities for UK mental health research based on current strengths and weaknesses

Question 1:
What weaknesses in UK research into mental illness and wellbeing are apparent and in which areas could the UK make an impact with some targeted investment?

Question 2:
Related to the above, what are the research opportunities in the light of other UK and international activity? What strengths should the UK play to, and what should we avoid doing?

Question 3:
What are the immediate and tractable priorities for investigation that would make an impact using existing resources (say £3-5m) in the short term (next 2 years)?

Question 4:
What should be the medium and longer-term aims of a mental health strategy that would improve public health for which additional investment would need to be sought at a level of, say £10m, over the next 2-7 years?

b. Research infrastructure and personnel

Question 5:
How best could we exploit current cohorts to examine factors influencing mental health and wellbeing? Are any new cohorts needed and if so, for what purpose?

Question 6:
What are the opportunities and barriers to access to biological resources (eg genetics, bioinformatics or biological samples), clinical networks, imaging etc?

Question 7:
How can information technology and e-resources be harnessed for the promotion of research into mental health and wellbeing?

Question 8:
What are the priorities in building capacity and providing research training for personnel in mental health?

c. Engaging stakeholders

Question 9:
How could users best be engaged in the design of studies?

Question 10:
Do you have any views on how the MRC could develop stronger links between academia and industry to facilitate drug development and evaluation?

Question 11:
What role could interdisciplinary research play in the longer-term strategy in delivering public health needs (ie within biomedical research and within population and social science)?

Question 12:
Consider how the MRC and OSCHR partners might develop a joint strategy with stakeholders to reduce stigma and raise the profile of the health needs of those affected by mental health issues.

d. Specific, thematic priorities

Question 13:
Are there any specific areas of UK mental health research that are under funded?

Question 14:
What are the specific priorities in the following topics?

Underpinning research and aetiology

Prevention of disease and conditions, and promotion of wellbeing

Detection, screening and diagnosis

Development and evaluation of treatments and therapeutic interventions (including clinical trials)

Management of diseases and conditions (including Service Delivery and Organisation)

Health and Social Care Services Research

Annex D

Analysis of Mental Health Research Funding

In this annex we review the major investments by the MRC and NIHR with brief reference to funding for mental health research in Europe and North America. This annex then proceeds to describe an analysis of the success rate for applications for research grants and training fellowships submitted to the MRC. Finally, this annex draws on a recent analysis of OSCHR members' training portfolios, making reference to mental health and psychiatry.

The classification of research for these analyses is set out in section D6. Where there are known caveats to the data presented, these are stated in the text.

D1. A snapshot of mental health research funding in the UK

This section reviews UK funding for mental health research and identifies the main funders and how much they spend (where known) on mental health research.

D1.1 The funders of mental health research in the UK

Mental health research in the UK is funded by Government Departments, the research councils, charities and industry. Four research councils invest in this area, the Medical Research Council (MRC) being the major funder of mental health research. The Biotechnology and Biological Sciences Research Council (BBSRC) funds research relevant to understanding normal brain function that underpins knowledge of mental illness; the Economic and Social Research Council (ESRC) supports social science, psychology and education research in the area of mental health and wellbeing and addiction; and the Engineering and Physical Sciences Research Council (EPSRC) supports research in underpinning technology development eg neuroimaging. The National Institute for Health Research (NIHR) is the other main public funder of mental research in the form of both infrastructural support for clinical and health research and 'programme' funding. The role of the MRC and the NIHR in funding mental health research is expanded upon in section D2.

The bulk of charity investment in this area comes from the Wellcome Trust with additional support from a handful of disease specific charities.

- The Wellcome Trust is the largest charity in the UK and supports biomedical research spanning genetics to epidemiology. A list of awards in mental health can be found on their web site at www.wellcome.ac.uk
- Autism Speaks Inc. has developed a strategic research plan underpinned by an annual research budget of around $30m. Although primarily a funder in the USA, it supports high quality international research and has funded significant projects in the UK in partnership with the MRC. Autism Speaks also has a UK arm, recently relaunched as Autistica, which is developing its own research activity.
- Research Autism is a UK charity exclusively dedicated to research into interventions in autism.
- SANE supports research that focuses on the social and psychological impact of mental illness.
- The Nuffield Foundation is a UK charitable trust which funds research advancing social wellbeing.
- Action on Addiction supports research specifically in the area of addiction, for example through funding the National Addiction Centre at the Institute of Psychiatry, King's Collage London.
- Mental Health Research UK[28] is a new charity that will raise funds for research into mental illnesses, their causes and cures.

D1.2 Total spend on research by UK funders of mental health research

The spend on mental health research versus the total spend on research by the major UK funders in the financial year 2007/08 is detailed in Table 1 below. OSCHR members alone spent over £1.3 billion on research in 2007/08 through grants, research centres and training fellowships. Of this, about 7 per cent (£91.5m) was spent on mental health research[29]. There was insufficient data available to accurately measure the total investment on mental research each year, but it is approximately £130m.

28 At the time of this review, at least two other mental health research charities were being set up or considered.
29 Data was not requested from Northern Ireland's Public Health Agency.

Table 1. Spend on mental health (MH) research versus all research in the financial year 2007/8 by some of the main UK funders of mental health

Funder	Total research spend (£)	Total MH research spend (£)	% of total in MH
CSO	52.8m	4.1m	7.8%
ESRC~	105.8m	1.4m	1.3%~
MRC (grant title analysis)*	579m	21.2m	3.7%*
MRC (HRCS analysis)**	579m**	34.0m	5.9%**
NIHR (infrastructure and programmes) _	702m	65.6m	9.3%
WORD °	2.4m	0.6m	26%
Total (MRC value used is the spend by grant title analysis)	**1442m**	**92.9m**	

Key:

Chief Scientist Office Scotland (CSO), the Economic and Social Research Council (ESRC), the Medical Research Council (MRC), the National Institute for Health Research (NIHR), the Welsh Office of Research and Development for Health and Social Care (WORD)

~ ESRC's remit is economic and social science. Therefore, spend on mental health research is expected to be lower than that for funding organisations that focus on medical and health research. ESRC is not an OSCHR member.

* Data based on an analysis of grant titles. See text following table 2 for explanation.

** This data is based on the Health Research Category Codes (HRCS) devised by the UK Clinical Research Collaboration for their UK Health Research Analysis, and includes components of other MRC investments relevant to mental health omitted in the 'grant titles' analysis. See text following table 2 for explanation.

_ NIHR research spend was estimated as set out at section D6.2. Spend includes funding for research programmes as well as support for research infrastructure. See text following table 2 for explanation.

° Total research spends in 'Research Funding Scheme'. Fellowships not included in this analysis.

The Wellcome Trust (WT), who spend around £600m a year on biomedical research, are major funders of MH research, however the Trust was unable to provide portfolio data for this report. In 2004/05 the UKCRC Health Research Analysis collected data suggesting that the Trust spent 5.3% of their total budget on mental health.

D2. Research spend in mental health by the MRC and NIHR

The section focuses on MRC and NIHR funding with a small section on the international perspective (section D2.3).

D2.1 Trends in research spend in mental health research by the MRC and NIHR

Total research spend in mental health research by the MRC and the NIHR in the financial years from 2005/06 to 2008/09 is detailed in Table 2 below and shown graphically in figures 1 and 2.

Table 2. Total annual spend in MH research by the MRC and NIHR in financial years 05/06 – 08/09

Organisation	2005/6	2006/7	2007/8	2008/9
MRC (grant titles)	£12.8m	£18.6m	£21.2m	£24.4m*
MRC (HRCS)	Data not available	£31.8m	£34.0m	£40.2m**
NIHR (infrastructure and research programmes)	£59.8m	£64.0m	£65.6m	£67.9m_

* Data based on an analysis of grant titles. This represents a conservative estimate as the spend exclude any grants for generic activities that might be relevant to mental health, large grants where some of component projects are on mental health and all neurodevelopmental, imaging technology and pharmacological studies at the basic end of the mental health research spectrum.

** This data is based on the Health Research Classification System (HRCS)- see D2.2 – and includes components of other MRC investments relevant to mental health omitted in the 'grant titles' analysis. It includes studies of normal psychology, cognitive function and behaviour where these are being undertaken with a view to informing mental health research.

_ Figures include all research and associated costs including direct research spend, infrastructure and support costs (please refer to the NIHR annual report for definitions at http://www.nihr.ac.uk/files/pdfs/NIHR%20Health%20Report%20final.pdf

NIHR total spend in 2008/09 was £819.2m, of which infrastructure spend was £397m and programme spend was £116m. The infrastructure spend on mental health includes the service support costs of HTA trials, the Biomedical Research Centre at the Institute of Psychiatry (see section D4) and the Mental Health Research Network (MHRN). The annual investment in MHRN is currently £4.2m per annum.

Figure 1. Total research spend in MH by MRC and NIHR in financial years 2005/06 – 2008/09

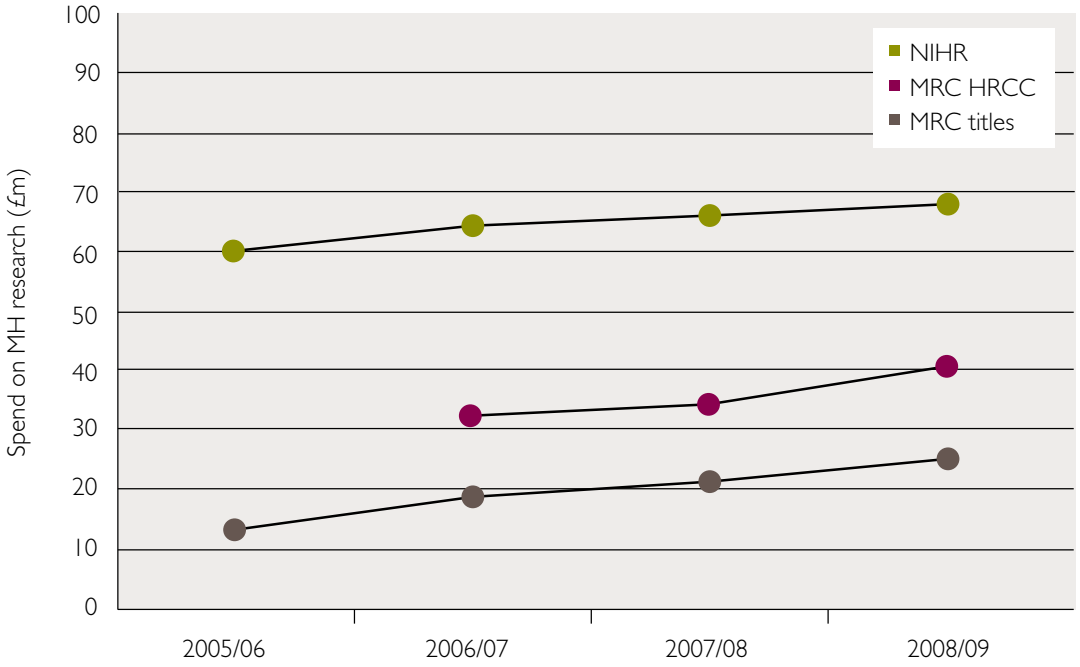
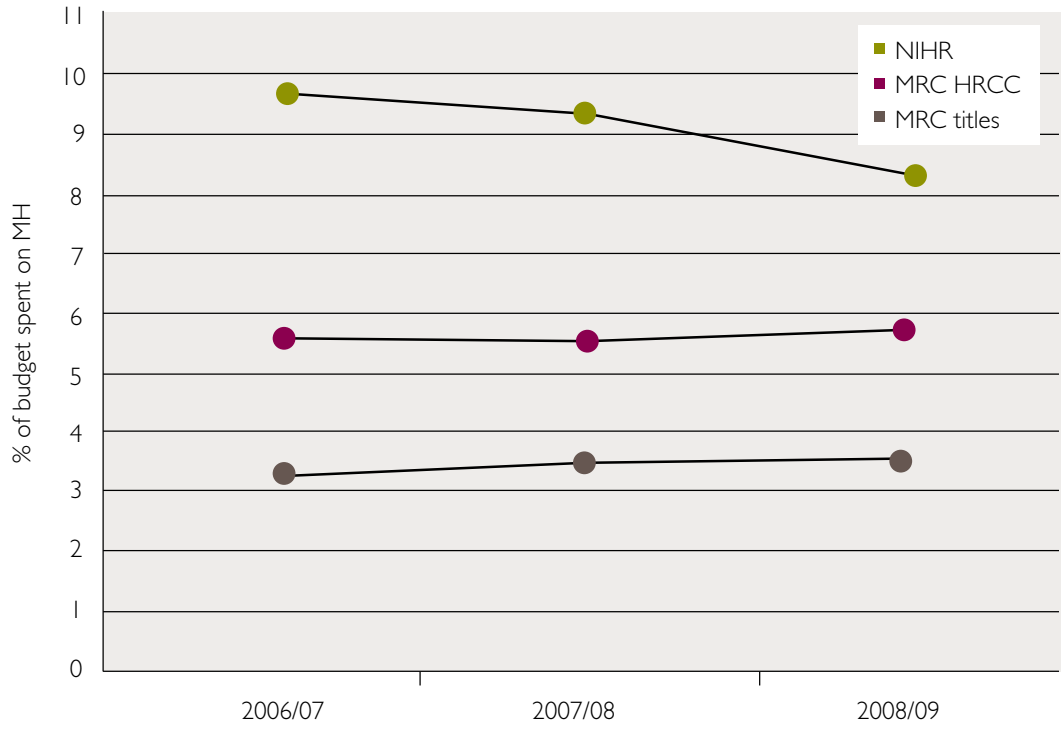


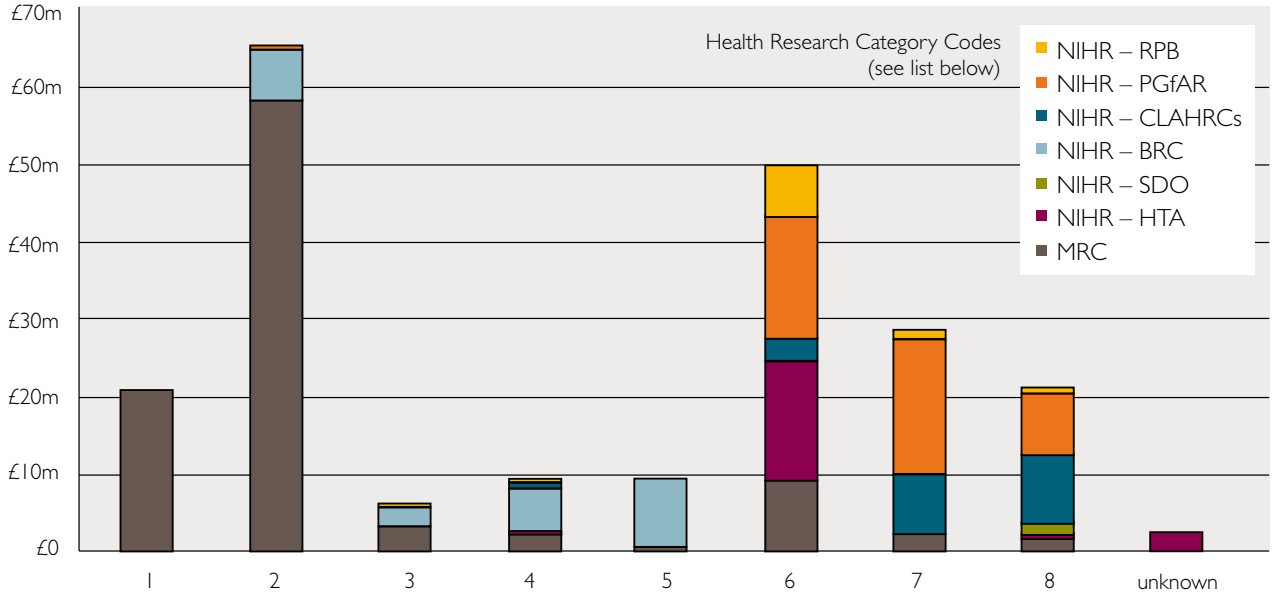
Figure 2. Proportion of total research spend by MRC and NIHR on MH research in financial years 2006/07 – 2008/09



D2.2 Research activities within mental health funded by the MRC and NIHR

The UKCRC Health Research Classification System (HRCS) describes broad areas of research activity in eight overarching categories (defined below). Whereas data presented in section D2.1 showed all mental health research funding data-coded by HRCS, in this section we divide the current[30] MRC and NIHR funding for mental health research as coded by HRCS into the separate research categories. This provides a pictorial view of the areas within the research spectrum (or translational pipeline) where investment has been made.

Figure 3. Live committed research spend in MH by the MRC and NIHR in 2009 according to UKCRC Health Research Classification System



Key to Figure 3

- UKCRC Health Research Activities are defined below. Note that HRCS category 5 is preclinical, and HRCS 6 is clinical development. Therefore all clinical trials, from healthy volunteers in Phase I and II, through to Phase III and IV, are all included in HRCS 6. Research that involves patients can be classified in HRCS 2 (aetiology): this is common in MH research.
- MRC schemes are not subdivided in the graph, however note that the live committed mental health research spend of £98.8m in June 2009 was distributed between grants (£77.3m), fellowships (£12.2m) and unit (intramural) programmes (£9.3m).
- Key to NIHR funding schemes: HTA - Health Technology Assessment, SDO – Service Delivery and Organisation, RfPB - Research for Patient Benefit, PGfAR - Programme Grants for Applied Research Programme, BRC – Biomedical Research Centres and CLAHRCs.
- Live committed spend in MH (excluding infrastructure and support costs) for NIHR in June 2009 was £67.0m with the majority of that commitment in the HTA, RPB and PGfAR schemes.

30 As of June 2009.

UKCRC Health Research Category Codes

1 Underpinning Research
2 Aetiology
3 Prevention of Disease and Conditions and promotions of Well-Being
4 Detection Screening and Diagnosis
5 Development of Treatments and Therapeutic Interventions
6 Evaluation of Treatments and Therapeutic Interventions
7 Management of Diseases and Conditions
8 Health and Social Care Services Research

Figure 3 shows that the areas receiving the least funding are: Prevention of Disease and Conditions and promotions of Well-Being, Detection Screening and Diagnosis, and Development of Treatments and Therapeutic Interventions. This is a common scenario in other health research areas as noted in the UK Clinical Research Collaboration UK Health Research Analysis[31].

A survey of the titles of the grants awarded by the MRC and NIHR indicated that research studies are funded across the full spectrum of psychiatric disorders, but that there was an emphasis on severe depression and psychosis. In contrast, relatively little funding for research was directed towards anxiety disorders, moderate or mild depression, bipolar disorder and child and adolescent mental health (including autism and ADHD).

D2.3 International Perspective

D2.3.1 European Union (EU) funding for mental health research

The EU mainly supports research through the European Commission's Framework Programmes (FP), which provide long-term support for collaborative research undertaken by European consortia, as well as support for pan-European training and research infrastructure. At the time of the review, the seventh Framework Programme (FP7) was underway.

Under FP6 (2002-2006), €17.5bn total science funding was made available, of which approximately €2.5bn was allocated within the Health Research Theme. Of this, €0.02bn was awarded for mental health research. FP7 was launched in January 2007 and at February 2009, €6.7bn funding had been allocated. Of this, €0.9bn was allocated within the Health Research Theme and of this amount, €0.018bn was awarded for mental health research. Mental health research therefore amounts to about 0.1-0.3 per cent of the total FP budget and around 2 per cent of the total health budget (the health budget amounts to around 10-15 per cent of the total science budget)[32].

D2.3.2 National Institutes of Health (NIH) USA

The NIH is part of the US Department of Health and Human Services and is the primary federal agency for conducting and supporting medical research. In the fiscal year 2007/08, NIH invested about $30 billion in medical research. According to the online reporting tool (RePORT) investment in mental health was £2bn, primarily through the $1.4bn provided by the National Institute of Mental Health (NIMH). Other funding for mental health comes via the National Institute for Drug Abuse (NIDA), the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and the Department of Veterans Affairs. Total federal investment in mental health research approximates to around 7 per cent of total research spend.

D2.3.3 The Canadian Institutes of Health Research (CIHR)

CIHR is a 'Departmental Corporation' which acts at arms length to government, but is accountable to the Canadian Parliament through the Minister of Health. In the fiscal year 2007/08, CIHR invested about C$870 million in research projects and personnel support across the full spectrum of health sciences research, of which $65.9m was directed towards mental health and addiction-related research. This represents between 7 and 8 per cent of the CIHR research project budget.

D3. Key MRC and NIHR investments in mental health research

This section provides brief details on some of the major strategic investments by the MRC and NIHR in mental health. Some of these investments are in partnership with other funders. The investments listed below provide a snapshot of some major activities. It is not intended to be a comprehensive or systematic analysis of all the key investments in mental health. For example, we have not described any of the numerous programme grants that both the MRC and NIHR fund on mental health.

D3.1 MRC Investments

D3.1.1 The MRC Centre for Social, Genetic and Developmental Psychiatry (SGDP)

The centre was launched in 1994 in partnership with the MRC and the Institute of Psychiatry at King's College London. The centre aims to bridge the gap between 'nature' (genetics) and 'nurture' (environment) as they interact in the development of complex human behaviour, such as depression, autism, ADHD and conduct disorders in children.

http://www.mrc.ac.uk/Ourresearch/Unitscentresinstitutes/UnitCentreDetails/MRC002070

31 http://www.ukcrc.org/researchcoordination/healthresearchanalysis/ukanalysis/
32 At the time of the review, plans were in place to award grants for addiction research under a call within FP7.

D3.1.2 The MRC Centre for Neuropsychiatric Genetics and Genomics (CNGG)

The MRC Centre for Neuropsychiatric Genetics and Genomics at Cardiff University is also supported by funding from the Welsh Assembly Government's Wales Office of Research and Development (WORD) and the university itself.

The centre will tackle mental illnesses like schizophrenia and bipolar disorder, developmental disorders like dyslexia and childhood depression, as well as degenerative brain diseases like Alzheimer's, Huntington's and Parkinson's.

http://www.mrc.ac.uk/Ourresearch/Unitscentresinstitutes/UnitCentreDetails/MRC006217

D3.1.3 The MRC / WT Behavioural and Clinical Neuroscience Institute (BCNI)

The University of Cambridge Behavioural and Clinical Neuroscience Institute, is supported by a joint award from the MRC and the Wellcome Trust. The institute links clinical research at the level of functional neural systems to basic work on the brain with a common theme of different neuroimaging modalities and neuropsychopharmacology. Its research programmes address a wide range of neuropsychiatric disorders and addiction.

http://www.mrc.ac.uk/Ourresearch/Unitscentresinstitutes/UnitCentreDetails/MRC002079

D3.1.4 The MRC Cognition and Brain Sciences Unit (CBSU)

The unit in Cambridge investigates fundamental human mental processes such as attention, memory, communication and emotion. Within the unit, clinical research addresses the assessment and management of a wide range of behavioural and brain disorders, including ADHD. Research also focuses on emotion, cognition and self-regulation, particularly in clinical conditions such as depression and post-traumatic stress disorder (PTSD).

http://www.mrc.ac.uk/Ourresearch/Unitscentresinstitutes/UnitCentreDetails/MRC002119

D3.1.5 The MRC Social and Public Health Sciences Unit (SPHSU)

This unit, situated in Glasgow, receives core funding from the Chief Scientist Office at the Scottish Government Health Directorates in addition to the MRC. The unit aims to promote human health via the study of its social and environmental influences. Research projects are investigating psychological morbidity in young people, predictors and consequences of anxiety disorder, development of psychiatric assessment tools and self-harm. Research outcomes from the unit's work have been important in guiding both local and national mental health policies and service provision in Scotland for children and young people.

http://www.mrc.ac.uk/Ourresearch/Unitscentresinstitutes/UnitCentreDetails/MRC002097

D3.2 NIHR Research Investments

NIHR investments are divided into infrastructure and programmed investments. This subsection highlights two of the main infrastructure investments in mental health that have been made by the NIHR. The NIHR also provides the NHS support costs of clinical trials and other well designed studies.

A significant investment in programmes grants for mental health research had been by NIHR at the time of this review.

D3.2.1 The Mental Health Research Network (MHRN)

The Mental Health Research Network (MHRN) is one of the Topic Specific Networks of the NIHR CRNCC (Clinical Research Network Coordinating Centre). The Network provides the NHS infrastructure to support commercial and non-commercial large scale research in mental health, including clinical trials. The MHRN encourages collaboration, which is facilitated by clinical research hubs. Each hub is comprised of academic and clinical organisations and user and carer networks, bringing together a wide range of skills and expertise in mental health research and service provision in order to support MHRN-adopted research.

Scotland has also established a Mental Health Research Network.

D3.2.2 Biomedical Research Centre for mental health at King's College London

The NIHR has created 12 Biomedical Research Centres to drive progress on innovation and translational research in biomedicine. The Centres receive substantial levels of funding to translate fundamental biomedical research into clinical research that benefits patients and they will be early adopters of new insights in technologies, techniques and treatments for improving health.

One Specialist Biomedical Research Centre focuses on mental health – this has been established at the Institute of Psychiatry, King's College London in collaboration with the South London and Maudsley (SLAM) NHS Trust.

D3.3 Cross-Council Investments

D3.3.1 Lifelong Health and Wellbeing and 'Ageing' centres

The Lifelong Health and Wellbeing Programme is a cross-council initiative to strengthen multidisciplinary and collaborative research in ageing. In phase one of the programme three new 'lifelong health' research centres were announced in 2008, funded by the MRC, the Biotechnology and Biological Sciences Research Council (BBSRC), the Engineering and Physical Sciences Research Council (EPSRC) and the Economic and Social Research Council (ESRC). The centres will carry out research on healthy ageing, targeting the major determinants of health and wellbeing over the whole life course and reducing dependency in later life.

The Centre for Cognitive Ageing and Cognitive Epidemiology at the University of Edinburgh investigates how ageing affects cognition (cognitive ageing), and how mental ability in youth affects health and longevity (cognitive epidemiology).

The Crucible Centre at University College London will integrate research on longevity with the aspiration of improving levels of wellbeing.

The Centre for Brain Ageing and Vitality at Newcastle University will develop two main programmes to address the relationship between the healthy ageing brain and the healthy ageing body.

D3.3.2 UKCRC Public Health Centres

The UK Clinical Research Collaboration (UKCRC) Public Health Research Centres of Excellence Initiative aims to produce excellent research that has potential for impact on health by building academic capacity, increasing infrastructure and promoting multidisciplinary working in public health research. The five UKCRC Public Health Research Centres of Excellence bring together leading researchers with practitioners, policymakers and members of the public to tackle complex public health issues. The Centres are listed at:

http://www.esrcsocietytoday.ac.uk/ESRCInfoCentre/research/centres/ukcrc.aspx

The MRC contributed to this £20 million, jointly-funded investment (£3m over five years).

D3.4 A Cross Funder Initiative (PsyGrid)

PsyGrid was set up to provide resources to clinicians, researchers and others interested in first episode psychosis through the use of 'Health Informatics'.

By collecting data through databases, e-learning resources, electronic records and communications systems, PsyGrid initially tracked a large, representative cohort of individuals with first episode psychosis to enable epidemiological and intervention research.

PsyGrid is an e-science project that has the potential to address many of the problems that arise within the healthcare system today. It is funded from several sources including the MRC, ESRC and NIHR. It operates in each of the geographic hubs of the MHRN.

D4. Success rates of MRC applications for mental health research[33]

This section reviews the outcome of an exercise by MRC to assess the success rates for applications to MRC for mental health research. This analysis was performed to better understand the contributory factors behind the concern that mental health research is under funded relative to burden of disease. This analysis, therefore, sought to ascertain whether there were issues of unintended bias in the peer review system or low research quality or capacity.

The MRC funds mental health research under a number of different schemes and through its research boards. Below is an analysis of award rates for

1. Two MRC boards (NMHB and HSPHRB);
2. The major MRC training fellowship schemes;
3. A previous dedicated initiative for neuroscience called 'Brain Sciences';
4. The new MRC schemes and initiatives set up under OSCHR to address 'translational bottlenecks'.

D4.1 Neuroscience and Mental Health Board (NMHB) and Health Sciences and Public Health Research Board (HSPHRB) 2004/05 to 2008/09

Table 4 lists the success (by number of applications and value of awards) of applications for mental health (MH) research submitted to the Neuroscience and Mental Health Board (NMHB) in a five-year period compared to the award rate of all applications (in all areas of neuroscience including mental health). Figures are based on total spend for each financial year between 2004/05 and 2008/09 in applications to NMHB.

A comparative analysis was also undertaken for applications to the Health Services and Public Health Research Board (HSPHRB). Here the comparison is between mental health and all other fields, conditions and disease areas. Composite data for HSPHRB is shown over five years as the numbers of applications to this Board is much lower than to NMHB.

In both analyses, mental health research was classified as set out in section D6.

33 Although analysis was restricted to MRC schemes, at the time of this review, the awards rate for NIHR programmes in mental health was 26 per cent (by number).

Table 4. Award rates in applications to MRC NMHB and HSPHRB

Year	Number of applications submitted		Award rate (number of applications)		Award rate (funding requested)	
	MH	All*	MH (%)	All (%)	MH (%)	All (%)
	NMHB**					
2008/09	72	345	15.3	16.2	22.9	22.2
2007/08	83	321	14.5	20.9	19.4	29.3
2006/07	63	276	22.2	21.0	26.6	26.9
2005/06	68	339	13.8	16.8	23.3	24.3
2004/05	57	227	49.1	31.3	44.8	33.3
	NMHB					
2004/08	340	1508	23.0	21.2	27.4	27.2
	HSPHRB***					
2004/08	53	408	33.5	36.3	33.1	41.1

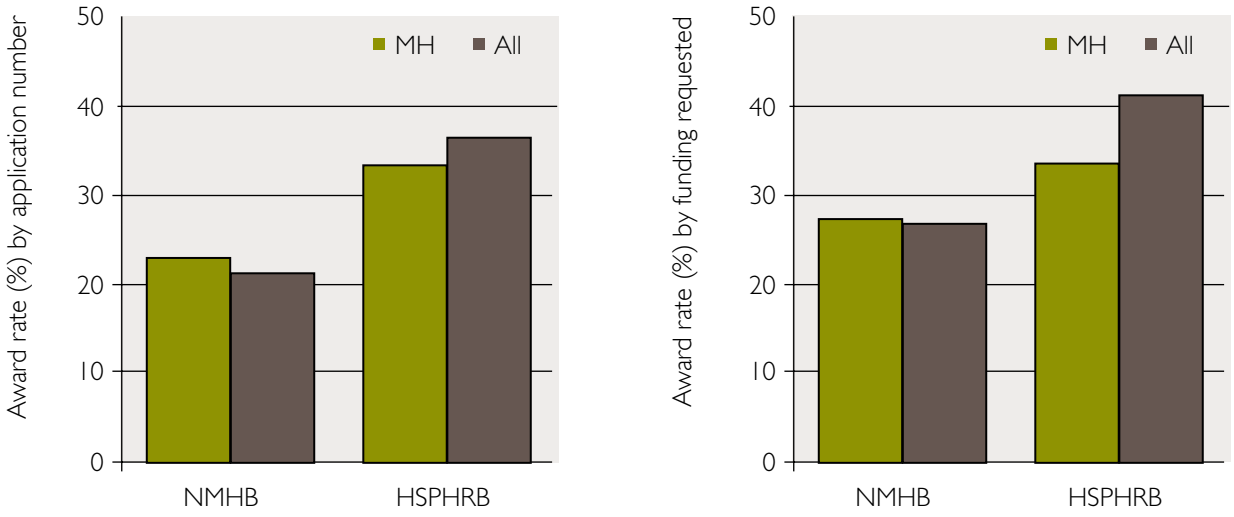
* All – includes applications for MH

** NMHB remit is programmes and funding in neurosciences and mental health

*** HSPHRB (now disbanded) remit was health services and public health research including methodology and clinical trials

Table 4 shows that over a five-year period there was very little difference in the award rates for applications for grants to fund mental health research in comparison to the award rate for all applications received. The award rates for MH research were slightly higher for those submitted to NMHB and slightly lower for HSPHRB. Taken together, the differences were not statistically significant. It therefore seems unlikely on the basis of this analysis that the low capacity in the field of mental health research is due to inferior quality or due to issues with peer review. The data is shown graphically in figure 4.

Figure 4. Award rates over five years between 2004 and 2008 in applications to the MRC NMHB and HSPHRB by numbers of applications (a) and by funding requested (b)



D4.2 Fellowship training schemes 2003 to 2009

The award rate of applications to MRC fellowship schemes for research training in mental health is similar to the award rate for all applications. The only exception is the Senior Clinical Fellowship scheme, where the award rate for mental health is much lower. However, the number of applications to this scheme is small – just five applications.

Table 5. Award rates in application number in MRC fellowship applications 2003 to 2009

Scheme	Application award rate	
	MH % (n)	All % (n)
Career Development Awards	25 (20)	21 (540)
Clinical Research Training Fellowship	34 (65)	35 (1139)
Clinician Science Fellowship	30 (30)	36 (299)
Senior Clinical Fellowship	20 (5)	43 (85)
Total	**31 (120)**	**32 (2063)**

D4.3 Brain Sciences

Following the UK Government's spending review in 2002, a £15m cross-research council initiative was set up to undertake research in brain sciences. The MRC launched two calls for proposals under this initiative to encourage project ideas in all areas of brain sciences but particularly those relevant to mental health and neurodegeneration. Two types of grant were provided: Pathfinder awards for high-risk, high pay-off research and Trial Platforms to help establish feasibility for future high quality trials. Table 6 summarises the award rates in these two calls, indicating that MH proposals were slightly more successful than the average across all brain science. Of the 17 Trial Platform grants awarded in mental health, 10 led to a successful application for a full clinical trial.

Table 6. Award rates in the MRC Brain Sciences Trial Platform and Pathfinder awards

Scheme	Application award rate		Funding requested	
	MH % (n)	All % (n)	MH % (n)	All % (n)
Trial Platform	21 (81)	16 (148)	23	18
Pathfinder	9 (150)	7 (491)	9	7

D4.4 MRC-led 'translational and bottleneck' schemes

This section reviews the awards in mental health made under the schemes established following the Cooksey Review, for the period 2008 to 2011, to promote translational research[34]. The MRC was allocated £132m over the three years to expand MRC's translational and public health activities, much of which has been allocated to managed programmes and targeted investments to address translational 'bottlenecks'. Of the schemes described below, some of the funding was delivered through one-off calls for proposals and where this was the case, the date of the call is provided in brackets. This analysis looks at the outcome of six schemes (Table 7).

34 The MRC's description of translational research was deliberately broad: "the process of the bidirectional transfer of knowledge between basic work (in the laboratory and elsewhere) with that of the person, in health or disease."

Table 7. Outcomes of MRC translational schemes captured in September 2009

Scheme	Total awards (n)*	Total awards (by value)	MH** awards (number)	MH awards (by value)	% By No.	% By value
Patient cohorts	13	£7.3m	1	£0.7m	8	10
Methodology (investigator-led)	19	£5.9m	2	£0.6m	11	10
Models	20	£10.6m	1	£0.6m	5	6
Biomarkers***	19	£9.9m	2	£0.7m	11	7
DPFS†	24	£8.3m	2	£0.7m	8	9
Developmental clinical science††	5	£6m	None yet	n/a	n/a	n/a
Total	**100**	**£48m**	**8**	**£3.4m**	**8**	**7**

* All disciplines including mental health

** MH – mental health

*** There were two calls under the biomarker initiative: the data show the outcome of one call that had a decision point in October 2008. The development of biomarkers is now expected to be part of the purpose of research grants funding considered through the established MRC funding mechanisms.

† DPFS supports the development of novel therapies, interventions and diagnostics and the research tools used in the development of therapies, interventions or diagnostics.

†† Developmental Clinical Studies are early stage clinical studies which are on the development pathway for a new therapeutic/diagnostic/device/public health intervention (or a new indication for an existing intervention).

Although the total number of applications awarded under each of these schemes was low (at least at the time of this review), Table 3 shows that proposals for mental health research were as successful as other disciplines, though the number of applications submitted for mental health research was small.

D5. Survey of funding for psychiatry within the training portfolio of 12 major UK funders

A report by the OSCHR Human Capital Workstream, entitled 'OSCHR UK-Wide Survey of Health Research Fellowships 2009', detailed the fellowship awards of 12 major funders[35] in a snapshot of live funding in March 2009. The MRC-led Fellowship survey returned data on 1,600 fellowships to build a high-level map of investments in growing and sustaining the research capacity in clinical, health services and public health research. The final report can be found on the MRC website[36].

The funders participating in this study coded their fellowship data to include medical specialty and UKCRC codes. The UKCRC codes were identified only at the most basic level (a single health category and the primary research activity for each fellowship). The data present a rough snapshot of funding and should be interpreted with caution. The specialty list was derived from the one used by the Medical Schools Council, with further specialties added to give a fuller, but manageable, list. For further information about how the data was collected, please see the final report (see footnote for web link).

Figure 5 shows the distribution of different funders' support for fellowships within the OSCHR fellowship survey across the UKCRC health categories. This highlights that mental health receives a substantial proportion of the funding for fellowships from public funders, but is lacking the charity support which benefit research training on cancer and cardiovascular disease.

35 Funders participated: NIHR (DH), Chief Scientist Office (Scotland), Welsh Office of R&D, Health & Social Care R&D Northern Ireland, MRC, ESRC, Wellcome Trust, British Heart Foundation, Cancer Research UK, Arthritis Research Campaign, Academy of Medical Sciences, HEFCE

36 http://www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC006501

Figure 5. Funding for fellowships recorded in the OSCHR survey 2009 broken down into funders and UKCRC Health Research Categories

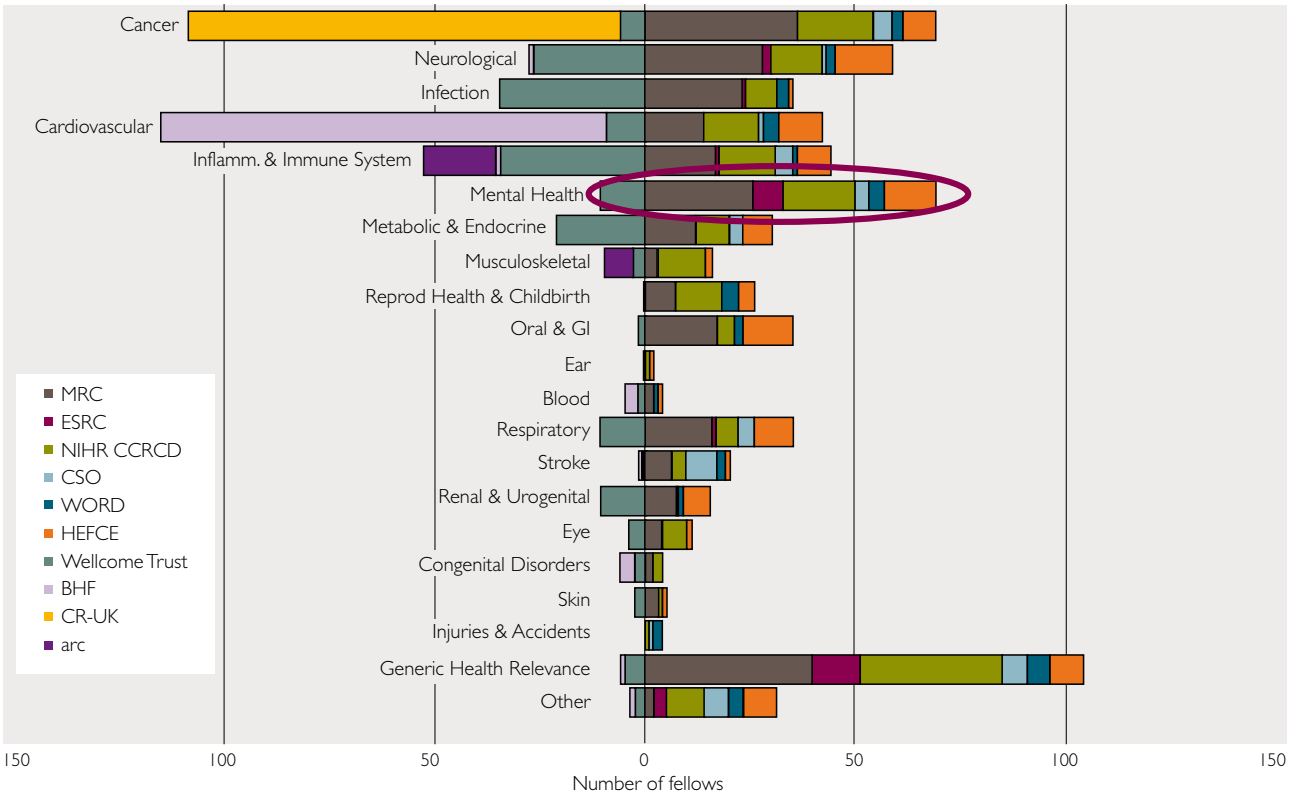
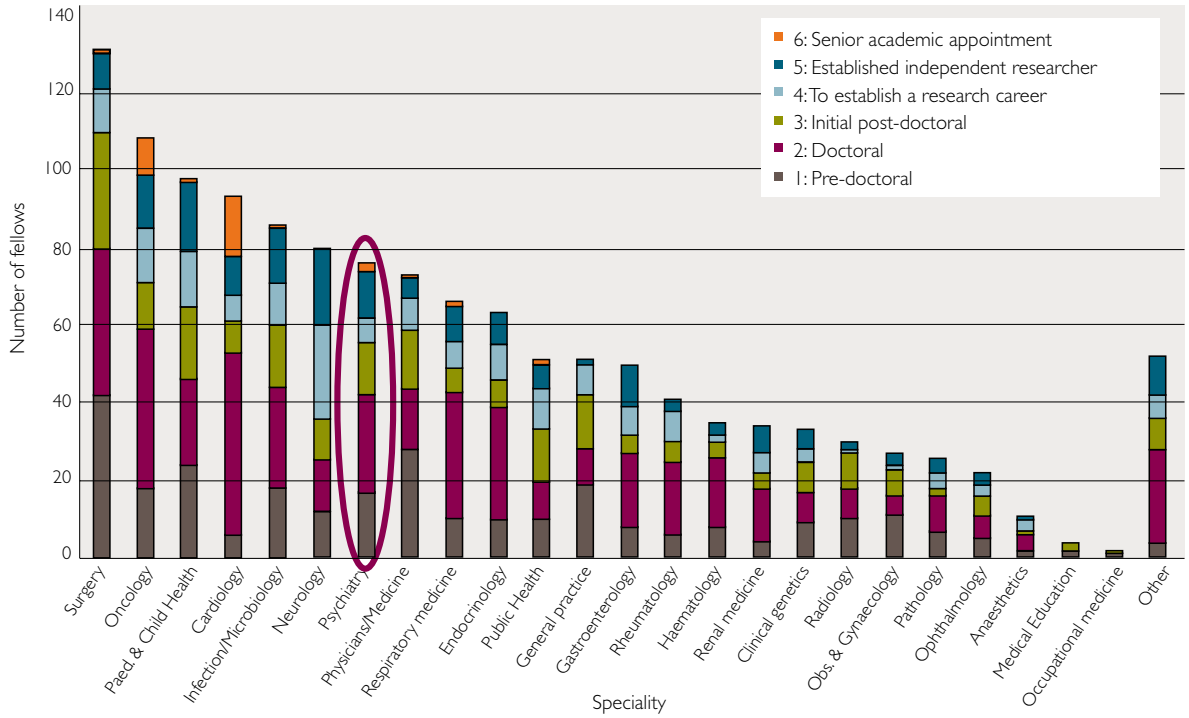


Figure 6 shows the number of fellowships reported in the OSCHR survey distributed across the different medical specialities (categorised by UKCRC Health Research Categories) broken down into the different career stages.

The OSCHR Fellowship survey indicates that psychiatry is neither one of the better nor one of the worst supported specialties.

The majority of awards are at pre-doctoral, initial postdoctoral and established independent researcher level. These positions have been supplemented in recent years by the NIHR-funded schemes to facilitate clinical research. The NIHR has invested in clinical training in mental health research with these schemes. One of the key findings of this report is that the integrated clinical academic career path of clinical fellowships (ACFs) and lectureships is beginning to have an impact.

Figure 6. The distribution of all medical fellowships in the OSCHR survey (excluding dentists) across speciality



The Medical Schools Council report many professorial positions for research active senior academics that are not captured on this graph.

D6. Classification of research for this analysis

D6.1 MRC data

The MRC total research spend used in this annex includes jointly funded programmes with other partners, including other research councils, Government Departments, research charities and external grant funding awarded to the MRC's own research units and institutes as well as international subscriptions.

To determine total funding and award rates in mental health, MeSH codes, UKCRC HRCS or, where necessary, identifying key words in the application title or abstract, were used. Combining all three methods ensured as accurate a representation of the funding in mental health as possible.

When assessing projects by title or abstract, research in the following areas was considered to be mental health research:

Addiction, substance use/misuse, autistic spectrum disorder, behavioural phenotype disorders, common mental disorders, eating disorders, neurodevelopmental disorders, personality disorders, psychiatric disorders, intellectual/learning disability, 5-HT, violence/risk taking/ other emotional behaviours.

For the purposes of this analysis, mental health does not include studies of neurodegenerative disease.

D6.2 NIHR data

Data collected by the NIHR for this report were categorised by UKCRC HRCS Coding. Therefore, the percentage of the total funding for each grant that was spent on mental health research was included in the data. The Biomedical Research Centre at the Institute of Psychiatry was assumed to be 100 per cent mental health research, but note that the NIHR-BRC is undertaking research into dementia.

D6.3 ESRC

Data collected by the ESRC for this report was for specific mental health projects and excluded some other streams of support such as those for psychology.

Below is a list of the key words used in the search for mental health research.

Neurobiology, pharmacological, psychosis, neuropsychology, anxiety, depression, bipolar, disorders, psychiatric, mood, learning disability, autism, schizophrenia, suicide, despair, neuroscience, psychopathology, paranoia, paranoid, hallucination, psychotherapy, hypnotherapy, ADHD, addiction, autism, amnesia, compulsions, obsessions, delusions, hyperactivity, dementia, neurosis, panic, self-harm, mania, neurodevelopment, mental health, inequalities, determinants, stress.

D6.4 Note of caution on all data and its interpretation

In this report data have been presented that were derived either through a bespoke analysis for this review or using existing data coded using the UKCRC-devised Health Research Classification System (HRCS). Both systems depend upon a subjective analysis, albeit by trained personnel, of what constitutes mental health research.

D7. General conclusions

The analysis highlighted two obstacles: the limited capability of UK mental health research to deliver the innovation needed, and the gaps in research in the area of prevention and treatment development. These obstacles to progress have to be addressed in any investment strategy for mental health research.

Annex D: Appendix 1

MRC and NIHR Programme Grants

MRC and MRC Programme grants that were 'live' during the period of the mental health review (Sep – Dec 2009).

NIHR programmes are awarded to an NHS Trust whereas MRC Programmes are awarded to a Higher Education institute (HEI).

The value of the award shown is the total value of the award. In the case of the MRC, this is 80 per cent of the Full Economic Costs.

Note that programme grants are usually funded for five years. The MRC has a specific definition of 'programme grant' and also a large portfolio of Research Grants. The latter mostly provide three years of funding, but some Research Grants also provide five years' support.

(MH = mental health)

MRC Awards

Lead Applicant	HEI	Title	Value of award
Professor Dale Hay	University of Cardiff	Early Prediction of Violence	£1,247,908
Professor Terrie Moffit	King's College London	Environment interplay in early-onset psychopathology	£3,131,833
Professor Sir Michael Marmot	University College London	Social influences on health	£1,495,963
Professor David Stephens	University of Sussex	Sensitisation to alcohol withdrawal: consequences and mechanisms	£1,287,002
Professor David Nutt	University of Bristol/ Imperial College London	Neurotransmitters in opiate and alcohol addiction	£1,177,198
Professor Robert Plomin	King's College London	Origins of learning difficulties and behaviour problems: from behavioural genetics to behavioural genomics	£1,750,976
Professor Lorraine Tyler	University of Cambridge	Cognitive neuroscience of normal and disordered language function	£801,117
Professor Barbara Maughan	King's College London	Adolescent conduct problems: a biosocial model of risk	£543,501
Professor Barry Everitt	University of Cambridge	Neural and psychological basis of compulsive drug seeking and relapse prevention in drug addiction	2,008,020
Professor Terrrie Moffitt	King's College London	Mental disorders from childhood to adulthood: the Dunedin Study	£785,827
Professor Philip Cowen	University of Oxford	Clinical Psychopharmacology of 5-HT	£1,698,637
Professor Mark Johnson	Birkbeck College	The typical and atypical development of the social brain during infancy	£1,694,860
Professor Jonathan Hill	University of Manchester	Social, emotional & biological processes in emergent conduct disorders: Wirral Child Health & Development Study 1-4 yrs	£1,796,024
Professor Michael Owen	Cardiff University	Molecular Genetics of Schizophrenia	£2,321,000

NIHR Awards

Lead Applicant	Contracting NHS Trust	Title	Value of award
Professor Thomas Burns	Oxfordshire and Buckinghamshire Mental Health NHS Foundation Trust	Coercion in mental health. Patterns and prevalence of coercion in mental health care and a trial of the effectiveness and costs of Supervised Community Treatment orders	£712,140
Professor Ulrike Schmidt	South London and Maudsley NHS Foundation Trust	Treatment of Anorexia nervosa: Translating experimental neuroscience into clinical practice.	£1,998,286
Professor Declan Murphy	South London and Maudsley NHS Foundation Trust	Crossing the divide. Effective treatments for people with neurodevelopmental disorders across the lifespan and intellectual ability	£1,999,319
Professor André Tylee	South London and Maudsley NHS Foundation Trust	A programme of research to develop and test stepped care for patients with depression and physical illness in primary care	£999,993
Professor Robin Murray	South London and Maudsley NHS Foundation Trust	Improving physical health and decreasing cannabis abuse in people with severe mental illness	£665,729
Professor Til Wykes	South London and Maudsley NHS Foundation Trust	Patient involvement in improving the evidence base	£1,999,618
Professor Graham Thornicroft	South London and Maudsley NHS Foundation Trust	Improving Mental Health Outcomes by Reducing Stigma and Discrimination	£1,999,538
Professor Christopher Dowrick	Liverpool Primary Care Trust	A R&D programme to increase equity of access to high quality mental health services in primary care	£2,000,000
Professor Anthony Morrison	Bolton Salford and Trafford Mental Health NHS Trust	Psychological approaches to understanding and promoting recovery from psychosis	£1,999,872
Professor David Challis	Manchester Mental Health and Social Care Trust	National Trends and Local Delivery in Old Age Mental Health Services: Towards an evidence-base	£612,847
Professor Swaran Singh	Birmingham and Solihull Mental Health NHS Foundation Trust	Ethnicity, Detention and Early Intervention: Reducing Inequalities and Improving outcomes for Black and Ethnic Minority (BME) Patients	£912,024
Professor David Gunnell	Avon and Wiltshire Mental Health Partnership NHS Trust	A multi-centre programme of clinical and epidemiological research in support of the National Suicide Prevention Strategy for England.	£926,382
Professor Shon Lewis	Lancashire Care NHS Trust	Early phase treatment for the prevention of relapse in first episode schizophrenia.	£1,406,726

NIHR Awards

Lead Applicant	Contracting NHS Trust	Title	Value of award
Professor Peter Jones	Cambridgeshire and Peterborough NHS Foundation Trust	Understanding Causes and Developing Effective Interventions For Schizophrenia and Other Psychoses	£1,976,676
Professor John Gladman	Nottingham University Hospitals NHS Trust	Medical crises in older people	£665,124
Professor Steven Jones	Manchester Mental Health and Social Care Trust	Understanding and addressing risk in bipolar disorder: Practical approaches to help services users and health professionals reduce relapse, self harm and suicide	£1,997,431
Professor Jeremy Coid	East London NHS Foundation Trust	Improving risk management in mental health services	£1,997,415
Dr Mike Slade	South London and Maudsley NHS Foundation Trust	Developing a recovery focus in mental health services in England	£1,999,913
Professor Len Bowers	East London NHS Foundation Trust	Reducing Conflict and Containment in Psychiatry	£1,951,785
Dr Helen Killaspy	Camden and Islington NHS Foundation Trust	Rehabilitation Effectiveness and Activities for Life (REAL): a multicentre study of rehabilitation services and the efficacy of promoting activities for people with severe mental health problems	£1,241,856
Professor John Strang	South London and Maudsley NHS Foundation Trust	Developing a UK Evidence Base for Contingency Management in Addiction Treatment: Adjunctive Incentive-based interventions to improve treatments to reduce drug use and associated harms	£1,980,576
Professor Elspeth Guthrie	Manchester Mental Health and Social Care Trust	Developing effective strategies to reduce unscheduled care in chronic disease.	£666,000
Dr Hugh MacPherson	North Yorkshire & York Primary Care Trust	Acupuncture for chronic pain in primary care	£312,725
Professor Stefan Priebe	East London NHS Foundation Trust	Effective patient-clinician interaction to improve treatment outcomes for patients with psychosis	£1,024,917
Professor Edmund Sonuga-Barke	Southampton City Primary Care Trust	The development of an integrated early detection and intervention model for Attention Deficit Hyperactive Disorder	£1,999,790
Professor Gene Feder	Bristol Primary Care Trust	Improving the health care response to domestic violence	£953,336
Professor Guy Goodwin	Oxfordshire and Buckinghamshire Mental Health NHS Foundation Trust	Development and evaluation of SMS-based monitoring and management service for people with bipolar disorder	£706,674

Annex E

Recent Reviews of Mental Health

There have been a number of recent reviews into mental health which were influential in producing a starting point for this review and for informing the recommendations. Some influential reports on mental health include:

E1.1 Mental Health Research Funders' Group Strategic Analysis of UK Mental Health Research Funding (November 2005)

The Mental Health Research Funders' Group includes the Department of Health, UK research councils and charities funding mental health research. The group analysed its support for mental health and learning disabilities research in 2004. This was the first ever national review of research funding in this area. The full report can be found at

www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC002230

E1.2 Foresight Report on Mental Capital and Wellbeing (October 2008)

The aim of the Foresight Project on Mental Capital and Wellbeing was to advise the Government on how to achieve the best possible mental development and mental wellbeing for everyone in the UK. The Project used the best available scientific evidence to develop a vision for the opportunities and challenges facing the UK over the next 20 years. The full report can be found at

www.foresight.gov.uk/OurWork/ActiveProjects/Mental%20Capital/ProjectOutputs.asp

E1.3 Foresight Report on Brain Science, Addiction and Drugs: Drugs Futures 2025 (July 2005)

The aim of the Foresight project on Brain Science, Addiction and Drugs was to provide a challenging vision as to how scientific and technological advancement may impact on understanding of addiction and drug use over the next 20 years. The project looked at the ethical and economic issues associated with the findings and considered the issue from the perspective of the individual, community and society. It culminated in a report entitled 'Drugs Futures 2025'. The full report can be found at

www.foresight.gov.uk/OurWork/CompletedProjects/Brain%20Science/Docs/DrugsFutures.asp

E1.4 Academy of Medical Sciences working group report: Brain Science Addiction and Drugs (May 2008)

Following the Foresight Project above, the Academy of Medical Sciences was asked by the Department of Health to consider the societal, health, safety and environmental issues raised in the Foresight project and to formulate recommendations for future research needs and public policy. The resulting report considers issues around three types of substance: illegal and legal 'recreational' drugs; medicines for mental health; and a category of substances termed 'cognition enhancers'. The full report can be found at

www.acmedsci.ac.uk/p99puid126.html

E1.5 Global mental health

Although this review was not constituted to look at opportunities for mental health on the global stage, the Group noted the Lancet Series on Global Mental Health, launched in September 2007. This documented the global burden of mental disorders and the long-term neglect of the needs of the mentally ill, particularly in low and middle income countries (LAMICs). It is therefore timely and right to invest in substantially extending the evidence base in economically developing countries to identify cost-effective interventions suitable for scaling up to the national and international levels. See

http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(08)61556-1/fulltext

Abbreviations

ACFs – Academic Clinical Fellowship

ADHD – Attention Deficit and Hyperactivity Disorder

AHP – Allied Health Professionals

ALSPAC – Avon Longitudinal Study of Parents and Children

aMCI – Amnestic Mild Cognitive Impairment

AMS – Academy of Medical Sciences

ARMS – At Risk Mental States

BASIS – British Autism Study of Infant Siblings

BBSRC – Biotechnology and Biological Sciences Research Council

BCNI – Behavioural and Clinical Neuroscience Institute

BHF – British Heart Foundation

BRC – NIHR Biomedical Research Centre for Mental Health

CANTAB – Cambridge Neuropsychological Test Automated Battery

CBSU – Cognition and Brain Sciences Unit

CBT – Cognitive Behavioural Therapy

CDA – Career Development Award

CIHR – Canadian Institute of Health Research

CLAHRCs – Collaboration for Leadership in Applied Health Research and Care

CNGG – Centre for Neuropsychiatric Genetics and Genomics

CNVs – copy number variants

CRTF – Clinical Research Training Fellowship

CRUK – Cancer Research UK

CSF – Clinician Scientist Fellowship

CSLAs – Clinical Senior Leadership Award

CSO – Chief Science Office (Scotland)

CSP – Coordinated System for gaining NHS Permission

CVD – Cardiovascular Disease

DALY – Disability Adjusted Life Years

DH – Department of Health

DNA – Deoxyribonucleic acid

DPFS – Developmental Pathway Funding Scheme

DSM IV/V – Diagnostic and Statistical Manual of Mental Disorders (4 and 5)

EM – Experimental Medicine

EPSCR – Engineering and Physical Sciences Research Council

ESRC – Economic and Social Research Council

EU – European Union

GABA – Gamma Aminobutyric Acid

GxE – Gene x Environment

GRPD – General Practice Research Database

GWAS – Genome-wide Association Study

HALCyon – Healthy Ageing Across the Life Course

HEFCE – Higher Education Funding Council for England

HRCS – Health Research Classification System

HSPHRB – Health Services and Public health board

HTA – Health Technology Assessment

IoP – Institute of Psychiatry

IPFs – In-practice Fellowship

IRAS – Integrated Research Application System

IT – Information Technology

LAMICs – Low And Middle Income Countries

MeSH – Medical Subject Headings

METB –Medical Educations and Training Board

MH – Mental Health

MHC – Major Histocompatability Complex

MHRA – Medicines and Healthcare products Regulatory Agency

MI – Mental Illness

MRC – Medical Research Council

MRI – Magnetic Resonance Imaging

MRP – Methodology research programme

NHS – National Health Service

NICE – National Institute for Health and Clinical Excellence

NIH – National Institute of Health

NIHR – National Institute for Health Research

NIHR CCRCD – National Institute for Health Research Coordinating Centre for Research Capacity Development

NIHR CRN CC – National Institute for Health Research Clinical Research Network Coordinating Centre

NIMH – National Institute of Mental Health

NMHB – Neuroscience and Mental Health Board

MHRN – Mental Health Research Network

OSCHR – Office for Strategic Coordination of Health Research

PGfAR – Programme Grants for Applied Research Programme

PTSD – Post Traumatic Stress Disorder

RCT – Randomised Controlled Trial

RfPB – Research for Patient Benefit

SCF – Senior Clinical Fellowship

SDO – Service Delivery and Organisation

SGDP – MRC Centre for Social, Genetic and Developmental Psychiatry

SLAM – South London and Maudsley NHS Trust

SMI – Severe Mental Illness

SMHRN – Scottish Mental Health Research Network

SPHSU – MRC Social and Public Health Sciences Unit

SSRIs – Selective Serotonin Reuptake Inhibitors

SU – Service User

T1 – Phase 1 translational research

TEDS – Twins Early Development Study

UCL – University College London

UKCRC – United Kingdom Clinical Research Collaboration

WORD – Welsh Office for Research and Development

WT – Wellcome Trust

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