

From delivery science to discovery science: realising the full potential of global mental health

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The discipline of global mental health has been singularly associated with the generation of knowledge which seeks to reduce the treatment gap for mental disorders. Its priority research agenda has focused on delivery science, i.e. the science of implementing evidence-based interventions. Considerable new resources have furthered this agenda, leading to a flowering of innovations to address barriers to the delivery of interventions while also contributing to the growth and consolidation of research capacity in low and middle income countries. A significant, but as yet under-recognised, opportunity of this global mental health initiative is its potential contribution to discovery science, notably research aimed at identifying the aetiology of mental disorders and the development of novel interventions. This editorial considers a range of potential themes for such discovery science and its guiding principles. Given the limited knowledge that we currently possess about the nature of mental disorders or their effective prevention and treatment, this may well be the most important ultimate contribution of global mental health, i.e. generating knowledge which not only reduces the treatment gap but the actual global burden of mental disorders, and will finally do justice to the 'global' of this discipline.

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The discipline of global mental health, built upon the foundations of transcultural psychiatry and global health has been singularly associated with the generation of knowledge, which seeks to reduce the treatment gap for mental disorders (Patel & Prince, 2010). This research agenda of delivery or implementation science is motivated primarily by the driver of equity, i.e. the frank injustice that millions of people with mental disorders are systematically denied the interventions which could transform their lives. This agenda also represents the leading challenges emerging in multiple priority-setting exercises, most notably the Grand Challenges in Global Mental Health (Collins *et al.* 2011). It is reassuring to observe the emergence of research programmes, many led by institutions in low and middle-income countries and funded by a growing legion of funders, which has sought to address these priorities. The result is a flowering of innovations in the delivery of evidence-based interventions for a range of mental disorders (www.mhinnova.tion.net), in the process redefining several fundamental assumptions regarding mental health care, notably the

types of human delivery agents who are able to deliver these interventions, the settings in which interventions are delivered, and the content of the interventions. However, the very low investment by governments and development agencies to scale up these innovations (Gilbert *et al.* 2015; World Health Organisation, 2015) is a reminder that there remains a long way to go before this new knowledge has its intended impact on the ultimate goal of benefiting the lives of those affected by mental disorders. It goes without saying, then, that the effort to ensure the uptake of this knowledge is likely to remain an ongoing and challenging struggle. While delivery science will continue to play a crucial role in addressing these challenges, other strategies for generating political will and increasing demand from civil society are likely to take centre-stage, including mobilising people affected by mental disorders to become advocates for this cause.

A major dividend of the flourishing of this delivery science has been the development and consolidation of research capacity in key institutions in low- and middle-income countries, most notably exemplified by the NIMH-sponsored Hubs for International Mental Health Research (<http://www.nimh.nih.gov/about/organization/gmh/globalhubs/index.shtml>), and robust partnerships between these institutions with other institutions, including NGOs, research funders

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and Ministries of Health, in their regions, and with high-income countries. Within these institutions and networks are a growing legion of researchers, from diverse nationalities and disciplines, who are collaborating to pursue shared goals. A number of new resources for research and practice have emerged, including Master degree programmes, journals dedicated to the subject, textbooks and practice guidelines, and a calendar of dedicated scientific meetings. Importantly, these institutions and networks have gained acknowledgment by other public health disciplines, access to populations for large research projects, and buy-in from the local political leadership. Taken together, these new resources offer a sound basis for global mental health to continue to deliver knowledge of value to the implementation agenda. However, in this editorial, I wish to make the case that the potential of this resource goes well beyond its contributions to delivery science. A significant, but as yet under-recognised opportunity of this consolidated global mental health initiative, is its potential contribution to discovery science, notably research aimed at identifying the aetiology of mental disorders and the development of novel interventions.

The overwhelming majority of psychiatric research, measured by the metric of peer-reviewed publications, has its origins in a handful of countries, which together account for no more than a fifth of the global population (Patel & Sumathipala, 2001). This inequity is even greater for discovery science in psychiatry. Given the complex nature of mental disorders, where multiple social, genetic, biological and environmental determinants interact to lead to psychopathology, it is plausible that studying these disorders, using similar protocols in diverse global populations, may yield new insights into aetiology of mental disorders. This is no small opportunity for decades of research focused on a small fraction of humanity has yet to yield any findings which have led to a transformational advance in our understanding of the nature of mental disorders. A similar promise could be applied to the area of therapeutics, where the available interventions are imperfect not only in their effectiveness, but also their unwanted side effects. Mapping and investigating therapeutics developed and used in diverse populations across the millennia may help uncover new approaches to the prevention and treatment of mental disorders. Other branches of medicine are replete with examples of how global health research has contributed to our basic understandings of disease and its therapeutics, evidenced by research on disease mechanisms in HIV/AIDS and the re-discovery of artemisinin, now the most effective antimalarial drug in the world. Is now the moment for such a revolution in the scientific

foundations of psychiatry to be propelled by global mental health?

Discovery science aimed at understanding the risk and protective factors for mental disorders and developing novel preventive and early interventions for mental disorders are also amongst the key goals prioritised in the Grand Challenges initiative, albeit with a lower rank than implementation questions (Collins *et al.* 2011). One of the six major goals of the Grand Challenges is the identification of root causes, risk and protective factors of mental disorders, notably to identify modifiable social and biological risk factors across the life course; understand the impact of poverty, violence, war, migration and disaster; and to identify biomarkers for disorders. A second goal is to advance prevention and implementation of early interventions, notably by identifying components of community environments that promote physical and mental wellbeing throughout life; reducing the duration of untreated illness by developing culturally-sensitive early interventions across settings; developing interventions to reduce the long-term negative impact of low childhood socioeconomic status on cognitive ability and mental health; developing an evidence-based set of primary prevention interventions for a range of disorders; and developing locally appropriate strategies to eliminate childhood abuse and enhance child protection. Now that the priority delivery science agenda is bearing ripe fruits ready for picking by practitioners and policy makers, it may be an opportune moment to consider how the newly created opportunities offered by the global mental health research capacity may expand its horizons to address the discovery agenda.

At least four major themes of research could be considered relevant for this agenda. The first theme aims at promoting epidemiological research which seeks to better characterise the nature of mental disorders. A significant body of global research has already started to demonstrate the value of this approach. By demonstrating the universality of the associations between certain risk factors, such as child abuse or trauma, particularly in their most extreme forms, and mental disorders, these studies confirm that the pathways are fundamental to the aetiology of these disorders. However, the impacts of these exposures are heavily influenced by contextual factors, pointing to the interaction between such factors with the fundamental pathways. For example, the cultural interpretation of combat experiences may lead to varying degrees of posttraumatic stress disorder and other trauma-related illnesses, or even no illness at all, depending on the meaning attributed to the combat experiences. Such research has provided insight into the influence of socio-cultural factors and their intersection with

underlying mechanisms of risk and resilience. As another example, by studying differing frequencies of gene variants in different populations, for example in genetic population isolates in diverse settings, one may more easily identify the genetic bases of these disorders due to the greater frequency of variants of these genes in these isolates. Such research could also contribute to the ongoing debates about the most appropriate approach to the classification of mental disorders (Jacob & Patel, 2014). An example of recent research which has sought to address many of these strands of inquiry is the INTREPID Project, which sought to describe first-onset psychoses from a phenomenological and aetiological perspective in three countries (Trinidad, Nigeria and India), adopting methods which have been well-established in high-income countries, thereby allowing for the comparability of the findings (Morgan *et al.* 2015).

The second theme would aim at promoting the development of novel interventions which expand the armamentarium of interventions for mental disorders. Despite decades of investment in new therapies, one commentator recently noted that ‘a revival in psychiatric drug development is badly needed: there hasn’t been a breakthrough medicine for any of the common mental illnesses, including schizophrenia, bipolar disorder, or severe depression, in roughly 50 years’ (<https://www.technologyreview.com/s/528146/shining-light-on-madness/>). Even the evidence in support of some interventions which were once thought to be unassailable is now being questioned (Kirsch *et al.* 2008). In this somewhat dispiriting context, it is worth exploring how global mental health may contribute to novel interventions. No doubt this dismal situation is, to a significant degree, due to the complex aetiology of mental disorders which, in turn, is unlikely to be unravelled without a global research paradigm. Additionally, three distinct routes need to be considered. The *first* relates to the identification of novel psychosocial strategies which have been used in diverse cultures to address mental health problems; the example of mindfulness-based psychological treatments is an obvious one in this regard. Mindfulness, which owes its distant origins to meditative traditions in Buddhism and Hinduism, has now achieved status as an ‘empirically supported treatment’ and is being implemented, perhaps ironically, almost entirely within mental health care systems in high-income countries. *Second*, the goal of scalability is leading to the design of brief interventions which seek to address a range of psychopathology, including trans-diagnostically, with impressive effects. Developing and evaluating such brief interventions is more likely to be feasible in settings where human and financial resources are scarce. A recent series of trials of trans-diagnostic psychological

treatments for people affected by conflict in Thailand and Iraq based on common elements of psychotherapy is an example of how innovations delivered in very resource-poor settings are helping us redesign psychological treatments for all (Bolton *et al.* 2014; Weiss *et al.* 2015). *Third*, there is untapped potential in the systematic description and evaluation of herbal and physical remedies used in traditional systems of medicine around the world. Systems of medicine such as Traditional Chinese Medicine and Ayurveda have used a large number of remedies such as acupuncture, herbs and yoga for the treatment of mental disorders, and some of these have so far been standardised and studied for their potential to be integrated with and scaled up within conventional health care systems (Thirhalli *et al.* submitted).

The third major theme would involve investigation of the mechanisms which explain the co-existence of mental and somatic disorders, for example depression and diabetes. Such multiple morbidities have been shown to be very common and, indeed, even more common than single morbidities in ageing populations and in lower socio-economic groups. While there are many potential mechanisms to explain multiple morbidities, notably common risk factors or the impact of one condition on the risk of the other, there is the need for a specific hypothesis-driven research agenda, which seeks to assess the strength of each of these pathways to identify promising interventions which can reduce the burden and impact of multiple morbidities (Patel & Chatterji, 2015). At present, the only effective interventions are collaborative care, which seeks to integrate the management of multiple morbidities with several ongoing trials in low- and middle-income countries, investigating their effectiveness in low-resource settings. Beyond individuals, there is a higher level of aggregation of chronic conditions which has been largely neglected: the household. There are many examples of the increased risk of a mental or somatic disorder in those who live in the same household as a person with a mental or somatic disorder (consider the risk of depression in the spouse of a person with dementia as one classic example) but no research to examine the mechanisms of such aggregation of multiple morbidities at the level of households which would include, in addition to shared genetic and environmental risk factors, inter-personal behavioural mechanisms. Such research is being promoted by the recently established 4C (the Centre for the Control of Chronic Conditions) at the Public Health Foundation of India and seeks to discover novel interventions targeting households for the prevention of chronic conditions.

The final theme is the prospect of findings emerging from neuroscience, for example related to the

biomarkers of neuropsychiatric disorders such as autism and dementia, which may potentially translate to products and technologies which can lead to scalable diagnostics for the early detection of these disorders and the design of novel interventions targeting disease pathways. The emergence of eye-tracking as a potentially scalable technology for assessment of behavioural biomarkers of autism and the development of computer delivered game-based 'training' to 'stimulate' the brain and, potentially, delay age related neurodegeneration are examples of neuroscience informed technologies which can reduce the treatment gaps in low resource settings (Anguera *et al.* 2013).

There are a number of guiding principles across these research themes. The first is the inherent interdisciplinarity of the research, with partnerships among diverse clinical disciplines, and between public health, clinical sciences, basic sciences and engineering. The second is the use of technology in various ways, from diagnostic applications to the training of health workers and delivery of mental health care interventions. The final is the most important: the generation of knowledge with global application. Given the limited knowledge that we currently possess about the nature of mental disorders or their effective prevention and treatment, this may well be the most important ultimate contribution of global mental health, i.e. generating knowledge which not only reduces the treatment gap, but the actual global burden of mental disorders, and will finally do justice to the 'global' of this discipline.

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Conflict of Interest

None.

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