

Preventive Psychiatry

Siow Ann Chong,¹*MMED (Psychiatry), MD, FAMS*, Mythily Subramaniam,¹*MBBS, MHSM*, Patrick McGorry,^{2,3}*MD, PhD*

In medicine, measures that save the most lives and improved the quality of life of millions have largely been public health measures that in most instances, had been preventive measures. The most obvious examples are the infectious diseases which were – to use the cliché – the scourge of mankind a century ago and a number of which, by the end of the 20th century, have been brought under control or even eradicated, as with smallpox. To be sure, infectious diseases continue to be a problem, particularly in low income countries, but as the leading cause of mortality and disability worldwide, a new wave of non-infectious health problems (e.g. heart disease, stroke, cancer, diabetes mellitus and mental illness) has now emerged and gained ascendancy.¹

Scientific breakthroughs, advances and reforms in clinical care (including better deployment and delivery of existing treatments) and public preventive measures have produced a steady decline in the mortality rates of cardiovascular diseases, stroke, and cancer. In stark contrast, the morbidity and mortality of mental illness have not decreased significantly.²⁻⁴ If anything, the situation seems worse from the perspective of mortality in the case of schizophrenia, in which those who suffer from this illness die 12 to 15 years before the average population and this mortality difference has increased in recent decades.⁵ The Global Burden of Disease Study has projected that major depression will be the second leading cause of disability worldwide after ischaemic heart disease, and ahead of road traffic accidents, cerebrovascular disease, chronic obstructive pulmonary disease and human immunodeficiency virus-AIDS.⁶

Thomas Insel, Director of the US National Institute of Mental Health, has suggested that one main reason for the modest “incremental advances” in psychiatry was that researchers and clinicians have set the bar for mental health research too low. For decades the research approach has been what Insel described as “canonical,” i.e. following a standard formula of trying to understand the pathophysiology of mental illnesses and to develop drugs based on early prototypes that were effective in some of the symptoms of these disorders. The formula produced, instead of a significant elucidation

of the disease mechanisms, a plethora of “me-too” drugs.⁷

Another possible reason is the slower maturation of neuroscience and the lack of sophisticated technologies that could investigate effectively the higher mental processes of cognition and emotion, or disturbances therein, down to the system, cellular and molecular levels.

In the past decade, however, neuroscience has moved at a breathtaking pace, and we now have powerful tools to help us better understand mental disorders as brain disorders, that is, disorders of brain circuits and of biochemistry. The applications of new technology and tools in biomedical research like genomics, imaging and identification of biomarkers – which have transformed the diagnostic and therapeutic approach to other physical diseases – to neuroscience have increased both knowledge and insights into the workings of the brain. Mental disorders are, in most instances, the manifestation of a complex interaction of genetic factors, environmental factors, experience and evolving brain psychopathology. The emerging field of epigenetics is revealing how external factors interact and alter gene expression in the mechanism for learning,⁸ and provides a possible explanation for how early stressful experiences can have enduring effects on behaviour in the presence of genetic vulnerability.⁹

But over and above this willingness to embrace technology to shed light on the origins and nature of mental illness, there has been, using Thomas Kuhn’s phrase “a shift in paradigm”. This is perhaps most evident in the area of psychosis, in which a group of clinicians and researchers have the courage and perspicacity to try to prevent psychosis.

Schizophrenia and related psychotic disorders are among the most disabling disorders. They are one of the world’s greatest public health concerns with schizophrenia listed as among the 5 leading causes of disability worldwide. In Singapore, schizophrenia ranks ninth (along with breast cancer) among all diseases in terms of the burden of disease.¹⁰ Despite the low lifetime prevalence of psychosis, estimated to be about 3% worldwide, schizophrenia generates an enormous burden in both economic cost and human suffering. Most psychotic disorders – in particular

¹Research Division, Institute of Mental Health

²University of Melbourne, ORYGEN Youth Health

³University of Melbourne, ORYGEN Research Centre

Address for Correspondence: A/Prof Chong Siow Ann, Institute of Mental Health, Buangkok Green Medical Park, 10 Buangkok View, Singapore 539747.

Email: Siow_Ann_CHONG@imh.com.sg

schizophrenia – are now viewed as pathologies with a trajectory that reaches back long before the emergence of psychotic symptoms, in which a substrate of genetic vulnerability is acted upon by environmental stressors.

This relatively long path to the first psychotic break, and the plastic response of the brain to injury, have given hope that psychosis could be prevented with the right interventions at the right time points.¹¹ The present state of affairs with psychosis is where coronary artery disease was decades ago, in which it was diagnosed retrospectively after a myocardial infarction. Today, we are able to predict the risk of coronary artery disease based on plasma lipid concentrations and family history, identify those with ischaemic heart disease using stress tests and imaging, and to prevent myocardial infarction with angioplasty, stents, medication, and lifestyle changes. Another comparison is cancer, in which clinical staging is essential in guiding treatment and prognostication but staging is hardly – at this time- being practiced in psychiatry.

There are now a number of groups who are attempting to depict accurately the trajectory in psychosis, and to identify those at the highest risk of developing psychosis. This body of work has given us transforming insights into the stages of psychosis and supported the validity of an “at-risk concept”.¹²⁻¹⁵

The optimism is such that the American Psychiatric Association Workgroup of the Diagnostic and Statistical Manual of Mental Disorders (the DSMV) has proposed a category termed “Psychosis Risk Syndrome,”¹⁶ although this is viewed by others as premature and fraught with potential ethical pitfalls – in particular the dangers of mislabelling, unnecessary exposure to antipsychotic medication, denial of future insurability, and the stigma that might be faced by the “false positives,” i.e. those individuals who do not convert to psychosis in the end.^{17,18}

More research is needed to improve the positive predictive value of this “high psychosis risk” syndrome and to enable us to do clinical staging which would help clinicians to select the most appropriate and effective treatment in the early stages, that are less harmful than treatments given later in the illness.^{19,20} Staging therefore creates “a prevention-oriented framework for understanding pathogenesis and for evaluation of interventions”.²⁰ However, various studies to date have been hampered by difficulties in recruiting and retaining a sufficiently large cohort over an adequately period of time, such that the findings in the extant literature are mitigated by the lack of power.²

A comprehensive, well-powered cohort study that can determine the profile of clinical and biological risk factors evident during the prodromal phase of those with psychosis is needed before rigorous preventive trials can be designed. We are in the midst of such a study in

Singapore. Due to the structured nature of Singaporean society, the country's population densely located within a small geographical area, and its highly organised health, education and military systems, Singapore is possibly the best place in the world to implement a longitudinal study of individuals at high risk for psychotic disorders and other disabling mental disorders.

The challenge to complete the cohort study successfully should not be underestimated; audacity and tenacity coupled with a disciplined scientific approach to identify the risk factors and understand the pathophysiology are needed. Intervention studies, too, need to be woven into these cohort studies to examine not only their safety and effectiveness in these early and less well-defined stages, but also to determine the causality and malleability of putative risk factors. The payoff would be that if the pre-psychotic phase of this illness can be depicted accurately and comprehensively, then psychosis itself could be pre-empted with either psychosocial or medical interventions. This means that some of the complications and associated disabilities can be avoided, with positive public health consequences – only then can we talk meaningfully about preventive psychiatry in the universal and primary sense.

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