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Deconstructing the mental health crisis: 5 uneasy pieces

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One in 3 of us will experience mental illness in our lifetime, and yet the current treatments as well as the development of new strategies haven't been overly encouraging.¹ In economically developed countries mental illness exerts an enormous social and economic toll; in Canada, for instance, more than 500 000 people will not go to work daily owing to mental illness.² The problem, of course, is not restricted to developed countries; depression more than any other condition is responsible for "years lost" to disability worldwide. Indeed, the burden attributable to mental illness exceeds that of diabetes, cancer and pulmonary diseases combined. At the World Economic Forum held in Switzerland, mental disorders emerged as the single largest health cost, with global projections increasing to \$6 trillion annually by 2030.³ An important feature of mental illness is that it tends to "travel" in the company of other noncommunicable conditions (e.g., heart disease, dementia, diabetes), often sharing some underlying mechanisms (e.g., elevated inflammatory activity) and sometimes mutually affecting one another.⁴ The co-occurrence of these conditions make the toll of mental illness still more significant. Norman Lamb, Minister of State for Care and Support in the United Kingdom, has maintained for some time that there has been a gross imbalance in attention to mental versus physical illness, and when budgets need to be cut, mental illness invariably seems to lose out, and the result has been disastrous.⁵

To be sure, there have been enormous gains in the treatment of mental illness over the past few years, and various organizations, such as the Mental Health Commission of Canada and assorted federal and provincial granting agencies, have facilitated and encouraged analysis of the mechanisms and treatments of mental illness. At the same time, it is unfortunate that, despite best efforts, discovering effective new treatment strategies has been torturously slow. Multiple factors are responsible for this, and here we outline 5 intersecting issues at play in limiting success in the development of more effective treatment strategies: 1) stigma associated with mental illness; 2) the changing contexts regarding mental health needs; 3) the limited availability and/or application of technology and alternative modalities for assessing and

treating mental illness; 4) the dismal resourcing of mental health care and research, particularly in relation to the identification of the pathophysiology of mental illnesses; and 5) a dearth of effective partnerships in research.

Stigma

The difficulties in dealing effectively with mental illness begin with individuals failing to seek treatment. In some cases they might not recognize the symptoms of mental illness, but those who do — even medical personnel — often avoid seeking help because of self, cultural/social, or structural stigma.^{6,7} The good news is that various forms of stigma related to mental illness are dissipating, albeit modestly, and more people have been seeking help.⁸ However, for many individuals who carry shame and stigma as part of their identities, "outing" themselves may simply be too difficult, and fewer than 30% of those in need, including health professionals, seek help.⁸ Such problems are compounded when those seeking help have to face long wait times, which has been a persistent problem.⁹ Given the projected increase in demand for service, an already stretched system will become excessively challenged, potentially pushing patients to suffer in silence or seek alternative treatments, including self medication through alcohol or illicit drugs.

Changing contexts regarding mental health needs

Over the past several years, there has been a disturbing trend among many major pharmaceutical industries to retrench from research and develop new drugs for mental illness. To a considerable extent, this practice originated owing to the potential promise of medications, such as selective serotonin uptake inhibitors (SSRIs), not being realized. Indeed, the Sequenced Treatment Alternatives to Relieve Depression study of antidepressants,^{10,11} the Systematic Treatment Enhancement Program for Bipolar Disorder study of bipolar patients,¹² the Clinical Antipsychotic Trials of Intervention Effectiveness study of antipsychotics,¹³ as well as the Treatment of

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Early Onset Schizophrenia Spectrum Disorders study in teenagers,¹⁴ all yielded outcomes that were not as positive as hoped. Retrenchment was further encouraged by the heavy costs of bringing a drug to market, increasing regulatory processes and limited patent protection periods. The diminished appetite for drug development in brain-related mental illness has also been prompted by the lack of promising treatment targets, and reliable biomarkers of most mental illnesses have not been identified (but see the study by Vinkers and colleagues¹⁵).

The belief that very complex, multidimensional mental illnesses can readily be cured with simple drug treatments has dissipated to some extent, and the quest for novel drug treatments has been perceived to be in free fall, even though a fair number of new agents and several more in the pipeline may be effective in treating various mental illnesses. Yet the use of herbals and other nutraceuticals have been on the rise despite limited empirical data supporting their effectiveness. To be sure, their rise and that of several alternative treatments may be part of a desire to live more organically in the mistaken belief that natural products are necessarily better than those produced by "Big Pharma" or that obtained through behavioural therapy. Unfortunately, it may also reflect frustration and distrust that has arisen given repeated media reports pertaining to the ineffectiveness of drug treatments (perhaps creating a placebo effect in the process).

Treatment of psychiatric illnesses obviously requires a better understanding of the neurobiological processes contributing to specific attributes of illness phenotypes. This could potentially lead to more precise targets for drug development as well as to the development of biomarkers to detect and guide the treatment of specific forms of depressions (personalized medicine). There has been considerable movement toward such an approach, although this may ultimately be cumbersome and too expensive to be adopted effectively.¹⁶ This aside, an endophenotypic approach, including ambitious undertakings, such as using the Research Domain Criteria to assess mental illnesses, could have considerable practical and scientific ramifications¹⁷ that could be further enhanced by considering psychosocial and cultural factors that contribute to the development of mental illness.¹⁸ Such an approach might also point to individuals who would benefit from other (or additional) modalities of treatment, including cognitive therapy, mindfulness and meditative approaches as well as yoga-based practices, either alone or in combination with pharmacotherapy.

Technologies

Remarkable technological advances have been made over the past 2 decades, many of which have been used effectively in the diagnosis and treatment of cancer and heart disease, including imaging-guided treatments. But such technological advances have not been explored to their maximum capacity in relation to mental illness. Greater use of imaging procedures for early detection and diagnosis of mental illness and evaluating brain changes associated with treatment responses could help define predictive biomarkers. There might also be considerable promise in using various technol-

ogies to alter regional brain activity (i.e., neuromodulation). For instance, repetitive transcranial magnetic stimulation (rTMS), direct current stimulation and deep brain stimulation could be used alone or with other forms of treatment, and understanding their modes of action could be part of an arsenal of approaches linked to specific biomarkers. Additionally, mobile devices (smartphones, mobile Apps) that have the capacity to reach large numbers of people are being assessed to determine their effectiveness in providing appropriate interventions, even in developing countries, and these can be useful in remote Canadian communities where medical services are limited or largely unavailable.¹⁹

Resourcing mental health care and research

The industry retreat from research for mental illness came at a very bad time given that research funding from government agencies diminished relative to the number of researchers seeking funding. Investment in research related to identifying the mechanisms related to mental illness has been modest, with less than 5% of research dollars going toward these illnesses even though every dollar invested in depression and anxiety research has a \$4 return on investment.²⁰ The shortage of funds has also undermined the capacity to foster much needed intellectual capital, particularly among young researchers, potentially foreshadowing difficult issues that will follow. Given a fixed pie, more dollars spent on mental illness means that funding for research aimed at other illnesses is necessarily reduced, which is not something we would advocate. Clearly, the current situation leaves granting agencies in a miserable *Sophie's Choice* situation regarding what type of research is to be saved and what type is not. The remedy, obviously, is that the size of the pie must be increased to meet the translational and basic science objectives, or alternatively, more pies need to be served up. Hopefully the underfunding will come to an end, but it would be foolhardy to continue to rely on government agencies to meet research needs. Greater efforts should be enlisted to garner funds from elsewhere, including corporate entities and the private sector.

Partnerships in research

Within the United Kingdom, for every 1£ of government spending on cancer and heart research, more than 2.5£ and 1.2£, respectively, are contributed by the public.²¹ However, for every 1£ spent by the government for research related to mental health, a paltry 0.003£ is spent by the public.²¹ In the same vein, the activities of research networks focused on some illnesses (e.g., heart disease, different forms of cancer) have been beneficiaries of specific foundations dedicated to finding cures, but such foundations are relatively rare in the context of mental illnesses. It has been said in relation to resource allocation that mental illness is the orphan of the health care system and that research concerning mental illness is the orphan of the orphan.

This takes us to an essential issue concerning ways for the field to move forward. Several Canadian efforts have been

made to bring researchers with diverse interests and skills under unifying tents (e.g., Canadian Biomarker Integration Network for Depression, Canadian Network for Mood and Anxiety Treatments, Canadian Depression Research and Intervention Network as well as other directed research funding through Canadian Institutes for Health Research Strategy for Patient-Oriented Research and Ontario Brain Institute initiatives). Similar networks have been created in the United States (National Network of Depression Centers) and in Europe (European Alliance Against Depression), and hence there is an opportunity to create a network of networks to globalize the battle against mental illness. In this regard, consideration should also be given to the many comorbid conditions associated with mental illnesses. It would be practical and theoretically appealing, despite the challenges, to have researchers across disciplines and illness domains cooperate in data collection and interpretation, as this might facilitate the identification of underlying mechanisms for the comorbidities or the discovery of important biomarkers. Certainly, bigger isn't always better, but we have seen that for other disease conditions (e.g., cancer, heart disease) integrated, international research and clinical consortia can facilitate data sharing and the conduct of large clinical trials, especially those that include genomic analysis, and allow us to learn from obstacles encountered by our research partners. In essence, the emergence of collaborative networks may facilitate the harnessing of collective energy to uncover the mechanisms underlying mental illnesses, finding more effective treatments and talking unapologetically about the quest for cures, just as we do for cancer.

Conclusion

As the shadow of the stigma associated with mental illness diminishes further and the huge social and economic impact of mental illness becomes glaringly clear, political interests will escalate. The cries of the patients and their families; the financial loss owing to problems in the workplace; and the opinions expressed by clinicians, researchers and others are beginning to resonate politically and hopefully will result in more resources directed toward mental illness. Navigating through the 5 uneasy pieces will be difficult, requiring global thought leaders and national and international organizations to articulate plans and strategies for the development of specific targets and mechanisms for funding research. It would be important to ensure that as innovative treatments are developed, they are made accessible to developed and low-income countries as well as to vulnerable and marginalized groups within Canada. Nations should be held responsible for giving mental illnesses as prominent a place in health care as other noncommunicable diseases.

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