

From the Editor's desk

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Treatment resistant mental illnesses

Celebrate! Mental health is now an everyday conversation piece. It is no longer impolite to suggest you work to improve mental health. The importance of mental health to the success of society, the economy and in the future of our children is much better recognised. The media, charities and dedicated skilled professionals should be praised and encouraged. The plight of veterans returning from conflict zones, asylum seekers escaping persecution, children surviving trauma, violence, abuse and deprivation are all now recognised as important preventive targets.

A decade ago, I visited China to talk to psychiatrists and psychologists and government officials to explore different models and practices of care, especially as classifications systems, mental health legislation, and services were fast evolving. They were looking to our models of care to learn lessons. The clinicians in China work hard, they are determined to use evidence-based interventions, adopt advanced psychological therapies, and they know the social and cultural contexts and constraints within which they deliver care. However, they proffered a cautious optimism when it came to complementary and traditional Chinese medicine which we were learning more about. They suggested that 'when the Emperor has left that palace, it is hard to restore order'. The analogy of the mind as Emperor is pertinent to individual patients (how originally meant) but can also be seen to reflect leadership and societal mindfulness. For example, suicide rates had been very high in Japan, in part due to stigma and taboo about mental illness and suicide. Once the Japanese Royal Family and government spoke openly about mental illnesses, society took over the discourse and we see better mental health and more engaged and active professionals, public actors and charities.⁴ Their Royal Highnesses the Duke and Duchess of Cambridge and Prince Harry have given mental health a much higher profile in the public imagination and to motivate better care and services. They have set up a new charity to tackle stigma and encourage people to talk about mental health in the UK. Head Space supports mental health promotion, and is the official charity of the London marathon (April 2017). As a consequence, the media stories following this year's London marathon were dominated by stories of pursuing better mental health for people themselves, their families, and communities.

Common emotional distress and mental health problems not quite reaching the threshold of being seen as illnesses - are familiar to the public and are a part of everyday experience. These are the subject of novels and films. These can be related to relationship difficulties, loss, bereavement, sudden unexpected traumatic events, chronic adversity and harsh social experiences. Furthermore, adversity can trigger health risk behaviours, so leading to a higher risk of cancer, brain, heart, lung, liver or kidney disease. There is now much commitment to tackle common forms of distress, work stress, co-existing mental and physical illness and premature mortality in people with mental illness. Health and social care professions, public health agencies, local government, schools, employers and those responsible for the built environment are fully engaged. The greater public engagement can help frame and motivate more action and resources to realise better mental health with a fuller range of socially embedded, compassionate, humanistic, and evidence-based tools.

However, there is another story. Many people suffer very severe mental illnesses and live in abject poverty and appalling housing, are socially excluded, unable to secure work, have few friends or social supports, and their start in life has been tragically unkind and unfair; they report trauma, abuse and violence, often from a very early age. These patients are often seen in very specialist mental health services that are hard pressed to provide comprehensive and complex packages of care. People suffering with more persistent conditions with life-long causation do not easily respond to social, psychological and biological interventions. ^{5–7} The term often applied dispassionately, medically, and devoid of empathy is 'treatment resistance', meaning that they do not benefit from or respond to medication, psychotherapy, electroconvulsive therapy (ECT), or even new neuromodulatory treatments. ^{5,8}

We need to find better ways of classifying states of emotional distress that are part of human experience, what the popular campaigns seem to focus on, and illnesses that are hard to remedy and need specialist interventions. These classifications and corresponding treatments must be based on a better understanding of aetiology and mechanism. For example, patients with emotionally unstable personality difficulties suffering comorbid depression or transient states of psychosis find no one service suited to meet their total needs. Comorbid depression and personality disorders appear to benefit less from conventional treatments. Each service (personality disorder or generic adult services) operates different models of engagement and intervention on quite different timescales, with distinct practices around therapeutic boundary structures and balance between supportive or transformative interventions. Some patients persistently hear voices, or worry about taking their lives, or are so low in mood that there is nothing they enjoy in everyday life. Treatment-resistant illnesses are not as newsworthy, and rarely make it as stories of success and triumphant victory over nefariously portrayed disease characters. Research to benefit such illnesses is vital.

This edition of the BJPsych speaks to the tragic but vital task of tackling treatment resistance and not being able to predict rare events despite the best research. Structured assessment of suicide risk is riddled with missed contextual information that seems not to capture the actual concerns of patients. Several papers warn against the unthinking use of suicide risk assessments (Hawton & Pirkis, pp. 381-383; Owens & Kelley, pp. 384-386; Carter et al, pp. 387-395; Quinlivan et al, pp. 429-436). However, sustainable and simple interventions may help; for example, a WHO brief intervention including contact appears to be more effective than lithium and cognitive-behavioural therapy (Riblet et al, pp. 396-402). Ketamine is a controversial proposed treatment for treatmentresistant depression. 10,11 In an updated meta-analysis, McGirr et al (pp. 403-407) evaluated whether ketamine used as an anaesthetic in ECT produces any greater improvement than ECT without ketamine. A new trial also confirms that ketamine appears to offer no advantage over other anaesthetics in ECT (Fernie et al, pp. 422-428). Mood dysregulation is troubling and often persistent. It is often thought to be a consequence of experiences of lability of mood in parents, for example if parents suffer bipolar disorder. Contrary to expectation, Propper et al (pp. 408-412) show that depression in parents is more likely than bipolar disorder to be associated with mood dysregulation in offspring. These findings recommend more effective and earlier treatment of mental disorders, but especially in parents. Finally, to avoid treatment resistance and chronicity, clinicians need to better establish first-line interventions that have the best chances of long-term success. Berk et al (pp. 413-421) suggest that lithium appears to show advantages over quetiapine in maintenance treatment for first-episode psychosis, offering some precision. Much more is needed on precision around early intervention.

Another form of treatment resistance, or persistence of wicked problems in healthcare, is the complaint from patients that they face discrimination at work, in society, and in services. May holidays in the UK have been dominated by talk of the general election. What is remarkable is that political parties are now promising better mental healthcare, a new mental health act, more mental health professionals, and that it is time to end discrimination against people with mental health problems. However, the parties differ in their approach to securing the necessary resources, and in their ability to engage and motivate staff, to garner trust and cooperation, and to capitalise on the values, commitment to social justice and goodwill of mental health professionals. Short-term solutions will not work, and one might question whether a change of mental health legislation is the remedy to shortages in services and disproportionate levels of detention in some demographics, for example Black patients. I watch with excitement what unfolds in the coming weeks as healthcare is a societal commitment enacted through political representation and action.

- Ashton JR. Plans, hopes and ideas for mental health. BJPsych Bull 2017; 41: 3-6.
- 2 Mehta N, Davies SC. The importance of psychiatry in public mental health. Br J Psychiatry 2015; 207: 187–8.

- 3 Forsman AK, Wahlbeck K, Aaro LE, Alonso J, Barry MM, Brunn M, et al. Research priorities for public mental health in Europe: recommendations of the ROAMER project. Eur J Public Health 2015; 25: 249–54.
- 4 Akiyama T. Profile of psychiatry in Japan. Int Psychiatry 2007; 4: 35-7.
- 5 Howes OD, McCutcheon R, Agid O, de Bartolomeis A, van Beveren NJM, Birnbaum ML, et al. Treatment-resistant schizophrenia: Treatment Response and Resistance in Psychosis (TRRIP) working group consensus guidelines on diagnosis and terminology. Am J Psychiatry 2017; 174: 216–29.
- 6 Bennabi D, Aouizerate B, El-Hage W, Doumy O, Moliere F, Courtet P, et al. Risk factors for treatment resistance in unipolar depression: a systematic review. J Affect Disord 2015: 171: 137–41.
- 7 Post RM. Heading off depressive illness evolution and progression to treatment resistance. *Dialogues Clin Neurosci* 2015; 17: 105–9.
- 8 Anderson RJ, Hoy KE, Daskalakis ZJ, Fitzgerald PB. Repetitive transcranial magnetic stimulation for treatment resistant depression: Re-establishing connections. Clin Neurophysiol 2016; 127: 3394–405.
- 9 Newton-Howes G, Tyrer P, Johnson T. Personality disorder and the outcome of depression: meta-analysis of published studies. *Br J Psychiatry* 2006; **188**: 13–20
- 10 McGirr A, Berlim MT, Bond DJ, Fleck MP, Yatham LN, Lam RW. A systematic review and meta-analysis of randomized, double-blind, placebo-controlled trials of ketamine in the rapid treatment of major depressive episodes. *Psychol Med* 2015; 45: 693–704.
- 11 Malhi GS, Byrow Y, Cassidy F, Cipriani A, Demyttenaere K, Frye MA, et al. Ketamine: stimulating antidepressant treatment? *BJPsych Open* 2016; 2: 05.00