THIS WEEK

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No dishonour in depression

The stigma associated with mental illness discourages investment in finding cures — even though the burden of the disorders on society is immense.

Comedian and writer Ruby Wax, a regular on British television, has clinical depression. In her book published last week, *Sane New World* (Hodder & Stoughton, 2013), she describes her struggles with different therapies and her fear of being 'found out'. She is not alone. A 2010 survey in Europe revealed that 38% of people had a diagnosed mental disorder — including 7% with major depression. The proportion is likely to be similar in all populations, even in Africa, where psychiatric disease barely features on the health agenda.

The stigma attached to such disorders means that many people do not admit to their illness. The same stigma discourages investment, so that research funding is not proportional to the distress these disorders cause. Why lobby for better treatments for depression or schizophrenia when there are 'real' diseases out there, such as cancer?

Wax has been through the catalogue of available therapies and says that she has settled on an approach known as 'mindfulness', which helps to keep her depression under control. It may seem that the various therapies are inadequate, given that initial treatment of depression fails in 60% or more of cases. It is true that more treatment options are badly needed. Yet evidence-based cognitive behavioural therapies and drugs already developed by the pharmaceutical industry can work splendidly for long periods — if they are given to the right patients.

How do you recognize the right patients? Treatment decisions tend to be based on the preferences of physicians or their patients, often with a missionary zeal that gives no credence to the idea that a personalized approach would be more appropriate. Some hold that drugs have unacceptable side effects, whereas others say that cognitive therapy wastes time if the depressed brain is not first chemically lifted. It is becoming increasingly common to offer patients both treatments at once in the belief that drugs can prepare the brain to respond to cognitive therapy. That may be so, but it is also possible that the improved response rates are simply the result of catching two different populations.

The situation would improve drastically if simple tests could be developed to predict treatment outcome. Many exploratory clinical trials are now under way to search for biomarkers in genes or in the brain itself that might be predictive. This week sees the description of the first potential biomarker for discriminating between responders and non-responders to drugs or cognitive therapy in major depressive disorder (C. L. McGrath *et al. JAMA Psychiatry* http://dx.doi.org/10.1001/jamapsychiatry.2013.143; 2013).

The study, led by neurologist Helen Mayberg of Emory University in Atlanta, Georgia, used positron emission tomography (PET) scans to measure metabolic activity in various brain regions of people with untreated depression (see also *Nature* http://doi.org/mtc; 2013). Patients were randomized into groups and treated for 12 weeks with either a commonly used antidepressant drug or cognitive behaviour therapy. The study's results were clear-cut. Below-average activity in a brain area called the right anterior insula — which is linked with depression-relevant behaviours such as emotional self-awareness and decision-making — was associated with the patient showing a good response to cognitive behavioural therapy and a poor response to the drug. Above-average insula activity was predictive of the opposite.

This potential biomarker must still be tested in prospective clinical trials, which will assign patients to a treatment on the basis of their insula activity. It may fail. But if the biomarker comes up trumps, it could be transformative for many patients who would not have to endure two or three months of treatment trial and error.

"The stigma attached to mental disorders will fade when treatment becomes more effective."

If attitudes to mental illness do not change, even a successful biomarker of this type will have a hard time being accepted by health systems that foot the bills. Unlike a simple blood test, a PET scan is inconvenient because not all physicians have easy access to the technology and, at up to US$2,000 a shot, the procedure is not cheap. Although expensive treatments for other diseases and arguments about how to fund them are nothing new, this rational debate is harder for mental illnesses because of the irrational stigma that is attached to them.

Fifty years ago, the stigma surrounding cancer meant that physicians would sometimes lie to patients about the diagnosis from kindness. That has now faded because cancer is not always the death sentence it once was — thanks in part to the development of biomarkers that guide therapy. The stigma attached to mental disorders will also fade when treatment becomes more effective. But to break out of a vicious circle of underinvestment in a stigmatized disease area will require continued effort to get the problem recognized. This is a good week for that. ■

Track the trackers

Oversight and public debate about access to personal data are crucial to preserving privacy.

Access to phone records is all over the news at the moment, following media revelations of massive snooping by US intelligence agencies. Collecting phone records is in itself nothing new, and is legitimate — scientists have long done so for research. What is unprecedented is the government weaving together multiple huge data sets for secret state surveillance.

When researchers obtain electronic records of millions of people's calls for social science — including data on who called whom, when and from where, but not actual conversations — they must first make a strong case for why they need that information, and must comply with multiple layers of oversight and safeguards such as anonymization of