

bound to the BNAb has been characterized using x-ray crystallography and cryo-electron microscopy.⁴ Next, the naive B-cell repertoire residing in bone marrow and secondary lymphoid tissue must be engaged. That engagement will probably need to be accomplished through a process referred to as B-cell lineage immunogen design. Specifically, one or more clonally related BNabs must be isolated and, using next-generation sequencing, an antibody lineage constructed through inference that links the mutated BNAb-producing cell to its naive, germline ancestor. Next, recombinant antibody technology would express members of that BNAb lineage in order to select HIV-envelope constructs that optimally bind them. Finally, those envelope constructs would be used as immunogens in a prime–boost fashion to engage the naive B cell in vivo and iteratively stimulate B-cell “evolution” until BNAb-producing cells are elicited.

Just as B-cell vaccine science

is advancing, so, too, are T-cell approaches. These models could enhance B-cell responses by providing broad help to the B cells and eliciting immune-stimulating cytokines. Furthermore, it has been discovered that levels of T-follicular cells in the blood of HIV-infected persons correlate with the creation of BNabs, probably because these cells enhance hypermutation of B-cell genes. In addition, in experiments using a virus related to HIV, the simian immunodeficiency virus (SIV), a vaccine constructed by inserting SIV genes into a cytomegalovirus vector induced potent CD8+ T-cell responses that controlled SIV replication and resulted in viral clearance in roughly half the nonhuman primates studied.⁵

These advances demonstrate the dynamic nature of HIV vaccine discovery and the promise of impending breakthroughs. Therefore, while continuing to scale up the delivery of ART and deploying nonvaccine prevention methods, the HIV prevention

community should hold fast to its commitment to vaccine science. Ultimately, we believe, the only guarantee of a sustained end of the AIDS pandemic lies in a combination of nonvaccine prevention methods and the development and deployment of a safe and sufficiently effective HIV vaccine.

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From the Office of the Director, National Institute of Allergy and Infectious Diseases, Bethesda, MD.

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Transforming Lives, Enhancing Communities — Innovations in Global Mental Health

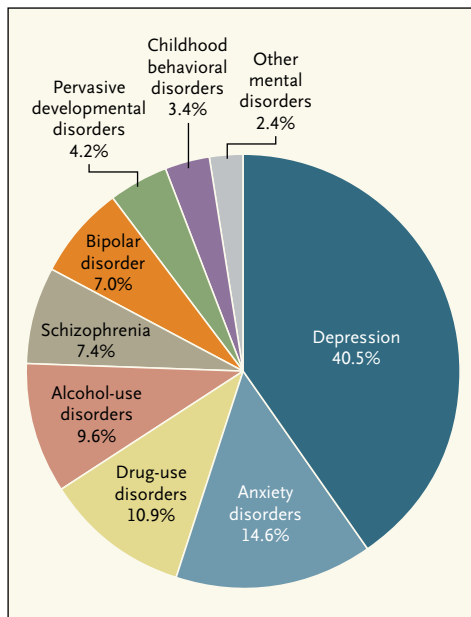
Vikram Patel, F.Med.Sci., and Shekhar Saxena, M.D.

Mr. K. spent nearly a year and a half bound to a log in his home village in northeastern Ghana. His crime? He had a psychotic disorder, and his family could not afford the \$17 for antipsychotic medication that would have stabilized his condition. Instead, they consulted a traditional healer, who pinned Mr. K.'s right leg inside a hole in the log and warned his family

not to free him lest the wrath of the gods be visited on them.

At least 10% of the world's population is affected by one of a wide range of mental disorders; as many as 700 million people had a mental disorder in 2010. The 2010 Global Burden of Disease Study showed that mental disorders account for 7.4% of the world's burden of health conditions in terms of disability-adjusted life-

years¹ and nearly a quarter of all years lived with disability — more than cardiovascular diseases or cancer (see pie chart for the contribution of different mental disorders to this burden). Incredibly, these numbers probably underestimate the true burden, since they do not include the effects of mental disorders on other high-priority health conditions — for example, the effect of maternal depression



Proportions of Global Disability-Adjusted Life-Years Associated with Mental Disorders Accounted for by Various Types of Disorders.

Data are from Whiteford et al.¹

on infant undernutrition in low-income settings.² Furthermore, the trends in the global burden of disease suggest that the proportionate burden of mental disorders will continue to grow.

There is a robust body of evidence testifying to the enormous personal and societal impact of this burden, from the distress associated with the experience of psychiatric phenomena to the hundreds of thousands of lives lost to suicide; indeed, suicide is a leading cause of death among young people globally. The economic effect of mental disorders, both due to the costs of formal and informal care and due to lost productivity, is staggering. The global economic costs of mental disorders were estimated at \$2.5 trillion in 2010 and are projected to reach \$6.0 trillion by 2030.³

But arguably the most important reason for action is the dis-

turbing evidence that people with mental disorders, like Mr. K., are subject to some of the most severe human rights violations encountered in modern times. Such experiences include being tied to their beds or kept in isolation in psychiatric institutions, being incarcerated in prisons, being chained and caged in the community, and being abused by some traditional healing practices.⁴ In short, the human rights abuses visited on people with mental disorders amount to a global emergency that requires immediate and sustained action.

At the heart of these injustices is a lack of access to evidence-based treatment and care. Despite the robust evidence testifying to the effectiveness of a range of pharmacologic, psychological, and social interventions that can transform lives and enhance communities,⁵ the majority of the world's population has no access to these interventions. In no country is the financial allocation for mental health care proportionate to the contribution of mental disorders to the burden of disease; the average allocation for mental health in low-income countries is

a meager 0.5% of the total health budget.

People with mental disorders are more likely than other people to die prematurely — even if those who commit suicide are excluded from the calculation. The lack of opportunities for healthy lifestyles and appropriate medical care for coexisting physical conditions are key reasons.

But there is, at long last, some good news. In May 2013, 194 ministers of health adopted the World Health Organization Comprehensive Mental Health Action Plan in the World Health Assembly, recognizing mental health as a global health priority and pledging action. Mental health is now discussed at the highest-level policy forums devoted to global health and development, such as the recent World Innovation Summit for Health (WISH) in Qatar and the World Economic Forum in Davos, Switzerland. On the scientific side, after more than a decade of sustained efforts to build knowledge, we are witnessing a flourishing of innovations that successfully address the health and social needs of people with men-

Policy Actions to Improve Treatment and Care of People with Mental Disorders.*

- Empower people with mental disorders and their families to, for example, provide support to one another
- Build a diverse mental health workforce — for example, of appropriately trained and supervised nonspecialist health workers — to deliver psychological treatments
- Develop a collaborative and multidisciplinary team-based approach to mental health care — for example, by integrating economic interventions with mental health care
- Use technology to improve access to mental health care — for example, by means of computer-assisted, self-guided psychological therapies
- Identify and treat mental disorders early — for example, by delivering school-based interventions for childhood mental disorders
- Reduce the rate of premature death — for example, by providing integrated care for physical health problems for people with mental disorders

* Adapted from the World Innovation Summit in Health Report of the Mental Health Working Group, 2013 (www.wish-qatar.org/app/media/381).

tal disorders, even in the most poorly resourced settings.

For the WISH, we published a report synthesizing the evidence supporting innovations in treatment and care, especially those that are the most promising for scaling up in diverse countries (see box). We launched an online database to document these innovations and facilitate their dissemination to policymakers, researchers, and practitioners (www.mhinnovation.net); this database already includes more than 60 innovations. Given the number of recent grants from funders such

part in this process — for example, by enhancing access to specialist care by means of telemedicine, enhancing adherence and follow-up with the use of mobile phones, and creating opportunities for self-care by means of Internet-delivered treatment.

Such care models must focus on the detection and treatment of mental disorders as early in the life course as possible, since most mental disorders begin before adulthood. They must also ensure the delivery of high-quality care for both physical and mental disorders. Mental health care

arguments for treatment and care, we would also emphasize the scientific and economic arguments. Innovative ways of delivering evidence-based care can reduce disability and suffering; increase the health, well-being, and productivity of people with mental disorders; and reduce the adverse economic effects of these problems on individuals, their families, and society.

A one-size-fits-all approach is not appropriate for scaling up mental health care globally. National contexts and cultures vary greatly, and if innovations in treatment are to be effective, mental health planners and policymakers must adapt them for local social, economic, and cultural conditions, including the availability of human resources. The choice of which policy actions to implement should be based on current gaps in mental health care in a particular context and on the priorities of policymakers and other stakeholders. Mental health is everyone's business. A wide range of stakeholders — from patients and their families to service providers, employers, policymakers, and researchers — need to work together to make a difference.

Our ultimate goal must be universal mental health care, providing a system that adequately addresses not only the mental health needs but, equally important, the social consequences of mental health problems. As many countries are showing, change is possible, regardless of the context and the constraints, and the keys to success lie in strong political commitment backed by adequate financial resources, planning and implementation guided by a rights-based and evidence-

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as the National Institute of Mental Health, Grand Challenges Canada, and the Wellcome Trust supporting global mental health initiatives, the database is expected to grow rapidly.

At the heart of these innovations lies the health care delivery model of integrated collaborative care, in which front-line care is delivered by appropriately trained and supervised community-based health workers, working in partnership with primary care physicians and mental health specialists. Collaborative care must incorporate an active role for patients and their families and must integrate mental health care with social and economic interventions. Technology can play a key

should be delivered in diverse settings; indeed, most care would be expected to occur outside traditional specialist delivery venues — for instance, in schools, primary health care facilities, the workplace, and patients' homes.

We know what works in treatment and care; now we need to implement that knowledge and take it to scale. These efforts must be guided by the principle that people with mental disorders have a universal right to a life of dignity, autonomy, and inclusion. The right to receive evidence-based treatment and care is an essential foundation of this goal. In addition to the compelling moral and humanitarian ar-

based perspective, and investment in evaluation and research to ensure that the many unanswered questions are addressed in due course.

There is no excuse anymore for inaction. The time to act is now.

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From the London School of Hygiene and Tropical Medicine, London (V.P.); the Public Health Foundation of India, New Delhi, and the Sangath Centre, Goa — both in In-

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