The Pulse on Global Trials

By Matthew Howes

Clinical development for mental health therapies remain an unmet need. Over the past decade, government-funded research initiatives in advanced countries have lagged in the area of mental health, and the private sector hasn't succeeded in filling the gaps.

In a recent report published by inVentiv Health, *An Advocacy Rx For Progress In Mental Health*, the authors point out that mental illness amounts to an unparalleled public health crisis. Beyond the impact of disease for the individual suffering, mental illness creates barriers to workplace productivity, places strain on families and drives costs throughout the healthcare system.

In Europe, for example, 27% of adults have experienced a mental illness. Protracted high unemployment across the continent increases stress levels, which can trigger depression. Increasing numbers of refugees and traumatized immigrants from war-torn nations to Greece, Germany and other countries contributes to health system strains.

Patient organizations are playing an increasingly vocal role in public policy debates, pushing for parity in how societies handle mental illness compared to other health conditions like diabetes, heart disease and many cancers. That will likely take many years, given the current budget pressure for healthcare services.

Payers are responding to the economic impact of mental illness therapies by asking for more data from clinical research sponsors on new treatments being brought to market. Many want more post-marketing surveillance studies, arguing that a six-week trial isn't helpful to them because patients may be on these drugs for decades. That means research must be expanded to learn more about compliance rates, relapse rates, changes in efficacy/resistance and other benefits and liabilities of long-term usage.

Fortunately, there are a couple of innovative ideas on how to improve the lives of people who struggle with major depression, schizophrenia, bipolar disorder and other serious conditions. Amidst great uncertainty in the healthcare environments of the U.S. and Europe, there is hope for new solutions that can address the unique challenges in mental health disorders.

Priorities for Progress in Mental Health

- Extend length of clinical trials to ensure real-world relevance
- Sponsor post-marketing surveillance studies of psychiatric drugs
- Increase gender/ethnicity/race representation in drug trials
- Develop and test more products for pediatric and geriatric use
- Seek clearance to test new drugs against the standard of care, not placebos
- Develop more "multi-morbidity" treatments to manage mental health conditions that are co-morbid with diabetes, cancer and other conditions

In the coming years, clinical trials for mental health therapies will be shaped by two key changes. The first will be extending the length of clinical trials to ensure real-world relevance. In the U.S., the 21st Century Cures Act endorses the use of patient-reported outcomes (PROs) in psychiatric drug trials. Advocates say these relatively simple tools can reduce the danger that regulator-approved dosages will lead to over-treatment, which can cause side effects such as precipitous weight gain and other metabolic problems.

When a trial relies solely on input from clinicians, disease symptoms may be logged as more severe than what the patient actually experiences, or how they describe that experience. By skipping the PRO, the trial sponsor may miss the fact that the optimal dose of an experimental drug is lower than clinicians think.

The second key change in clinical trials for mental illnesses is how the studies are designed. Most companies currently test new drugs for mental health conditions against a placebo, rather than giving patients in the control arm medications considered to be the current standard of care.

Currently, both in the U.S. and the EU, rules governing the registration of new mental health drugs are based on the concept of absolute efficacy, as measured against a placebo, not an active comparator. Some mental health advocates say regulatory guidance should be revised so that the concept of absolute efficacy is replaced by one of added value. Evidence should show that the new drug is at least as safe as the current standard of care, and also more effective.

Guidance that requires placebo controls also adds to the challenge of recruiting patients for trials. Many people with mental health conditions are anxious about being on a placebo for several months with no access to medications that work. Researchers looked into the recruitment issue in 2011, with help from the National Institute of Mental Health (NIMH), and found that more than one third of patients they interviewed cited fear of being placed on a placebo as the primary reason for declining to participate in trials of psychiatric drugs.

Advocacy groups also note that placebo controls—considered the gold standard by scientists—are not the general rule in areas such as oncology. For trials of most new cancer drugs, patients placed in the control arm are given anti-cancer medications with a proven track record, not placebos. Moving forward, many experts across stakeholder groups believe standard of care will also become the control in trials for mental illness therapies.

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