Washington State Health Care Authority

Final key questions and background

Pharmacogenomic testing for selected conditions

Background

In 2014, there were an estimated 43.6 million (18.1 percent) adults in the United States with a mental illness in the previous year. This includes approximately 9.8 million (4.2 percent) adults with serious mental illness. Based on data from 2002, the National Institute of Mental Health (NIMH) estimates that the total direct and indirect costs of serious mental illness exceeds $300 billion per year. In 2010, neuropsychiatric disorders, which include mental and behavioral disorders, accounted for the largest proportion of health-related disability in the U.S. In 2008, 13.4 percent of adults in the United States received treatment for a mental health problem. This includes all adults who received care in inpatient or outpatient settings and/or used prescription medication for mental or emotional problems. The following mental illnesses are the focus of this report: depression, psychosis, anxiety, mood disorders, attention deficit hyperactivity disorder (ADHD), and substance use disorder. Substance abuse will focus specifically on opioid and alcohol abuse.

Depression, psychosis, mood disorders, and anxiety are treated by various medications, including tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), typical antipsychotics, and atypical antipsychotics. However, there is a 30 percent to 50 percent failure rate with initial treatment, and rates of attrition and nonadherence during treatment are reported to be high. While some patients experience benefits from these medications, response varies significantly among patients and can range from no response at all to medication-related toxicity and serious side effects after a standard dose. The reason for such variability is not fully understood, although it is believed that both genetics and environment play a role.

Attention deficit hyperactivity disorder (ADHD), a neurodevelopmental disorder, can affect young children, adolescents, and adults. Symptoms vary from mild to severe. Data from 2011 indicate that 6.4 million (11%) children ages 4 to 17 years in the U.S. had been diagnosed with ADHD at some point in their lives, and 3.5 million (6%) 4 to 17 year olds were taking medication for ADHD. Approximately 4.1 percent of adults in the U.S. in 2005 reported having ADHD in the previous year, and 41.3 percent of this group are considered to have “severe disorder.” Medications such as stimulants and non-stimulants may be prescribed for the treatment of ADHD.

Substance use disorder affects approximately 20 million adults in the U.S. and is a frequent cause of illness, injury or death and subsequently places a significant burden on the health care system and individuals and families. It includes misuse or dependence on drugs and alcohol. Medication-assisted treatment may be used to reduce cravings or symptoms of withdrawal from opioids or alcohol. The medications generally act to either reduce or eliminate sensations associated with using a substance or cause a negative reaction when a substance is taken.

Pharmacogenomics aims to identify relationships between variations in genes that affect medication response and clinical outcomes and ultimately identify patients likely to respond to treatment or experience adverse events from specific medications. Numerous enzymes and other types of effector molecules are known to be involved with drug uptake, distribution, metabolism, target engagement, and action. Specific variants in the genes encoding these molecules may result in an absence of function, reduced activity, or increased activity, thereby affecting drug function. The labels of several medications include a discussion of pharmacogenetics or drug interactions for some genes; far fewer include recommendations for how to use this information in patient management. Many tests for these variants are commercially available in the U.S. Targeted tests of individual genes and multi-gene panels designed to test several selected genes at once are available to identify specific variants in each gene that are believed to be associated with drug response or potential adverse reactions. Available panels have some overlap in the genes included in each panel, but not all panels test the same genes. Those that do may not assess the same variants for a given gene. Potential uses for the information gleaned from both types of tests include drug and dose selection for initiating or changing medications with the intent to improve patient outcomes and experiences with treatment.

Policy Context

A growing number of new laboratory tests and computer based predictive algorithms are available to assess an individual patient's potential metabolic response to various drugs. Potential benefits include better application of the drugs for a specific individual. Concerns relate to whether specific tests result in improved treatment decisions and health outcomes, as well as rapid emergence and uptake of pharmacogenetics tests generally. Concerns are considered low for safety of these tests, high for efficacy, and medium/high for cost-effectiveness.

Scope

Population: Adults and children initiating or changing medications for any of the following diagnoses: depression, mood disorder, psychosis, anxiety, attention deficit hyperactivity disorder (ADHD), and substance use disorder (specifically opioid and alcohol abuse)

Interventions: Genetic tests to inform the selection or dose of medications for specified disorders

Comparators: Usual care/no genetic testing

Outcomes:

- Effect of genetic testing on patient management decisions about medication selection or dose
- Effect of genetic testing on patient adherence to treatment regimen
- Effect of patient management decisions guided by genetic testing on response to treatment and adverse events as a result of treatment
- Direct harms of genetic testing such as consequences of false positives or negatives, and risks associated with sample collection
- Costs and cost-effectiveness

Settings: Inpatient or outpatient settings, any country.

Key Questions

1. Effectiveness: What is the clinical utility of genetic testing to inform the selection or dose of medications for individuals diagnosed with depression, mood disorders, psychosis, anxiety, attention deficit hyperactivity disorder (ADHD), or substance use disorder?
    a. Does genetic testing to inform the selection or dose of medications change the drug or dose selected by physicians and/or patients compared with usual care/no genetic testing?
    b. Do decisions about selection or dose of medications guided by genetic testing result in clinically meaningful improvement in patient response to treatment, or reduction in adverse events as a result of treatment compared with decisions based on usual care/no genetic testing?
2. Harms: What direct harms are associated with conducting genetic testing when it is used to inform the selection or dose of medications?
3. Special populations: Compared with usual care/no genetic testing, do decisionmaking, patient outcomes, or harms following genetic testing to inform the selection or dose of medications vary by:
    a. Clinical history (e.g. prior treatments, whether the diagnosis is initial or recurrent, duration of diagnosis, severity of illness, or concurrent medications); or
    b. Patient characteristics (e.g. such as age, sex, or co-morbidities)?
4. Costs: What are the costs and cost-effectiveness of genetic testing to guide the selection or dose of medications?

Public Comment & Response

No comments were received regarding the draft key questions.