Pharmacogenomics and Psychiatric Disorders

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More than 40 different antipsychotic/antidepressant drugs are available to treat severe mental disorders such as schizophrenia, bipolar disorder and major depression. Drug choice and dose adjustments are empirical and it is common for patients to need several medication changes. There is evidence that genetic factors influence response and adverse reactions to antipsychotics/antidepressants and for many of these medications there are clinical guidelines recommending drug selection/dose adjustments based on genetic variation. However, pharmacogenetics testing is not used in UK mental health practice.

We will present analyses of the UK Biobank, a large cohort study including more than 35,000 participants taking psychotropic medication for psychosis or depression. We investigate if variation in key CYP2D6/CYP2C19 genes influence antipsychotic-induced weight gain or antidepressant-related sedation. We are also investigating polygenic risk scores for schizophrenia/bipolar disorder and how these may identify disease risk in independent samples in order to facilitate prompt access to treatment.

Compared to the general population, people with severe mental disorders face 18-year average reductions in life expectancy, primarily due to poor physical health. Antipsychotic and antidepressant drugs have important adverse reactions such as sedation, metabolic syndrome or arrhythmias. Severe mental disorders, especially psychosis, are highly heritable, and our understanding of their genetic architecture is advancing rapidly. Evidence-based pharmacogenomic interventions have the potential to optimise the prescribing for severe mental disorders.