

# Why is it so difficult to implement precision psychiatry into clinical care?

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Precision Psychiatry has been envisaged as a tool capable of delivering targeted clinical care to groups, or optimally to each individual patient with a mental disorder.<sup>1</sup> But what is the clinical reality today? In Europe, one in ten people is diagnosed with a mental disorder and is in need of treatment. Of these, two-thirds benefit from the available treatment options, while one-third does not. This latter group significantly contributes to the individual and economic burden caused by mental illness. Even when clinical guidelines are rigorously applied, patients who respond unfavorably often need to go through all available therapeutic options before arriving at an effective treatment. During this period, the risk of developing unfavourable outcomes due to accumulating disease exacerbations, symptom recurrences and untreatable residual symptoms gradually increases. Despite all treatment efforts, a group of patients remains that unfortunately develops treatment resistance (TR) characterized by poor recovery and quality of life.<sup>2</sup>

Is this avoidable? One major argument for this situation is the poor quality of diagnosing mental illnesses. However, contrary to common belief, the diagnoses of mental disorders have good to very good reliability but only fair validity.<sup>3</sup> This means that based on clinical criteria such as ICD-11 or DSM-5, the replication of the diagnostic process by another clinician yields similar results. Compared to other medical disciplines like neurology, the reliability of the clinical diagnosis of multiple sclerosis (MS) is comparable to that of schizophrenia.<sup>3</sup> What schizophrenia lacks, compared to MS, is a defined pathophysiology rooted in biomarker-based subtypes. Using biomarkers from blood and cerebrospinal fluid (CSF), as well as imaging and electrophysiology, allows for the definition of different outcomes and specific treatment regimens per subgroup. The example of MS shows that precision medicine relies on the pathophysiological understanding of the illness, allowing to optimally choose

mechanistically informed treatment options for the given patient or patient group.

What needs to be done in psychiatry? So far, single biomarkers in mental disorders have failed to replace clinical diagnoses or predict outcomes and therapy responses. Instead, biomarkers need to supplement the information obtained from trained clinical appraisal.<sup>4</sup> Recent models show that clinicians' estimates significantly contribute (by 65%) to predicting the likelihood of progression from prodromal to the first-episode psychosis.<sup>5</sup> Information from brain imaging or genetics each adds only a few percent, but combined, they raise prognostic precision to a level that is useful for individualized preventive interventions. To implement such biomarker-augmented approaches into clinical care, the data should stem from routinely acquired clinical information, which is not confined to specialized centres. The information needs to be easily accessible, quantitative and standardized so that machine learning algorithms can quickly calculate the likelihood of a given diagnosis, outcome, or response to established treatments.

In a recent prospective study,<sup>6</sup> admission data from general practitioners' outpatient clinics were used to predict whether patients had depression. About 10% of patients were found to have depression that was not previously recognized. Routine examination data such as waist circumference, weight, lab results related to lipid metabolism, and ECG data related to heart rate variability were used to predict the likelihood of depression. Based on this information, further standardized clinical diagnoses can follow, offering specific treatment options.

In psychiatry, the goal should be to utilize routine clinical information from admissions or initial outpatient contacts. This data can be used to calculate the likelihood of a clinical diagnosis, estimate outcomes, and suggest treatment responses for a range of somatic and psychosocial treatment options. This approach allows for specific treatments to be offered to each patient based on a "risk/outcome score," preventing many trial-and-error attempts and reducing the risk of chronic illness.

Finally, the implementation of precision psychiatry requires that the heterogeneity of disorders with poor diagnostic reliability is resolved into more homogeneous, biopsychosocially informed disease entities. The



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detection of therapeutically amenable dimensions and subtypes of diseases in large representative datasets using artificial intelligence is pivotal to this process. By integrating diverse data sources such as clinical records, genetic information, imaging, and biomarkers, machine learning algorithms can help to stratify patients into more precise categories. This approach can improve the understanding of individual variations in disease presentation and treatment response, leading to more personalized and effective interventions.

#### Contributors

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#### Declaration of interests

None.

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