Providing the most appropriate care to our *individual* patients

Andrea Cipriani,[1,2] Anneka Tomlinson[1,2]

With 350 million people affected in the world, depressive disorder is one of the top 20 causes of the overall global burden of disease.[1] The high costs, both direct and indirect, of major depressive disorder are largely due to the significant deficits in treatment provision[2] and therefore remediable with current therapies. A key international challenge is to determine how best to implement currently available and effective treatments.

There are a number of efficacious pharmacological and non-pharmacological interventions for depressive disorder.[3] Antidepressant drugs are recommended and frequently used as first-line therapy for adults with moderate to severe depressive disorder, and in the UK, about 80% of people in primary care receive an antidepressant prescription in the first year of diagnosis.[4] However, a significant proportion of these prescriptions are for less than 30 days, while an adequate trial of antidepressants is generally recommended to be 6–8 weeks before changing or stopping the medication.[3] A too short duration of treatment limits both the therapeutic effect[5][6] and increases the risk of withdrawal symptoms.

A number of factors contribute to the suboptimal treatment duration of antidepressant drugs, and the two most recognised contributing factors include the initial side effects of the medication and their perceived marginal efficacy. These factors are exacerbated by our current limited ability to predict which drug will cause the fewest undesirable side effects for a specific patient and which will work most effectively. Improved methods to tailor specific treatments to individual patients are needed. While the need for such an approach is widely recognised by the National Institute for Health and Care Excellence guidelines, this still remains an unmet clinical need, with no currently reliable ways of doing so.[3]

In fact, however, there are *major* opportunities to improve patient outcomes using existing therapies by the efficient use of available clinical trial data combined with the technical advances in data synthesis and long-term outcomes from real-world datasets[6] Such analyses can now predict the probability of response for a specific subgroup of patients or estimate the chances that a person will have a particular side effect[7] By matching individual patients to individual specific antidepressant drugs, clinicians can precisely customise treatment to patients' individual needs and preferences to ultimately improve their clinical outcome.

Internationally, precision medicine is now a leading aim of healthcare[8] Currently, the process of matching patients to treatments is too often by trial and error, delaying clinical improvement and increasing the risks and costs associated with ineffective treatment. Pooling an analysis of data from clinical trials may provide 'personalised' estimates of comparative effectiveness, stratified for specific subgroups of patients to predict 'individualised' response to treatment. Despite important progress in trying to identify depressed patients who may respond differently,[9] psychiatry continues to lag behind other specialties like cardiology, oncology and stroke (where simple clinical variables were used to target aspirin and heparin to individual patients).

Factors influencing an individual's drug response in depressive disorder include environmental (eg, co-medications, smoking and food), clinical (eg, severity of illness, previous treatments) and personal or demographic variables (eg, age, gender and family history). However, the wealth and variety of these factors creates its own challenges.[10] New methodologies and tools are needed which:

▶ Are based on robust evidence;
▶ Are acceptable to patients and clinicians;
▶ Guide and direct treatment personalisation, incorporating patients' views and values, and clinical judgement;
▶ Support probabilistic decision-making. For instance, a difference in efficacy between interventions of, say, 5% might mean more to one patient than to another and it does not precisely exclude a benefit that clinicians and patients might find meaningful. Or, vice versa, the same result could allow some doctors and patients to choose to avoid the treatment after carefully considered tolerability, risk and uncertainty.

When several treatment options are available, standard meta-analyses provide only partial information because they can only answer questions about pairs of treatments.[11] This fragmented approach does not support optimal clinical decision-making,[12] and the need for a robust method to summarise evidence across several, indeed many, interventions has been increasingly recognised.[13] Network meta-analysis has been developed to (1) synthesise evidence across a network of randomised trials, (2) allow the estimation of the relative effectiveness of several interventions and (3) produce ranked treatment options.[14] A further advancement is individual patient data network meta-analysis (IPD-NMA).[15] IPD-NMA allows the comparative efficacy of different treatments to be assessed, as well as providing a prediction of the clinical outcome, looking for instance at time to response or temporal trajectory of side effects. This is a novel and exciting development which will hopefully drive forward evidence-based practice.

Treatment algorithms have contributed to advances in many fields of medicine including psychiatry, but studies have consistently shown that the initial benefits of algorithm implementation are not sustained once the implementation support is withdrawn. Computerised decision systems have been developed to provide ongoing assistance to clinicians. However, all algorithms developed to date lack the ability to apply the best knowledge directly to the individual patient and selectively provide information relevant to the characteristics and circumstances of that patient in their specific situation. This requires human interpretation and clinician–patient interaction.[16] So, as we recently said,[17] 'is it now time to move away from a 'one size fits all approach' and move towards precision mental health, providing the most appropriate care to our patients individually?'

[1]Department of Psychiatry, University of Oxford, Oxford, UK
[2]Oxford Health NHS Foundation Trust, Warneford Hospital, Oxford, UK

Correspondence to Professor Andrea Cipriani, Department of Psychiatry, Warneford Hospital, University of Oxford, Oxford OX3 7JX, UK; andrea.cipriani@psych.ox.ac.uk

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