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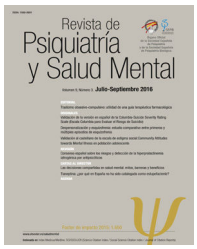

EDITORIAL

Waiting for Godot or the use of biomarkers in clinical practice

Esperando a Godot o el uso de biomarcadores en la práctica clínica

Emilio Fernández-Egea

University of Cambridge, Addenbrooke's Hospital, Psychiatry, Cambridgeshire and Peterborough N, Cambridge, United Kingdom

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The Irish playwriter Samuel Beckett premiered '*Waiting for Godot*' in 1953, a two acts tragicomedy in which a group of characters await and wait for Godot... who never arrives. In a sombre way, it reminds the situation of clinical biomarkers in schizophrenia and other psychotic disorders, as we are still only relying on interview skills for most to all clinical decisions. But one might wonder if we are just ignoring all the accumulated knowledge.

For instance, clozapine therapeutic drug monitoring (TDM) is a tool that can provide clinicians with relevant information for the treatment of schizophrenia or schizoaffective disorders [1]. Clozapine and its metabolite norclozapine blood levels can be used to evaluate the clinical response and could predict psychotic relapses. Of course, it has limitations, such as considering the genetic background [2] or the potential interaction in routine practice [3]. Still, it can provide significant guidance to clinicians to monitor response, control side effects and predict relapse [4]. Additionally, there is increasing evidence of the role of clozapine:norclozapine ratio in the cognitive function in patients with schizophrenia [5], a common symptom in patients with a harmful impact on their daily functioning.

Surprisingly, routine clozapine TDM is not recommended by most international clinical guidelines, and it is limited to non-compliance screening or toxicity assessment. Nevertheless, clinicians are increasingly using annual routine clozapine TDM in countries like the UK, Germany or others. Still, in Spain, we have not even an audit of how many patients are regularly tested or whether all Community mental health teams (CMHT or CSM) have access to this technology. The situation is even more puzzling when compared with other TDM such as lithium, which is far more accepted and regularly done.

But why limit to clozapine? There is growing evidence that TDM for other antipsychotics can also be of great use. A novel forthcoming CIBERSAM/Healthcare Research Fund-supported large multi-centre study aims to characterise and understand the causes of the second episode of psychosis [6], which occurs in up to 80% of patients after FEP. Blood and saliva TDM will be analysed within the project, including many antipsychotics such as aripiprazole, risperidone, paliperidone, olanzapine, and quetiapine. The expectation is to include reliable biomarkers (TDM and neurocognition and imaging) to improve relapse prediction and treatment algorithms.

Of course, many other biomarkers could be potentially added to the clinical guidelines, from cognitive testing [7] to neuroimaging or other blood markers [8] evidence for these tests is, at present, perhaps less solid than for TDM. As we all know, changing clinical guidelines in the traditionally biomarker-aversive field of psychiatry is not an easy step. In this sense, TDM and the markers of physical health offer the best cost-effective balance to be used in practice to guide

E-mail address: ef280@cam.ac.uk

clinical decisions. Importantly, this would represent the first signal that Godot might be finally coming to visit us.

Incidentally, *Waiting for Godot* was first shown precisely the same year that chlorpromazine was first marketed. The delay in novel therapeutic mechanisms for schizophrenia is even more shocking, but this is for another play.

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