## Reconceptualising treatment-resistant depression as difficult-to-treat depression

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We are heartened that our consensus statement[1] on difficult-to-treat depression has provoked robust debate. As pointed out by Lisa Cosgrove and colleagues,[2] our proposed definition and model of care for difficult-to-treat depression is not derived from a systematic review or a Delphi technique. The term difficult-to-treat depression had previously been proposed to address semantic and conceptual issues with the so-called treatment-resistant depression model, for patients where achieving sustained remission proves elusive.[3] We aimed to extend the discussion regarding this proposal, focusing on practical clinical advice. As the concept of difficult-to-treat depression is new, there is no literature to systematically review. The literature around the management of so-called treatment-resistant depression has been reviewed on many occasions, but this literature was only of partial relevance to our aims. Not only is there no universally accepted definition of treatment-resistant depression, but those that are used rarely if ever take into account psychotherapeutic or neurostimulatory treatments, or how to account for differential efficacy among treatments.[4,5] At the core of the proposed difficult-to-treat depression model is the importance of taking a holistic approach and considering all treatment options available. A systematic review of all treatments for depression was not practical. As a result, our consensus was based on the culmination of extensive discussion and deliberation among 15 international experts in the management of depression from across three continents, and the national guidelines for the treatment of depression from the countries represented. Rather than through a Delphi technique, we arrived at a consensus through many iterative reviews of the manuscript until all 15 contributors were comfortable with all the statements being discussed. However, we wish to clarify two key points that we feel Cosgrove and colleagues might have misunderstood.

First, they argue that a better way to address deficiencies of the current treatment-resistant depression model is to strive for a better understanding of why treatment success remains low for some patients. We fully agree with this statement, and this is precisely the central tenet behind the difficult-to-treat depression model. We suggest that when depression is proving difficult to treat, the next step is for the clinician, collaboratively with the patient, to do a comprehensive biopsychosocial assessment of the factors relevant to this, addressing any that are tractable using all appropriate therapeutic modalities. Thus, the difficult-to-treat depression model does precisely what Cosgrove and colleagues argue that it should.

Second, Cosgrove and colleagues' main concern regarding the difficult-to-treat depression model is that they view it as a diagnostic label that is broader and even more susceptible to subjective interpretations than treatment-resistant depression. They suggest that study sponsors could easily take advantage of such loose criteria when designing pivotal trials for new drug applications. We concur that broadening diagnostic criteria can have negative consequences including overmedicalisation and might, as Cosgrove and colleagues have suggested, erode the threshold above which riskier and more expensive treatments are offered to patients. However, once again it seems that what we mean by the term difficult-to-treat depression has been misunderstood. We are not professing that the term is a diagnosis per se, but rather a framework or model of care. We stipulated in our consensus paper that the model was aimed primarily at clinicians, and not regulators. Furthermore, we specifically acknowledged the limitations of our proposed model and noted in particular that difficult-to-treat depression is insufficient to define clinical populations for regulatory trial purposes. Importantly, we intentionally did not indicate where in any particular treatment algorithm specific treatments should be used. Instead, we highlighted an earlier paper that argued for a threshold well above conventional definitions of treatment-resistant depression and including multiple therapeutic modalities, which could help clinicians decide when it might be appropriate to utilise potentially more risky and expensive treatments.[5]

Finally, it is important to note that the proposed difficult-to-treat depression model of care is not appropriate for all patients with depression, and not even for all those who would normally be classified as having treatment-resistant depression. However, the model is a useful concept for both patients and clinicians when management is mutually perceived as difficult, because it serves the aim of averting the development of therapeutic nihilism.

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1 McAllister-Williams RH, Arango C, Blier P, et al. The identification, assessment and management of difficult-to-treat depression: an international consensus statement. *J Affect Disord* 2020; **267:** 264–82.

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# Reporting on suicidal behaviour and COVID-19—need for caution

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News reporting on suicidal behaviour can have a considerable influence on suicide and self-harm in the general population.[1] This issue is particularly relevant during the COVID-19 pandemic. With a rising number of deaths from COVID-19 infection and negative effects of the pandemic on key factors that are associated with suicide, including social isolation, unemployment, and financial problems, there is understandable concern that suicide rates might