

## REFERENCES

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## Dr Leon Replies

**To the Editor:** I thank Dr Siris for the thoughtful comments and for his innovative suggestions to promote discovery of interventions in psychiatry. Clearly, there is a need for the field of psychopharmacology to identify novel treatments. Unfortunately, the promise of translational research in the search for novel mechanisms of action has yet to be fully realized.

In referring to psychopharmacology's initial and highly productive decade, Dr Siris suggests that "broad-ranging serendipity in psychiatric medication finding may still be available" in electronic medical records. Providing researchers access to these rich data, which document an array of clinical encounters, certainly holds potential for treatment development. However, there are several caveats that must be considered.

First, the electronic medical record represents uncontrolled, observational data. Without a comparator, one must rule out the natural history of the illness when evaluating within-patient change over time. Second, in lieu of randomized treatment assignment, patients receive interventions based on clinician or self-selection. As a result, those who receive an intervention will quite likely have clinical profiles very different from those who do not. For example, a clinician might experiment with a novel treatment only in patients who are most treatment refractory. Therefore, statistical approaches appropriate for observational data, such as the propensity adjustment,<sup>1</sup> must be used to account for selection bias. Furthermore, the sensitivity of results to the assumptions of the statistical models must be examined. Third, findings from electronic medical record analyses must be considered preliminary; they require replication before clinical application.

Perhaps the most formidable challenge with electronic medical records is the accuracy of reporting. All too often, reimbursement policy encourages creative reporting of the clinical encounter. For electronic medical record data to be of value for treatment discovery, the administrative system must provide an environment that encourages accurate recording of diagnoses, symptoms, treatments, and outcomes (though they are less readily available). After all, it is only the off-label medication use that will lead to serendipitous findings.

Dr Siris' "search for serendipity" with electronic medical records could serve as a valuable endeavor. We must acknowledge, however, this does not replace the function that clinical observation served in serendipitous findings of psychopharmacology's initial decade.<sup>2</sup>