## Genetics Guideline Is Excellent, but the Pharmacogenetics Section Is Weak

**To the Editor:** Nurnberger et al[1] should be congratulated for their article on psychiatric genetics, which I sent to our Residency Training Director as soon as I saw it. Unfortunately, Nurnberger and colleagues[1] commented on pharmacogenetics, an area with which they may be less familiar because, not surprisingly, pharmacogenetics was not developed by geneticists but by pharmacologists. They did not consider the most important advance in psychiatric pharmacogenetics, the guidelines written by the Clinical Pharmacogenetics Implementation Consortium (CPIC), a group of pharmacologists with expertise in pharmacogenetics. Psychiatrists need to be familiar with the CPIC *CYP2D6* and *CYP2C19* genotyping guidelines for tricyclic antidepressants,[2] selective serotonin reuptake inhibitors,[3] and atomoxetine.[4]

Instead of relying on CPIC experts, Nurnberger et al[1] relied on the US Food and Drug Administration (FDA) and pharmaceutical companies. There are multiple pharmacogenetic tests marketed for psychiatry in the United States that do not demonstrate clinical validity or clinical utility, and only limited analytic validity,[5] yet the FDA has no authority over the marketing of pharmacogenetic tests.[5]

Pharmaceutical companies have opposed pharmacogenetic testing since 2001.[5] As proof of these companies' unreliability regarding pharmacogenetic testing, psychiatrists should know that pharmaceutical company data suggest that atomoxetine was approved using doses that are too low for cytochrome P450 2D6 (CYP2D6) ultrarapid metabolizers, 1.5% of the US population, and possibly for CYP2D6 normal metabolizers with 2 active genes, around one-third of US Caucasians.[6] Independent investigators with limited resources completed the pilot atomoxetine study[7] that the company should have produced and further extended with their resources. If we combine the lack of knowledge of psychiatrists, the lack of US regulation over pharmacogenetic testing, the uncooperativeness of pharmaceutical companies, and the hype from marketers of nonvalidated commercial pharmacogenetic tests, the future of pharmacogenetics in psychiatry does not look good.[8]

### References


1. Nurnberger JI Jr, Austin J, Berrettini WH, et al. What should a psychiatrist know about genetics? review and recommendations from the Residency Education Committee of the International Society of Psychiatric Genetics. *J Clin Psychiatry*. 2018;80(1):17nr12046.
2. Hicks JK, Sangkuhl K, Swen JJ, et al. Clinical Pharmacogenetics Implementation Consortium guideline (CPIC) for *CYP2D6* and *CYP2C19* genotypes and dosing of tricyclic antidepressants: 2016 update. *Clin Pharmacol Ther*. 2017;102(1):37–44.
3. Hicks JK, Bishop JR, Sangkuhl K, et al; Clinical Pharmacogenetics Implementation Consortium. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for *CYP2D6* and *CYP2C19* genotypes and dosing of selective serotonin reuptake inhibitors. *Clin Pharmacol Ther*. 2015;98(2):127–134.
4. Brown JT, Bishop JR, Sangkuhl K, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6 Genotype and Atomoxetine Therapy. *Clin Pharmacol Ther*. 2019; Epub ahead of print.
5. de Leon J. Pharmacogenetic tests in psychiatry: from fear to failure to hype. *J Clin Psychopharmacol*. 2016;36(4):299–304.
6. de Leon J. Translating pharmacogenetics to clinical practice: do cytochrome P450 2D6 ultrarapid metabolizers need higher atomoxetine doses? *J Am Acad Child Adolesc Psychiatry*. 2015;54(7):532–534.
7. Brown JT, Abdel-Rahman SM, van Haandel L, et al. Single dose, CYP2D6 genotype-stratified pharmacokinetic study of atomoxetine in children with ADHD. *Clin Pharmacol Ther*. 2016;99(6):642–650.
8. de Leon J, Spina E. What is needed to incorporate clinical pharmacogenetic tests into the practice of psychopharmacotherapy? *Expert Rev Clin Pharmacol*. 2016;9(3):351–354.



**Jose de Leon, MD**[a,b,c]
jdeleon@uky.edu

[a]Mental Health Research Center at Eastern State Hospital, Lexington, Kentucky

[b]Psychiatry and Neurosciences Research Group (CTS-549), Institute of Neurosciences, University of Granada, Granada, Spain

[c]Biomedical Research Centre in Mental Health Net (CIBERSAM), Santiago Apostol Hospital, University of the Basque Country, Vitoria, Spain



***Potential conflicts of interest:*** Dr de Leon declares no competing interest during the last 36 months and is not a member of the Clinical Pharmacogenetics Implementation Consortium.

***Funding/support:*** No commercial organizations had any role in writing this letter.

***Acknowledgments:*** Dr de Leon thanks Lorraine Maw, MA, from the Mental Health Research Center at Eastern State Hospital, Lexington, Kentucky, for editorial assistance; Ms Maw declares no competing interest during the last 36 months.

***Published online:*** April 9, 2019.

*J Clin Psychiatry 2019;80(3):19lr12741*

***To cite:*** de Leon J. Genetics guideline is excellent, but the pharmacogenetics section is weak. *J Clin Psychiatry*. 2019;80(3):19lr12741.

***To share:*** https://doi.org/10.4088/JCP.19lr12741