Genetics Guideline Is Excellent, but the Pharmacogenetics Section Is Weak

To the Editor: Nurnberger et al1 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 colleagues1 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 al1 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 study7 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

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