Efficacy of Varenicline for Smoking Cessation

To the Editor: In their clinical trials of varenicline for smoking cessation, Dr Gonzales and colleagues,1 Dr Jorenby and colleagues,2 and Dr Tonstad and colleagues3 used broad exclusion criteria, particularly for psychiatric disorders of major depressive disorder within the past year; history of or a current panic disorder, psychosis, bipolar disorder, or eating disorder; or alcohol or drug abuse or dependency within the past year. In addition, Tonstad et al3 excluded potential participants who were taking antidepressants, antipsychotics, or mood stabilizers or anticonvulsants.

However, it is estimated that 30% of smokers have some form of mental illness.4 Moreover, Lasser et al5 estimated that persons diagnosed as having a mental disorder within the past month consumed 44% of all cigarettes smoked in the United States. Therefore, the extensive psychiatric exclusion criteria in these trials may make it difficult to apply their results to the general population of smokers. In addition, patients with psychiatric disorders are frequently heavy smokers. Rates of quitting smoking are lower in smokers with psychiatric disorders.5 Therefore, from a public health perspective, the effect of varenicline also should be assessed in individuals with psychiatric disorders.

Finally, the participants included in the 3 studies examining the efficacy of varenicline on smoking cessation were not assessed using structured interviews for the diagnosis of psychiatric disorders according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, or the International Statistical Classification of Diseases, 10th Revision. Appropriate instruments include the Diagnostic Interview Schedule and the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Because such instruments are necessary to make an accurate research diagnosis, the study results may have been biased.

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In Reply: We are in agreement with Drs Dervaux, Kanit, and Laqueille that all smoking cessation therapies, including varenicline, merit evaluation in population-based effectiveness trials following US Food and Drug Administration approval. These varenicline trials were phase 3 clinical trials designed to investigate safety and efficacy of an investigational drug prior to Food and Drug Administration approval. The exclusion criteria that were specified, including those for psychiatric conditions, were similar to those used in prior studies of investigational drugs for smoking cessation.1,2 They were chosen for several reasons.

First, investigational drug studies generally exclude participants with poorly controlled medical conditions or use of medications that might compromise either participant safety or evaluation of safety or treatment effects of the drug being studied. Second, because participants in the studies by Gonzales et al1 and Jorenby et al2 could have been assigned in a random, double-blind manner to either varenicline, bupropion, or placebo, all participants had to meet safety criteria for the comparator drug (bupropion sustained-release) as well as those for varenicline. As a result, the exclusion criteria regarding psychiatric disorders were designed to be similar to prior bupropion studies.1,2 Third, the use of the same exclusion criteria used in key bupropion sustained-release smoking cessation trials made possible a more valid scientific comparison between the active treatments. Given that these 3 studies demonstrated efficacy and safety in a healthy population, the next step should be to examine the effectiveness of varenicline in more medically compromised and diverse populations.6

Dervaux et al question the assessment of psychiatric disorders in these studies. While self-report was used rather than structured interviews to assess psychiatric history and...
adverse events, it is likely that the double-blind design of all 3 studies controlled adequately for any potential bias in the study results.

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Use of Computed Tomography to Assess Coronary Artery Stenosis

To the Editor: In their study of the accuracy of 16-row multidetector computed tomography (MDCT) for assessment of coronary artery stenosis, Dr Garcia and colleagues concluded that MDCT angiography may be useful to exclude coronary artery disease in selected patients in whom a false-positive stress test result is suspected. We have a number of questions about this conclusion and the study.

First, to establish such a role, there must be an assessment of the correlation between clinical pretest probability and diagnostic accuracy of 16-row MDCT for the assessment of coronary artery stenosis. The study included patients with intermediate or high probability of coronary artery disease who were referred for coronary angiography. The 32% prevalence of obstructive coronary artery disease, defined as at least 1 segment with luminal narrowing of more than 50%, was lower than anticipated, given that all patients had clinical indications for diagnostic catheterization, and 136 (86%) of the 158 patients who had undergone stress testing prior to enrollment had a positive or equivocal result. We are currently performing subgroup analysis to address the utility of MDCT according to stress test results and clinical stratum.

Regarding the overall performance characteristics of 16-row MDCT coronary angiography in our study, the positive predictive value was low (50%) but the negative predictive value was high (99%) in a patient-based analysis for...

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In Reply: Drs Hakeem, Bhatti, and Chapman raise several important issues. The primary objective of the Coronary Assessment by Tomographic Scanning and Catheter Angiography (CATSCAN) study was to measure the diagnostic accuracy of 16-row MDCT for the assessment of stenotic coronary artery disease. The study included patients with intermediate or high probability of coronary artery disease who were referred for coronary angiography. The 32% prevalence of obstructive coronary artery disease, defined as at least 1 segment with luminal narrowing of more than 50%, was lower than anticipated, given that all patients had clinical indications for diagnostic catheterization, and 136 (86%) of the 158 patients who had undergone stress testing prior to enrollment had a positive or equivocal result. We are currently performing subgroup analysis to address the utility of MDCT according to stress test results and clinical stratum.

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