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Response to Kaufman and Harper Letter

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To the Editor

A great deal of research shows that the *CHRNA5-CHRNA3-CHRNB4* haplotypes are associated with measures of smoking quantity (1–4). However, earlier research presented inconsistent results with regard to the association of these haplotypes with smoking cessation likelihood. Our findings show that these haplotypes can predict cessation success and also that their association with cessation likelihood differs depending on the use of smoking cessation pharmacotherapy in the quit attempt. In essence, we obtained a significant interaction effect between haplotype and treatment condition such that individuals with haplotypes that confer a heightened risk of relapse benefited much more from cessation pharmacotherapy than did individuals without such haplotypes.

In our study, we used both the Cox proportional hazards model to estimate the likelihood of smoking relapse over time and the logistic regression model to estimate the odds of smoking abstinence, and both showed greater benefit from pharmacotherapy in individuals with risk haplotypes than in those without such haplotypes. However, at one point in the article, we discussed the odds ratio generated by the logistic regression as if it reflected relative risk. In their letter, Kaufman and Harper note that the odds ratio and the relative risk ratio diverge for analyses of common events.

We agree with Kaufman and Harper's observation and appreciate their pointing out that the results of our research appear even more striking when portrayed in terms of number needed to treat. In our study, the number needed to treat is seven when computed across all individuals regardless of their haplotype status, supporting the established effect of pharmacotherapy. However, this number varies widely depending on the individual's haplotype. Based on their absolute risks, the number needed to treat is four for smokers with the high-risk haplotype, seven for smokers with the intermediate-risk haplotype, and >1,000 for smokers with the low-risk haplotype. We agree with Kaufman and Harper that a number needed to treat of four is an impressive finding compared with the numbers needed to treat of many existing pharmacotherapies. The wide variation between smokers with different

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haplotypes supports the notion that personalized smoking cessation intervention based on genotype could meaningfully increase the efficiency of such treatment.

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