

while the Veling et al. Dutch study investigated the potential effect up until approximately age 30. However, because the greatest impact in the Dutch study was observed in individuals migrating early in life, this cannot explain the differences in the observed results.

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Deficiency of the Odds Ratio for Common Outcomes

TO THE EDITOR: The article by Chen et al. (1) in the July issue provides a fascinating account of the interaction by genotype in the context of a smoking cessation trial. Participating smokers were randomly assigned either to placebo (N=132) or to various combinations of active treatments (N=941). The authors then reported the proportion with confirmed 7-day abstinence after 8 weeks, stratified by three common haplotypes (defined by two single-nucleotide polymorphisms on chromosome 15 that have established associations with nicotine and cocaine dependence). Despite clear evidence of statistical interaction between haplotype group and successful smoking cessation, the authors' stated conclusion that "[s]mokers with the high-risk haplotype were three times as likely to respond to pharmacologic cessation treatments as were smokers with the low-risk haplotype" is not correct. As shown in Figure S4 of the online data supplement that accompanies the Chen et al. article, treatment approximately doubled (not tripled) the 8-week abstinence proportion in the high-risk haplotype group, from about 24% to about 50%. In contrast, there was no treatment effect in the low-risk haplotype group.

The explanation for this large discrepancy is that the authors made the common error of interpreting odds ratios from logistic regression models as relative risks. This interpretation is not valid for outcomes that are not rare. It has been repeatedly noted in the biomedical literature that this is a serious deficiency of the odds ratio (2, 3), and many authors have therefore urged that for cohort analyses such as those used in the Chen et al. study, the odds ratio is not a parameter of interest and should be avoided (4). It is simple in these settings to estimate risk ratios or differences (5), and this also facilitates useful calculations such as the number needed to treat (i.e., the inverse risk difference) (6). For example, manipulation of these absolute risks shows that the number needed to treat in

order to prevent one relapse among the high-risk haplotype subpopulation is approximately four. This is an impressive finding that is completely obscured in the published analysis.

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Response to Kaufman and Harper Letter

TO THE EDITOR: A great deal of research shows that the CHRNA5-CHRNA3-CHRNA4 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