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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CARSTEN BØCKER PEDERSEN, DR.MED.SC.
Aarhus, Denmark

ELIZABETH CANTOR-GRAAE, PH.D.
Lund, Sweden

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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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JAY S. KAUFMAN, PH.D.
SAM HARPER, PH.D.
Montreal, Quebec

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Response to Kaufman and Harper Letter

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

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LI-SHIUN CHEN, M.D., M.P.H., Sc.D.
St. Louis

TIMOTHY B. BAKER, Ph.D.
Madison, Wisc.

LAURA J. BIERUT, M.D.
St. Louis

The authors' disclosures accompany the original article.

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Research on Medical Marijuana

To the Editor: In the June 2012 issue, Drs. Kleber and DuPont (1) conclude that there is no place for medicinal cannabis based on a selected and incomplete review of the data. First, they suggest that evidence for marijuana's efficacy is anecdotal. This is incorrect. There are results from at least five recent clinical trials reported in peer-reviewed publications (2–6); all of these indicate medicinal cannabis' efficacy, particularly in the management of neuropathic pain and possibly for multiple sclerosis spasticity. Second, they suggest that medical marijuana laws may lead to increased marijuana abuse as a result of reduced perception of risk. Actually, recent epidemiologic studies concluded that, after adjustment for other factors, such laws had no effect on recreational marijuana consumption (7). Additionally, in their review of the situation in California following passage of Proposition 215, the authors, while correctly pointing to the problems of unregulated dispensaries that followed in its wake, failed to mention a more positive development: California established the Center for Medicinal Cannabis Research at the University of California, the first such center in the nation, to conduct clinical trials to shed light on this topic (http://www.cmcr.ucsd.edu/index.php). Recently, we provided an update on medicinal cannabis research along with a possible algorithm to guide evaluation and decision making by physicians who may be in a position to recommend medicinal cannabis (8).

It is timely to consider the state of the science in medicinal cannabis; however, this needs to be done with full awareness and balanced consideration of all the relevant facts. Hopefully, our letter will facilitate this process by addressing some issues that were missed in the commentary.

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