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Reply to Dr Umanoff

Reply: Do Self-Reports Reliably Assess Abstinence in Cocaine-Dependent Patients?

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Sir

Dr Umanoff has identified an important aspect of our study, and that of substance abuse research in general. Unlike disorders with reliable biological markers (hypertension, pneumonia, cancer, etc), cocaine dependence lacks a precise outcome measure, forcing researchers, and clinicians to rely on a urine drug screen (UDS) to measure the persistent cocaine metabolite, benzoylecgonine (BE). Urine testing is a rough measure of clinical outcome, and often plagued by missing data, which cannot be presumed to be random because active users are more likely to miss clinic visits. Self-reports provide an alternative means of assessing cocaine use, but are limited by the veracity of cocaine-dependent patients. Unfortunately, it is well documented that cocaine-dependent patients often under-report their cocaine use (Myrick *et al*, 2002), which is why researchers and clinicians rely more on urine testing than reported use. Cocaine-dependent patients might under-report cocaine use due to forgetfulness, denial, or force of habit, and sometimes to please providers or avoid treatment consequences. Regardless of why under-reporting occurs, it is too prevalent for self-reports to constitute an acceptable primary outcome measure in cocaine clinical trials sponsored by the National Institute of Drug Abuse (NIDA) (Ehrman *et al*, 1997; Hser *et al*, 1999; Morral *et al*, 2000; Appel *et al*, 2001). Simply stated, urinary BE testing is currently the scientific standard.

Over-reporting of cocaine use is much less of a problem, and we acknowledge that it would be an extremely unusual occurrence. That said, small amounts of cocaine used 3 days before urine testing could certainly go undetected, and give the false appearance of 'over-reporting.' Given these considerations, we are frankly puzzled by the following statement in Dr Umanoff's letter:

The peer reviewers should have insisted that the discrepancy be resolved either by showing the urine tests were erroneous or that the patients, when asked again about their coke use, admitted lying about it, lying about using more coke than they actually did, something I've never heard of.

If we are interpreting his statement correctly, Dr Umanoff has assumed that modafinil-treated patients over-reported cocaine use, without considering the more likely explanation of under-reporting by placebo-treated patients. Dr Umanoff also criticized our omission of the actual self-report data, and our decision not to discuss this nonsignificant data in the *Abstract* and *Discussion* sections of our paper.

We believe we followed accepted practice by omitting the nonsignificant self-report data. We also note that for both self-reported use variables (dollars spent and days of use), the mean responses in the modafinil group were lower than those in the placebo group for each of the 8 weeks of the study. While this difference was consistent with that shown by the UDS results, the statistical comparison between the two groups showed no significant difference, and we believe that the discrepancy between the two sets of hypothesis tests reflects the unreliability of self-reports by cocaine-dependent patients. Since Dr Umanoff requested specific relevant data, we provide below a comparison between our UDS data and that obtained from the Timeline Follow Back (TLFB), our most rigorous measure of patient self-reports.

There were 1063 urine samples collected in our study, of which 559 were cocaine-positive and 504 were cocaine-negative. To assess concordance between urine testing and TLFB self-reports, we used a cutoff of 3 days, based on a conservative estimate of BE urinary persistence. Patients were considered to be under-reporting when they submitted a positive urine sample on a given date, but denied cocaine use for the three prior days. They were considered to be over-reporting when they submitted a negative urine sample on a given date, but reported cocaine use during

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the three prior days. We found under-reporting in 24% of urine samples (affecting 158 urine test results), and over-reporting in only 2% of urine samples (affecting 12 urine test results). These findings clearly indicate that over-reporting cannot explain the nonsignificance of our self-report data. In the placebo-treated group, a total of 21 patients (66%) under-reported their cocaine use at least once, affecting 94 (19%) of their cocaine-positive urine samples. Of the modafinil-treated group, a total of 14 patients (47%) under-reported at least once, affecting 64 (11%) of their urine samples. The higher proportion of under-reporting in the placebo group would explain some of the discrepancy between the UDS and self-report results. Under-reporting probably occurred at a greater frequency because patients with consecutive missed visits did not provide UDS samples, so their self-reports of abstinence could not be compared to urine testing and were not included in the analysis.

These data indicate that patients in our study were much more likely to under-report than over-report cocaine use, especially since 'over-reporting' could reflect actual cocaine use that was undetected by urine testing. Under-reporting cocaine use occurred in both groups, but was much more prevalent in the placebo-treated patients and may be associated with poor clinical outcome, especially since honesty is an important element of recovery (Dackis and O'Brien, 2001). These data substantiate the widely held view that self-reports do not provide a reliable means of assessing abstinence in cocaine trials.

Although new technologies might ultimately provide better objective measures of clinical outcome in cocaine dependence, the field currently utilizes BE testing, which demonstrated significant improvement in our modafinil-treated patients. Therefore, we stand by our conclusion that 'further research should be conducted to determine whether modafinil might become a first-line treatment for cocaine dependence.' Three large NIDA-sponsored clinical trials are currently assessing modafinil treatment for cocaine dependence. These studies will provide a more definitive test of the efficacy of modafinil, and permit a more complete consideration of the dual roles of objective and self-reported measures of use.

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