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Reply to Discrepant Results for Smoking and Cessation Among Electronic Cigarette Users

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Dr. Rodu and colleagues have made several comments regarding our article[1] that merit a response.

First, Rodu et al identified an inconsistency in the reporting of our analyses examining whether electronic cigarette (E-cigarette) users and nonusers differed in their smoking cessation outcomes. Shortly after the online publication of our article, we discovered a formatting error (reference group mislabelings) in Table 2, resulting in a discrepancy between the text and table reporting of the findings.[1] An erratum was submitted and published on November 25, 2014. The text and table are now consistent in reporting the equivalence of follow-up smoking cessation outcomes for e-cigarette users and nonusers using the complete case analysis (CCA) and the higher abstinence rate for nonusers with the intent-to-treat (ITT) analysis. We regret this inadvertent error.

Second, Rodu et al raise concerns regarding selection bias. We are aware that selection bias may be a concern in observational studies in which an important predictor is not randomized. In this specific case, Rodu and colleagues critiqued that the patients' current use of E-cigarettes was not randomized. In an effort to address these concerns, a straightforward propensity score adjustment was performed and it made no substantive difference in our main conclusions. Specifically, the propensity score model fitted log odds of current E-

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cigarette use as a function of age, sex, cancer diagnosis, and other factors found to be associated with the use of E-cigarettes. We then added this propensity score covariate to the logistic regression models reported in Table 2.[1] This adjustment made slight changes in the odds ratios, but no difference in the statistical significance of the covariates at the .05 level. In future studies, more sophisticated matching algorithms to address potential selection bias may be applied.

Next, Rodu et al questioned our presentation of CCA and ITT analyses. Consistent with recommended standards for reporting smoking abstinence in treatment programs and clinical trials,[2-4] we present both CCA and ITT analyses. For the ITT analysis, we included all patients who enrolled in the tobacco treatment program in the outcome analyses and assumed all patients whose follow-up smoking status could not be determined to be smoking cigarettes. We acknowledge the limitations of these analytic models,[5,6] appreciate the challenge of dealing with missing binary data when reporting cessation outcomes (particularly within the context of differential rates of follow-up), and chose to present both the CCA and ITT models. This method is consistent with current abstinence reporting practices[2,3] and readily allows for comparisons between our outcomes and those of other prior studies. In a recent analysis of missing data models, Witkiewitz et al concluded that missing data did not appear to significantly influence smoking outcomes after controlling for nicotine dependence level and therefore we included nicotine dependence in our analyses.[7] The clinic coordinator responsible for the follow-up assessment was blinded with regard to patients' E-cigarette use status. The follow-up data collection efforts were identical for E-cigarette users and nonusers. We know of no peer-reviewed recommendation for reporting smoking abstinence that assumes that patients lost to follow-up be treated as nonsmokers. This assumption is not consistent with the high rates of persistent smoking reported among patients with cancer.

Rodu et al further requested that we more fully explore potential selection bias in current E-cigarette use by revising Table 1 in our study[1] to include, in addition to the 414 completers, dropouts (367 patients who were lost to follow-up or had died at the time of last follow-up) and patients who were not yet due for outcome assessment (293 patients). This would not resolve the bias issue because it would only introduce additional nonevaluable abstinence outcomes, including the missing data for the 367 dropouts and unknown abstinence data for the 293 patients not yet due for outcome assessment. Although it would add more descriptive data regarding the differences between E-cigarette users and nonusers, it would not shed any new light on the abstinence rates through better control over a possible selection bias in the covariate of current E-cigarette use. Existing statistical methods, such as the propensity score adjustment described above, would delete a case by default unless the adjustment or propensity matching is linked to an evaluable, nonmissing outcome (barring ITT or imputation). This leaves the 414 completers, the only pragmatic and possibly most prudent choice of a sample in a selection bias adjustment. As reported in Table 1, the only significant difference was found in the number of past quit attempts (at least 2 vs never or once),[1] which was included in our attempt in propensity score adjustment above.

We agree that the dramatic observation of a 3-fold increase in the use of E-cigarettes among tobacco-dependent patients with cancer is striking and suggestive of patients' effort to mitigate the risks of persistent smoking of combustible cigarettes. However, these trends should be compared with use patterns among smokers, particularly those who are likely motivated to quit, rather than the general population.[8] We strongly agree that further research examining the potential benefits and harms of E-cigarette use among patients with cancer who are trying to quit is warranted. The risks of persistent smoking among patients with cancer should guide oncologists to discuss the known and unknown safety and efficacy of E-cigarettes and recommend evidence-based cessation treatment[9].

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