DOI: 10.1093/jnci/djr558
Advance Access publication on January 25, 2012.

Enhancing the Effectiveness of Smoking Cessation Interventions: A Cancer Prevention Imperative

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The emergence of the epidemic of tobacco addiction, primarily to cigarette smoking, in the United States and other developed nations in the first half of the 1900s was a global public health tragedy of untoward proportions. After the deleterious health effects of cigarette smoking began to be recognized, a major public health accomplishment was the success of tobacco control efforts in initiating a turnaround in the epidemic. In the United States, the prevalence of current smokers was reduced by 55% (from 42% to 19%) between 1965 and 2010 (1).

Major progress remains to be achieved; with approximately one in every five adult Americans a current cigarette smoker, smoking remains far too common. Smoking persists as a major cause of disease and death because of this substantial prevalence combined with the broad spectrum of diseases caused by smoking in many different organ systems. Cigarette smoking contributes heavily to the overall cancer burden; roughly one-third of all cancer deaths in the United States are attributable to cigarette smoking, because of its established role as a cause of cancers of the lung, oral cavity, larynx, esophagus, bladder, pancreas, kidney, cervix, and stomach, as well as acute myeloid leukemia (2). Consequently, any intervention that reduces smoking prevalence, either by preventing the uptake of smoking among youth or promoting smoking cessation among addicted smokers, represents a powerful cancer prevention strategy. This assertion is demonstrated by the fact that the decline in smoking prevalence is a major contributing factor to the current decline in cancer death rates in the United States (3).

The health benefits of smoking cessation are well documented (2); compared with persistent smoking, cigarette smokers can reduce their risk of smoking-caused disease by quitting smoking at any age. Two efficacious smoking cessation interventions are 1) counseling, which can be delivered via telephone quitlines, and 2) smoking cessation pharmacotherapies, including both nicotine replacement therapy (NRT) and non-nicotine therapies such as bupropion and varenicline.

Increasingly, the heterogeneity within the smoker population is recognized as a potentially important factor that may influence the effectiveness of smoking cessation interventions. In this issue of the Journal, articles by Zhu et al. (4) and Cox et al. (5) incorporated interventions known to work in the overall population of smokers to assess the usefulness of interventions in targeted segments of smokers that were at least partially defined by ethnicity. Zhu et al. (4) tested the effectiveness of counseling delivered via a telephone quitline tailored for Asian American smokers, and Cox et al. (5) tested bupropion in a population of African American light smokers.

In California, Zhu et al. (4) carried out a randomized controlled trial (RCT) of more than 2200 smokers of Chinese, Korean, and Vietnamese ancestry, who spoke their native languages, to test the efficacy of ethnically tailored telephone counseling in native language on quitting smoking compared with ethnically tailored self-help materials. Careful consideration was given to the tailored features of the intervention, such as use of a directive and authoritative counseling style, emphasizing that counseling was provided by university experts, and differences in approach based on the sex and age of the smoker. Each Asian ethnic group was represented in approximately equal numbers, and not only did the overall results indicate that the ethnically tailored and language-specific quitline intervention led to a statistically significantly greater likelihood of 6-month prolonged abstinence compared with self-help materials (16.4% vs 8.0%, $P < .001$) but this benefit was present within each Asian ancestry subgroup.

The tailored intervention in Asian immigrants provided clear evidence of the efficacy of telephone quitlines in smokers of Asian ancestry (4). This suggests that telephone quitline interventions are also likely to be highly transportable to Asian countries. This is relevant to global tobacco control because Asia is one of the current epicenters of the worldwide tobacco addiction epidemic (6).

In an era of increasingly scarce resources, factoring in cost is essential because tailored services add to the cost of providing quitline services. Zhu et al. (4) considered this issue and suggested the practical alternative of offering this tailored service through the national quitline. The study demonstrated that the tailored quitline

intervention tested was more efficacious than self-help materials, and provided some support for this alternative, but the evidence in support of the tailored intervention would have been strengthened if the tailored intervention was tested against a non-tailored quitline intervention, which is known to be efficacious in the overall smoker population (7). By using self-help materials as opposed to a non-tailored intervention as the control condition, the relative impact of a tailored vs non-tailored intervention remains an open question.

Cox et al. (5) carried out a randomized placebo-controlled trial of bupropion plus counseling vs placebo plus counseling in a population of 540 African American light smokers, who smoked 10 or less cigarettes per day. The smoking-caused risks of disease and death are dose dependent, but this should not be construed as minimizing the need for treatment even among light smokers. On average, light smoking is associated with less cancer risk than heavy smoking, but even light smoking is a potent risk factor compared with most other established cancer risk factors. Furthermore, nicotine dependence is evident in light smokers (8), and these light smokers comprise a growing segment of the smoking population (9). Compared with white smokers of European descent, evidence indicates that African American smokers are more susceptible to smoking-caused cancer [eg, (10)] and are more likely to smoke fewer cigarettes per day (11). The evidence in light smokers is sparse but suggestive that pharmacotherapy is efficacious (12). Most previous RCTs of smoking cessation pharmacotherapies were in predominantly white populations of European descent, but the existing evidence suggests the efficacy of cessation pharmacotherapy is comparable between these white populations and other ethnic groups (13).

The use of a non-nicotine medication, bupropion, was an attractive choice because of its potential appeal to smokers who harbor negative perceptions of NRT, perceptions more widely held by African Americans than other ethnic groups (11,14). Conversely, bupropion is a prescription medication, posing a barrier to access, often a key consideration in disseminating treatments to minority populations.

The results indicated that the intervention was efficacious in the short term during the time of intervention delivery, but after 26 weeks of follow-up, results based on self-reported smoking abstinence showed a statistically significant benefit for the intervention (odds ratio [OR] = 1.57, 95% confidence interval [CI] = 1.04 to 2.42, $P = .033$), whereas for the primary study outcome of biomarker-verified abstinence, the results were not statistically significant (OR = 1.39, 95% CI = 0.82 to 2.35, $P = .23$). Despite the lack of statistical significance for the outcome of biomarker-verified smoking abstinence at the end of follow-up, the odds ratios of 2.9 at end of treatment and 1.4 at final follow-up were consistent with previous evidence of pharmacotherapy among nonwhite smokers (15).

Cotinine is a well-validated and frequently used biomarker of recent smoking. Because cotinine-verified smoking abstinence was the primary study outcome, it is important to report specific methodological details of the study to remain consistent with the optimal use of biomarkers in population studies. This includes reporting the extent of missing data, whether the laboratory was blinded to intervention arm (important because bupropion metabolites were measured only in the intervention arm), and sending blinded quality control samples to the laboratory to quantify the study-specific real-time assay variability. Thorough and transparent reporting of such details is helpful because as with any type of measurement, even the best biomarkers are imperfect and potentially susceptible to measurement error.

The study findings remind us that it may be false to presume that intervening on light smokers is more easily accomplished than intervening on heavy smokers, at least among African Americans. The treatment regimen of evidence-based cessation medication (bupropion for 7 weeks) and six in-person psychosocial counseling sessions was a robust intervention for smokers who smoked less than 10 cigarettes daily. In fact, except by adding post-intervention booster sessions, a more robust intervention for light smokers is difficult to envision. This study highlights the continuing need for additional treatments for African American light smokers that result in long-term sustained abstinence. Beyond ethnic ancestry, substantial gains in efficacy of smoking cessation pharmacotherapy are theoretically possible by tailoring therapy using a pharmacogenetic approach, if clinically useful genetic markers were characterized that reliably predicted response to specific smoking cessation pharmacotherapies (15).

To reduce the enormous burden of cancer caused by cigarette smoking, improved and intensified tobacco control efforts are needed to accelerate progress toward reducing what can currently be characterized, alarmingly, as endemic levels of smoking prevalence. In addition to developing new smoking cessation intervention strategies, an important need is to refine understanding of existing intervention strategies known to be beneficial by characterizing whether they work in important segments of the smoker population. The two studies reported in this issue of the Journal (4,5) remind us that the population impact of smoking cessation interventions is a function of both its 1) efficacy and 2) reach. By applying smoking cessation interventions of proven efficacy to assess their value within subgroups of the smoker population, these studies have advanced understanding of the potential value of tailored interventions vs a "one size fits all" approach.

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Funding

National Institutes of Health (R01 CA154992 [to M.J.C.], P30 CA138313, UL1 RR029882).

Notes

The authors declare no conflict of interest.

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