Smoking Reduction and Tobacco-Related Cancers: The More Things Change, the More They Stay the Same

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Forty years ago, on January 11, 1964, the U.S. Surgeon General released a report that officially recognized that smoking causes cancer and other diseases (1). Since the release of that seminal report, knowledge about tobacco use, addiction, and tobacco-related disease has increased dramatically. With this knowledge has come major public health improvements: The prevalence of tobacco use has been cut in half, the number of former smokers nearly equals the number of current smokers, and some gains have been achieved in reducing lung cancer incidence and mortality rates (2,3). However, it is clear that we have not solved the problems associated with tobacco use. Approximately 23% of adults in the U.S. currently smoke, almost twice the target goal of 12% outlined in the Healthy People 2010 initiative (3,4). More than 440,000 Americans and approximately 5 million people worldwide die prematurely each year as a result of tobacco use and tobacco smoke exposure (5).

In this issue of the Journal are two quite different, yet complementary, articles on the impact of tobacco use on cancer. The first article, by Hecht et al. (6), evaluates the impact of nicotine replacement-assisted reduced smoking on biomarkers of cancer risk—particularly levels of major metabolites of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), a potent tobacco-specific lung carcinogen. The second article, by Vienis et al. (7), summarizes epidemiologic data which demonstrates that tobacco use is causally related to an even greater number of cancer sites than were identified in a 1986 International Agency for Research on Cancer (IARC) Monograph (8). Together, these articles serve as a poignant reminder that tobacco’s role as a cancer initiator and promotor is not only multifactorial and complex, but also remains one of the greatest global public health challenges.

Although we know that smoking cessation will reduce future cancer risk, we know little about smoking reduction or transition to other tobacco products (such as smokeless tobacco) as methods for reducing cancer risk. For example, do smokers who use nicotine replacement products (e.g., gum, patch, inhaler, or lozenge) to reduce, but not quit, smoking, decrease their intake of potent carcinogens and thus reduce future cancer risk? The study by Hecht et al. (6) addressed that question and concluded that although reduced smoking and concomitant reductions in biomarkers of cancer risk can occur with behavioral and pharmacologic support, reduced smoking is of ‘limited value’ as a means of reducing NNK exposure. More specifically, despite finding statistically significant reductions in NNK metabolites, Hecht et al. (6) speculated that smokers compensate for the reduced smoking by becoming more efficient smokers; thus, even a large reduction in smoking often led to only a modest reduction in levels of NNK metabolites. Although this observation is consistent with other studies (9,10), it is yet another reminder that standardized methods for assessing tobacco constituent exposure, such as the one adopted by the U.S. Federal Trade Commission, cannot adequately account for variations in human smoking behavior (11).

There are additional reasons why the study by Hecht et al. (6) does not provide much support for smoking reduction as a means of decreasing cancer risk. Their study revealed that a whole battery of tests, rather than one assay, is needed for evaluating tobacco products and assessing reductions in harm from tobacco. To evaluate total harm reduction, methods need to assess the myriad of toxins and carcinogens in cigarette smoke in addition to NNK. Choosing a surrogate marker of exposure to one carcinogen in the particulate phase of cigarette smoke does not allow for drawing conclusions about reduced exposure to other harmful smoke constituents, such as carcinogenic benzene and 1,3-butadiene, released in the gas/vapor phase. In addition, we do not know the threshold of exposure reduction that would translate into reduction of harm. For example, because no linear dose response relationship has been established for NNK, reducing NNK uptake by 50% may or may not reduce cancer risk. Modest exposure to NNK in the presence of other smoke constituents may be sufficient to cause lung cancer in some individuals at greatest genetic risk. Consequently, such individuals would need a much larger reduction in their exposure to substantially reduce their cancer risk. Moreover, even if we could demonstrate that a reduction in a single biomarker corresponds with a decreased lung cancer risk, we would need to track multiple biomarkers of cancer risk in multiple organ systems, given the conclusions of Vienis et al. (7) that tobacco use causes even more cancers than we previously recognized.

In 1986, the International Agency for Research on Cancer (IARC) concluded that tobacco smoke causes not just lung cancer, but also cancer in several other organ systems, such as head and neck, bladder, and pancreas (8). In an update to that report, Vienis et al. (7) summarize the IARC Monograph 83 findings that tobacco use also causes myeloid leukemia, as well as cancer of the stomach, kidney, liver, and cervix (12). Furthermore, the IARC Working Group concluded that involuntary smoking (exposure to secondhand or “environmental” tobacco smoke) is carcinogenic to humans (12). This new IARC report...
is nothing short of a new “call to arms” and reminds us that 40 years after the release of the 1964 report by the Surgeon General and despite substantial progress in reducing smoking rates, we have taken only modest steps in confronting this enormous public health threat. As Vineis et al. (7) note, if current smoking patterns continue there will be 1 billion deaths attributable to tobacco use worldwide during the 21st century, with the death toll reaching 10 million per year by 2030.

Now that tobacco use and secondhand tobacco smoke exposure have been shown to be causal factors for an expanding list of cancers and other diseases, how do we prioritize efforts to optimally reduce or eliminate tobacco-related disease? It is essential to implement whenever and wherever possible the approaches and interventions that have been shown to be effective. In the United States, the evidence suggests that certain policy changes have effects on the population that impact both smoking uptake and decisions to quit. For example, there is considerable evidence that increasing the cost of tobacco not only decreases youth tobacco use by creating a larger economic barrier to smoking, but also motivates adults to try to quit (13). We also know that effective behavioral and pharmacologic treatments exist and do work when they are affordable, widely available, and used properly in clinics and communities (14,15).

There are those who suggest that now is the time to implement “harm reduction” approaches because so many smokers cannot or will not quit smoking (16). However, as the study by Hecht et al. (6) clearly shows, there are major challenges to demonstrating a public health benefit of a “harm reduction” approach, and certainly insufficient data to support the practice of encouraging smokers to pursue reduced smoking as a harm reduction strategy. Given the current dearth of evidence supporting the viability and benefits of reduced smoking as a harm reduction strategy, and given the strong evidence that smoking cessation can have a dramatic impact on future tobacco-related morbidity and mortality, the IARC working group (12) correctly concludes that the most dramatic health benefits in the next half century will occur if we can significantly increase the number of smokers who quit.

REFERENCES


