

Message from the Series Editor

This volume is the twentieth of the Tobacco Control Monograph series of the National Cancer Institute (NCI). The series began in 1991 with a visionary blueprint for public health action on tobacco prevention and control. In the years since, it has disseminated important cross-cutting research in areas such as the impact of tobacco control policies, the risks associated with smoking cigars and low-tar cigarettes, systems approaches to tobacco control, and the role of media in promoting and reducing tobacco use.

The subject matter of this monograph began with an informal review and critique of the behavioral genetics literature related to smoking. This review showed that genotyping is restricted to only a few phenotypes (usually current and former smokers) and that standard definitions of smoking behavior are not commonly used. For example, in the United States, an “ever smoker” has been defined generally in the epidemiology and surveillance literature as someone who has smoked at least 100 cigarettes in his/her entire life. Similarly, there is consensus about the need to separate current smokers into “every day” and “some days” smokers. This distinction is rarely made in smoking genetics research. The lack of use of standard definitions of these and other aspects of tobacco use behavior (for example, smoking cessation) not only hinders comparisons among genetics studies, but also the ability to put results from these studies into context of knowledge gained from other disciplines. The need for standard definitions and measures of tobacco use behavior is critical to furthering our understanding of the genetic and environmental determinants of tobacco use.

Much of the tobacco literature examines genetic susceptibility to smoking initiation and cessation only among very broad groups without an understanding of the complexities or variations within these categories in patterns of smoking behavior. Combining very different subgroups of smokers into a few common phenotypes (for example, the current smoking phenotype often includes both light and intermittent smokers with heavy daily smokers) and then using such heterogeneous groups in research studies may be hindering progress in our understanding the role of genetics in complex behaviors such as smoking.

Another limitation of genetics research is that it is often based on small, nonrepresentative samples of the population, which limits the generalizability and interpretability of the findings. The frequency of genetic variants determined from nonprobability-based samples may not reflect the true underlying frequency in the general population. Therefore, epidemiologic and etiologic conclusions based on these results may be misleading. Only through the analysis of population-based samples will we be able to examine the relative contribution of genetics and environment, as well as gene-gene interactions and gene-environment interactions, to explaining variations in tobacco use behavior, dependence, and disease risk. Population-level genetic analyses will also help us determine if previously identified genetic variants are truly associated with smoking and whether conflicting findings in the literature are due to population stratification (selection bias).

Finally, while the effect of single genetic variants is likely to be small for complex behaviors such as smoking, previous research has not studied the joint effects of different genetic variants on tobacco use behavior, dependence, and disease risk. Large, national samples are needed to allow us to examine the potential impact of these multiple genetic variants.

This monograph was originally intended to demonstrate the need for standard definitions of tobacco use behavior and to explore the utility of using epidemiologic data from national surveys, as well as data from a multitude of other sources (such as smoking topography) and disciplines (such as psychology and pharmacology) to identify unique smoking phenotypes for genetic analysis. In addition, the original proposal called for exploring the conceptual and measurement issues related to describing the entire continuum of smoking behavior, from the first few adolescent puffs to “hardcore” dependence. Several steps were outlined to achieve these objectives: (1) synthesize the existing literature; (2) conduct original data analyses and develop innovative methods to address the research gaps; (3) examine the application and usefulness of the potential phenotypes for genetic, epidemiologic, and behavioral research; and (4) make recommendations for future conceptualization (theory/model building), methods development (new measurement, innovative analytic approaches), and new data collection and empirical research.

Researchers within and outside NIH also reached the conclusion around this same time that there were a number of questions, including those related to behavioral genetics, which could be most effectively addressed only if a clear definition for nicotine dependence was developed. These researchers, many of whom have subsequently edited or authored this monograph, were particularly interested in finding ways to define various groups of smokers along meaningful dimensions (such as dependence) that could help to advance the field of behavioral genetics of smoking. One of the most significant obstacles identified in behavioral genetics research of smoking was the lack of valid and useful phenotypes.

Although the content of this monograph has changed somewhat to focus more on nicotine dependence phenotypes, it has remained true to the original vision. The publishing of this monograph comes at a critical time. The field of behavioral genetics is evolving rapidly. Efforts are underway to develop core sets of standardized measures to use in genetic studies. The need to identify a broad range of homogeneous phenotypes of nicotine dependence has never been clearer. While the literature on the relationship between genetic variation and treatment outcomes was not addressed, new and important discoveries presented in this monograph concerning the assessment, development, and maintenance of nicotine dependence may help clinicians target interventions more effectively—to specific components of nicotine dependence and to windows of opportunity for more precise timing of intervention delivery. Moreover, more refined phenotypes may provide more sensitive indicators of the impact of treatment for nicotine dependence and, ultimately, lead to a stronger evidence base for pharmacogenetically-informed treatments.

Moreover, a better understanding of the role of genetic susceptibility may help the public health community enhance already effective public policies for tobacco prevention and control. Much progress in reducing tobacco use has already been made and much is already known to work; however, even in this context, knowledge gained from genetic studies may play an important role in designing new and innovative environmental and policy interventions. We hope the science presented in this monograph guides the field for many years to come.

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Monograph Series Editor
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