

# CEBP Focus: Nicotine and Tobacco-Control Research

## The Future of Tobacco-Control Research

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### Abstract

Recent epidemiologic data on the stabilization of adult and youth smoking rates underscore the need for vigorous research across the cancer control spectrum on tobacco use interventions. The steady decline in adult rates of smoking has stalled for the first time in 8 years, and certain race, ethnic, and population groups are disproportionately at risk to tobacco-related cancers because of disparities in tobacco use or access to effective interventions. Although substantial progress has been made across levels of basic through applied research, tobacco-control research across the discovery and delivery continuum must be accelerated to further reduce the cancer

burden. Following a brief review of the prevalence and trends affecting tobacco use initiation and cessation, we identify and describe four domains of extraordinary research opportunities: genetics and gene-environment interactions, bioinformatics and health informatics, disparities and disproportionate risk, and prevention and treatment. Evolutionary scientific changes, like rapidly advancing technology and emphasis on the paradigm of team science research approaches, provide both a challenge as well as unparalleled opportunities for scientific advancement and public health progress. (Cancer Epidemiol Biomarkers Prev 2007;16(6):1077–80)

### Tobacco Prevalence and Health Issues

Smoking has been the chief preventable cause of illness and death in the United States for more than three decades and is responsible for 440,000 deaths annually. Tobacco use is a major worldwide contributor to deaths from chronic diseases. Findings from the Global Youth Tobacco Survey suggest that the current dire warnings of a doubling of the death toll to 10 million deaths per year by 2020 could be a conservative estimate (1). Cigarette smoking is a primary cause of death from lung cancer, coronary heart disease, chronic obstructive pulmonary disease, and stroke. It is tied to multiple cancers besides lung, including cancers of the larynx, oral cavity, esophagus, bladder, kidney, and pancreas (2). Approximately 44.5 million adult Americans, representing 20.5% of the population, are smokers (3). These rates reflect dramatic decreases since 1965 when 42% of the population and 52% of males were smokers. In 2006, overall cancer rates dropped for the first time in a century, a milestone attributed to the significant reductions in smoking.<sup>3</sup> Thun posits that there would have been virtually no reductions in cancer mortality since the early 1990s without reductions in smoking (4). Although the reductions over the last four decades are significant, recent evidence is cause for concern. Although adolescent smoking rates steadily declined from over 36% in 1997 to 23% in 2005, this downward trend is now flattening. Furthermore, rates of adult smoking held steady from 2004 to 2005, after declining steadily for 8 years (5). Although the vast majority of smokers wish to quit, less than 5% are successful, pointing to a need to develop more effective treatments, better disseminate proven treatments, and employ effective community interventions and policies.

Smoking, from initiation to regular use to cessation, is determined by multiple factors, including biological, genetic, behavioral, social, and environmental (6). Discoveries emerge from epidemiologic inquiries and other basic or fundamental research in disciplinary areas, including biomedical sciences, psychology, sociology, anthropology, and economics. Intervention research builds on the evidence base from epidemiologic studies and fundamental research and then attempts to discover effective means to apply what has been learned at all levels of the health system and community (7). In tobacco-control research, this includes interventions at the individual (e.g., behavioral and pharmacologic treatments), health care system (e.g., insurance reimbursement and electronic medical records that prompt providers to treat), and population (e.g., smoke-free policies and tax increases) levels. Surveillance in tobacco-control, in addition to assessing initiation and cessation broadly and across subgroups, identifies disparities, research, and treatment gaps. Surveillance is also essential to identify changing and emerging tobacco products. For example, new smokeless tobacco products are being widely developed, and current smokeless tobacco products are now promoted for use when or where smoking is prohibited. Other products such as flavored cigarettes and the current trend of hookah pipe use are of particular concern among youth and young adults.

The President's Cancer Panel recently proposed a systems model for rapidly translating new discoveries into more effective approaches to prevent and treat cancer with special attention to dissemination and adoption to all Americans. This same model is essential for advancing the prevention and treatment of tobacco use (8). Similarly, NIH has created a

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<sup>3</sup> The contributions of behavioral and social sciences research to improving the health of the nation: a prospectus for the future (Draft Report). NIH, Department of Health and Human Services, Office of Behavioral and Social Sciences Research. 2006. Accessed 10/27/06: <http://www.conceptsystems.com/OBSSR/OBSSR-Prospectus-final.pdf>.

national consortium, funded through Clinical and Translational Science Awards, that will enable researchers to provide new treatments more efficiently and quickly to patients (9). These research frameworks are essential for speeding smoking prevention and cessation products to the market so that we can more rapidly reduce smoking prevalence and reduce tobacco-related disease.

**Trends Affecting Uptake and Cessation.** The reduction in smoking prevalence rates over the last four decades have been a tremendous victory for public health. This reflects both effective prevention efforts that curb rates of smoking initiation as well as cessation among smokers, where fully half of all Americans who have ever smoked have quit (10). Several social-environmental factors have been identified as significant in changing patterns of tobacco use on a community societal level. Banning smoking in public places, smoke-free work site policies, increasing cigarette price, and mass media counter-marketing campaigns have all been implicated in reducing cigarette consumption and increasing cessation (11, 12). Additionally, the argument can be made that such policies de-normalize smoking, thereby exerting a preventive force on youth uptake. Furthermore, the cost of behavioral and medication treatments and other treatment access variables will also affect the proportion of individuals who quit smoking. Closely linked to access to treatment are factors affecting consumer demand for treatment and prevention services, such as perceptions of their effectiveness and safety. Tobacco industry marketing, directly through advertising and introduction of new products and indirectly through sponsorship of sporting and civic events, continues to be a destructive vector in tobacco-control efforts.

**Populations.** Those with less education and lower income are disproportionately at risk for tobacco-related diseases. Among individuals with a masters degree or higher, only 7.1% were current tobacco users compared with 43.2% who had a GED diploma. Living below the poverty level is a risk factor for smoking, as well, with higher rates (29.9%) compared with others (20.6%; ref. 5). A higher percent of service and blue-collar workers are smokers (31% and 35%, respectively) compared with white-collar workers (20%; ref. 13). Although there are mixed findings regarding the question of whether current smokers are more hardcore than two decades ago, there is general agreement that there clearly a subpopulation that has been alternatively characterized as recalcitrant or unreachable. There is increasing concern about high rates of smoking and difficulty quitting among those with psychiatric disorders. For example, individuals with a diagnosis of schizophrenia have disturbingly high smoking rates, approximating 90% (14).

**Delivery Channels.** Interventions have been delivered using varied channels. Over 70% of smokers visit their physician every year, and over 50% of smokers see a dentist every year, providing practitioners opportunities to employ treatments and strategies as outlined in the PHS Clinical Practice Guideline Treating Tobacco Use and Dependence (15, 16). Health care system level interventions include provision of dedicated staff and resources, establishment of smoking cessation treatments as covered services, and practitioner reimbursement. Full insurance coverage for smoking intervention services has been shown to increase cessation attempts, cessation rates, and utilization of medications (17, 18).

Innovative use of communication technologies hold much promise for reaching greater numbers of smokers and for enhancing effectiveness of existing treatments. Web-assisted

treatment interventions, interactive telephone applications, and mobile phone text-messaging can be tailored or personalized to the individual and can be efficient modalities for smoking cessation (19, 20). Perhaps the broadest reach is afforded by policies restricting smoking in the workplace, restaurants, and other public areas.

### Extraordinary Research Opportunities

Across the landscape of tobacco-control research, vectors of scientific progress, cancer disparities, and new technologies converge to create an opportunity to accelerate progress in tobacco-control research. Table 1 provides a summary of key research directions and challenges.

**Genetics and Gene-Environment Interactions.** Inherited genetic variation is important in explaining individual differences in incidence of tobacco-related cancers, nicotine dependence, cessation, and response to treatment. The interaction of genetic factors with environmental factors is a fruitful area of inquiry. Environmental factors (e.g., culture, SES, family discord, stress, and peer smoking) interact with genetic factors to determine susceptibility to, development, and progression of nicotine dependence and smoking behaviors. Moreover, different gene-environment interactions are likely to exert influence at different points in the development of tobacco use (i.e., from initiation to maintenance to cessation/relapse; ref. 21).

Maternal smoking during pregnancy, for example, has been found to be a risk factor for subsequent nicotine dependence among offspring (22). Although the value of genetics research on the etiology of nicotine dependence has been challenged (23), this work provides new avenues for identifying novel and more effective behavioral and pharmacologic treatment approaches. Recent work, for example, illustrates emerging research in pharmacogenetics exploring how genetic variation in drug-metabolizing enzymes and drug targets can influence responses to pharmacotherapies (24).

**Bioinformatics and Health Informatics.** Technological advances in informatics have set the stage for accelerating progress reducing the burden of cancer. Innovative measurement methods track exposure to and use of tobacco products as well as compliance with medications and monitoring of mood and urges for cigarettes. Electronic medical records not only provide clinicians with immediate risk-factor information and intervention prompts but can also easily permit tracking of smoking status, interventions, and outcomes for individual patients as well as permit practitioners to perform profiles of their practice or group practice (or larger systems) concerning patterns of change. The linking or merging (or networking) of patient/subject information and data across studies and populations can vastly improve the ability to develop and then

**Table 1. Key research opportunities**

Genetics and gene-environment interactions influencing tobacco use and cessation
Bioinformatics and health informatics: development of standardized measures of exposure
Disparities: vulnerable, at risk, and underserved populations
Interventions: development of new medications and novel behavioral approaches
Methodology and measurement: refinement of smoking phenotypes and increase research on effectiveness of treatments
Team science: expansion of interdisciplinary and transdisciplinary research

deliver innovative, effective interventions. The National Cancer Institute is leading the development of a bioinformatics platform (caBIG) that includes common terminology and tools to connect scientists and institutions (25). Key research opportunities in informatics are the need for standardized measures of exposure for all cancer patients and linking of epidemiologic, clinical, pathology, genomic, and proteomic databases.

**Disparities.** It is well known that many population groups suffer disproportionately from cancer. Gender, ethnicity, and socioeconomic status are among the major factors that influence disparate rates of cancer incidence, morbidity, and mortality (26). Certainly, the social and demographic variations of tobacco use, mentioned above, are significant with regard to tobacco-related cancers and underscore the vital need and extraordinary opportunity for advances in this realm. This was a key/principal recommendation in the NIH State of the Science statement: "Tobacco Use: Prevention, Cessation, and Control" (14). Much more must be done in developing tailored, effective prevention and treatment approaches to populations that are vulnerable, at-risk, underserved, and/or unreached.

**Interventions.** Despite clear progress, many are still at risk for initiating smoking, and the majority of smokers who wish to quit are unsuccessful. The State of the Science report recommends that research on population-level interventions is needed regarding their active components/critical features as well as research on the science of disseminating these interventions more broadly (14). Tobacco harm reduction strategy approaches, including potential reduced exposure products, merit research (27). The medication armamentarium for smoking cessation is steadily increasing, with multiple nicotine-delivery systems and two non-nicotine smoking cessation aids (28). Continuing research into novel compounds, new indications for existing medications, with attention paid to specific effectiveness in special risk populations, is critically important (29). These populations include those with psychiatric disorders, who are pregnant, and who are diagnosed with cancer or other serious diseases.

## Challenges and Opportunities

**Methodology and Measurement.** The technological advancement of measurement methods that allow real-time behavioral data capture (e.g., ecological momentary assessment, accelerometers, and GPS technology) are being increasingly applied in tobacco-control research. More refined phenotypes for nicotine dependence and withdrawal will help guide us in developing tailored treatments.

With the emergence of informatics grids integrating data sets, the field is being challenged to agree upon constructs and terminology, develop and adopt data-sharing guidelines, and manage intellectual property issues. With regard to measurement of outcomes, scientists are urged to move beyond evaluating efficacy in the controlled clinical setting to studying effectiveness across diverse groups of smokers.

**Team Science.** Traditional, unidisciplinary, single-investigator research has been a fundamental building block in all cancer-related research, including cancer control research. Team science is being recognized as a useful approach to accelerating progress. The recognition of the complex, multi-dimensional nature of tobacco use has been an optimal area to use cross-disciplinary team science approaches. Embodied by the Transdisciplinary Tobacco Use Research Centers,

these research paradigms provide the opportunity for integrative research across disciplinary boundaries. Cross-disciplinary research may extend the reach beyond unidisciplinary approaches, which remain essential to discovery. Finally, it is recommended that a key priority is improving the dissemination of successful interventions and increasing community participation throughout the research, noted as a key area in the President's Cancer Panel report (8).

## Conclusion

The battle against the disease burden imposed by tobacco use still endures. It is critically important that tobacco-control research maintain its course in developing and delivering effective prevention and treatment approaches to practitioners, communities, and individuals, including those disproportionately at risk. In addition to investigating novel approaches, proven programs that have yielded significant public health gains should be sustained and improved. Scientists must be prepared to respond to the rapidly changing landscape of tobacco-control. Populations (e.g., youth initiation, established smokers, and patterns of use), tobacco-control resources (e.g., funding and research capacity), and the tobacco industry (e.g., product evolution and marketing) are dynamic. These vectors of influence also are interactive: what happens with tobacco industry marketing affects patterns of use; use patterns influence research priorities. The new evidence of stabilization of smoking rates underscores that the critical challenge for tobacco-control research is accelerate progress to achieve the goal of reducing the burden of tobacco-related cancer and other diseases.

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