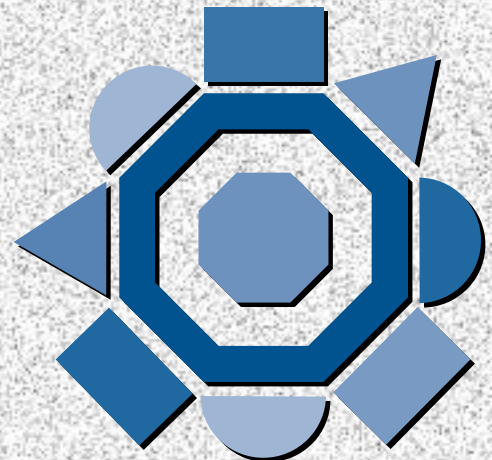


The National Cancer Institute

Tobacco Research Implementation Plan

**Priorities for
Tobacco Research
Beyond the Year 2000**



**Prepared by the
Tobacco Research Implementation Group
National Cancer Institute
National Institutes of Health**

November 1998

The National Cancer Institute

**TOBACCO RESEARCH
IMPLEMENTATION PLAN**

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Beyond the Year 2000**

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Tobacco-related cancers exact an exorbitant toll on the Nation's public health. Tobacco use in the United States is responsible for over 450,000 total deaths and 170,000 cancer deaths every year. More than 30 percent of all cancer deaths are caused by tobacco. The magnitude and complexity of the public health problem created by tobacco use and its accompanying diseases heighten the importance of the National Cancer Institute's (NCI) tobacco-related research.

A constellation of scientific advances, public policy, and social and legal developments presents the scientific community with an unprecedented opportunity to expand research that can dramatically reduce the burden of death and disease caused by tobacco use. Seizing that opportunity, however, poses significant challenges for the NCI and the research and public health communities. In a field where every need seems pressing, it is imperative that we meet the challenge of identifying where tobacco-related research is most needed and how best to prioritize and achieve research objectives that will be financially responsible and have the greatest impact.

To accomplish this goal, the Director of the NCI created the Tobacco Research Implementation Group (TRIG), which includes more than two dozen leading scientists and experts from within the NCI, the National Institute on Drug Abuse (NIDA), and the Office of Behavioral and Social Sciences Research (Office of the Director), and from the extramural research community, as well as representatives of major NCI review and advisory committees. The TRIG was charged with establishing the NCI's tobacco-related cancer research priorities for the next 5 to 7 years.

The TRIG began by reviewing the extensive recommendations of four

earlier advisory groups. Each of these earlier reports produced major recommendations for tobacco control research; however, no single previous report considered the entire spectrum of tobacco control research, from basic biological research to dissemination research. Furthermore, a number of the recommendations of these earlier review groups already had been partially or completely implemented. Therefore, in addition to reviewing these earlier reports, the TRIG analyzed NCI's current portfolio of tobacco research. Finally, the group sought input from representatives of other Federal agencies and private organizations around the Nation.

Through a consensus-building process, the TRIG identified and prioritized a core set of tobacco-related cancer research opportunities. Within this core set, nine unique, overarching research opportunities were identified as the highest priorities, requiring immediate implementation. These opportunities cover the range of tobacco control research from basic biological and basic biobehavioral research to clinical intervention, policy, epidemiology, surveillance research, and support for research infrastructure. The research priorities presented in this report also emphasize the unique opportunities and challenges of tobacco initiation, regular use, addiction, and cessation among youth and populations at disproportionate risk.

The TRIG emphasized that formation of strategic partnerships in the implementation of this research agenda is critical for success. The NCI must collaborate with partners in both the public and private sectors, such as NIDA, the Centers for Disease Control and Prevention, the American Cancer Society, and the Robert Wood Johnson Foundation.

This report includes two main components. A detailed Executive Summary

is provided for readers who want an overview of the top recommendations. The full report, following the Executive Summary, provides a detailed background and rationale for the highest priorities and other important research recommendations. The considerable overlap between the Executive Summary and the report was crafted by design to meet the needs of different readers. The nine highest priorities are summarized below.

1. **Transdisciplinary Tobacco Research Centers should be created to study the initiation of tobacco use, prevention of tobacco use, addiction to tobacco, and/or treatment of tobacco addiction and tobacco-related cancers.**

Increasingly, tobacco control research must rely on transdisciplinary teams of experts in diverse areas, including, but not limited to, genetics, epidemiology, tobacco-induced carcinogenesis, medicine, health psychology and other behavioral/social sciences, policy, and marketing. Specialized, transdisciplinary tobacco research centers should embrace a range of disciplines and investigations, consolidate expertise, facilitate collaboration, and provide the foundation for major scientific advances as well as productive training programs that address the urgent need for producing the next generation of tobacco researchers. Within the broad spectrum of tobacco research, the levels of specialization would vary from center to center. All centers would focus on priority issues, where major gaps in knowledge (e.g., adolescent smoking) create important barriers to advancing the field. Such centers would provide unique opportunities for innovative approaches to research.

The TRIG has made creation of these centers its top priority, envisioning them as part of a collaborative funding effort among NIH partners, especially the National Institute on Drug Abuse (NIDA), and private foundations. The centers are

the most effective way to achieve the Institute's priorities in all areas of tobacco research. These centers should lead the Nation and the world in conducting tobacco research and in discovering new ways to combat tobacco use and its consequences.

2. **Basic biobehavioral research should be conducted to understand the sociocultural, psychological, physiological, and genetic factors that influence the initiation of tobacco use, progression to nicotine addiction, and smoking cessation among children, adolescents, and adults.**

Among the critical and fundamental unanswered questions facing researchers is why some people

adopt or cease tobacco use, while others do not. Tobacco use results from a complex interplay of biological, behavioral, and environmental influences. Gaps in fundamental knowledge about tobacco adoption, maintenance, and cessation highlight the need for research to understand the interacting effects of these influences. Recent research breakthroughs in genetics now make it possible to examine the complex biological and behavioral foundations of tobacco use and nicotine addiction. For example, recent studies have identified genes

that modify nicotine metabolism and the activity of neurochemicals that affect the reinforcing properties of nicotine. There also have been new findings concerning important biological differences in nicotine metabolism among individuals and ethnic groups. Research in this area may identify innate vulnerabilities to tobacco use and addiction in the context of sociocultural and psychological influences. Research to determine the critical thresholds for progression from occasional use of tobacco products to nicotine addiction would aid in identifying appropriate levels of intervention at different stages of tobacco use. In this effort, special attention must be given to the primary and interactive effects of developmental factors, psychological comorbid disorders, and tobacco product design and marketing influences. Research also

It was the unanimous and fundamental conclusion of the Tobacco Research Implementation Group that an unequivocal commitment of the NCI to a comprehensive but focused program of research on tobacco use can help to reverse the epidemic of tobacco-related cancers.

is needed into the basic neurobiological processes and mechanisms related to nicotine addiction. Research in animals and cellular models would be needed since these processes and mechanisms would most likely entail cellular and molecular studies of the brain. This research will lead to improved treatments and intervention programs by increasing understanding of the biobehavioral underpinnings of tobacco use and nicotine dependence. This will help clinicians and public health providers better target prevention and treatment strategies. Much of the research in this area should be conducted in partnership with NIDA.

3. Research concerning the treatment of nicotine addiction should be conducted to find the best ways to tailor tobacco cessation interventions to specific sociocultural, psychological, physiological, and genetic subgroups.

As new pharmacological treatment products become available, research is needed to evaluate and maximize their effectiveness in specific patient populations. Research also is needed to evaluate the relative effectiveness of behavioral modification approaches and pharmacological therapies, treatments that combine the two, and combinations of pharmacologic agents. These new combinations hold particular promise for increasing tobacco cessation rates. This research also will determine the effectiveness of these approaches for different subgroups of tobacco users, such as heavy smokers, pregnant women, African-Americans, and adolescents. It will help define optimal treatment for individuals with different psychological, physiological, or genetic profiles. Advances in genetics may offer many new and unexpected opportunities for the rational tailoring and matching of treatments to individuals based on genotype. The new digital electronic media also can be used, in combination with other strategies, to tailor programs based on information needs and preferences. Much of the research in this area should be conducted in partnership with NIDA.

4. Research should be conducted to improve community and state tobacco control programs and to increase the effectiveness of these programs for populations at disproportionate risk.

Ultimately, promising interventions developed through research should be assessed at the community and state levels. Understanding societal influences on the decision to use tobacco is critical to reducing the tobacco-related disease burden. The need for useful research on the effectiveness of community and state interventions to reduce tobacco use has never been greater. New tobacco control programs are underway in almost every state, and major questions remain about the relative effectiveness of different components of these programs. Additionally, new validated measurement tools and systems to support this complex research are needed. Research in this area will provide a scientific basis for designing and implementing effective interventions, such as counter-advertising campaigns, and for improving a wide range of other programs that prevent the initiation of tobacco use and promote cessation. In developing these community and state tobacco control programs, special emphasis should be given to high-risk populations, especially low-income groups, where tobacco use is increasingly concentrated. The wide-ranging impact of state programs on large populations has been well documented, and further research can increase the effectiveness of these programs.

5. Research should be conducted to identify mechanisms for optimal dissemination of proven prevention and treatment interventions at the community and state levels.

As interventions for prevention and treatment are found to be effective in particular population groups, dissemination and diffusion trials are needed to evaluate the optimal methods for applying these approaches within entire health care systems and at the national, state, and community levels. There has been only modest attention to the challenging question of how to disseminate evidence-based tobacco control programs. Yet, there are exciting opportunities to adapt and disseminate proven interventions. For example, we know that few Americans (particularly the poor) currently have access to the most effective school-based prevention programs or to physician counseling and self-help cessation programs. There is a great need for a stronger science of dissemination

and technology transfer and for research to evaluate policies and strategies that increase dissemination. Research also is needed to determine the types of system change needed to institutionalize tobacco control interventions. Effective dissemination of proven interventions will have a significant impact on tobacco use.

- 6. Research should be conducted to understand the impact of tobacco policies, including taxation and pricing, clean indoor air policies, marketing restrictions, youth access restrictions, and tobacco product and nicotine replacement regulation.**

Policy research can potentially influence some of the most wide-ranging interventions currently used in tobacco control. Public and private policies, such as those listed above, can reduce tobacco use among populations of entire states and nations. For example, policies that increase the price of tobacco, restrict its marketing, and limit where it can be used have resulted in a decrease in tobacco use. But numerous questions remain about the impact of other types of policies, such as youth access restrictions, as well as the relationship between policies and tobacco adoption, use, addiction, and cessation. For example, how do tobacco advertising and promotion interact with biobehavioral factors to increase youth susceptibility to tobacco use? How does product design, including amount of nicotine and mode of delivery, influence nicotine use and dependence among users? And what are the relative costs and benefits of mandating Medicaid coverage for nicotine addiction treatment? Additionally, opportunities exist to learn from effective foreign tobacco control policies, and the NCI is uniquely positioned to take the lead in research examining cross-national policy differences. International research could be especially useful in clarifying the impact of advertising restrictions on tobacco use.

- 7. Basic biological research should be conducted to identify and validate biomarkers of tobacco exposure and tobacco-induced cellular events as they relate to the different stages of carcinogenesis.**

Recent advances in defining the genetic and epigenetic basis of cancer will allow us to expand knowledge of the origins and processes of tobacco-

co-induced cancers. This should lead to new ways to prevent, detect, diagnose, and treat cancer and discover why tobacco-related cancers are so difficult to cure. The focus of our recommendation is on biomarker development founded upon basic carcinogenesis research that will broaden the approach to risk assessment of people exposed to tobacco and allow for rational selection of biomarkers. These biomarkers include carcinogen-macromolecular adducts, assays to measure enzymes involved in critical cellular processes, methods to detect DNA damage and decreased DNA repair, RNA-based methods to identify changes in expression, genetic variations that increase vulnerability or resistance to cancer-causing chemicals, and metabolites of procarcinogens or cancer-causing agents. Basic research to explore mechanisms of tobacco-induced molecular damage at different stages of carcinogenesis will increase understanding of how tobacco carcinogens cause their deleterious effects and what the specific molecular changes and genetic targets are for these effects. More knowledge is required about how tobacco smoke carcinogens drive the stages of carcinogenesis, leading from early, pre-neoplastic events to tumor growth and metastasis, as well as how these carcinogens affect cancer susceptibility genes that have caretaker and gatekeeper functions within the cell. Research to understand these basic changes and to identify and validate biological markers is essential. The identification and validation of biomarkers, based upon new understandings of tobacco-induced carcinogenesis, will allow us to evaluate populations where we can directly assess human cancer risk using a wide range of biomarkers that represent different effects on the cell at the various stages of carcinogenesis. Ultimately, this knowledge will lead to more rational prevention methods and ways to identify who is at risk for the most aggressive cancers. Finally, basic biological research can make critically important contributions by examining tobacco-induced carcinogenesis in women and in former smokers.

- 8. Research should be conducted to understand genetic and environmental interactions in susceptibility to tobacco-related cancers in order to identify subgroups at risk.**

Molecular and genetic epidemiology studies are needed to determine if tobacco-related cancer risks differ according to factors such as gender, race, and ethnicity and to discover the genetic and other biological factors responsible for these differences. Tobacco use provides an ideal model for the study of gene-environmental interactions.

Continued study of interactions among multiple genes and between genetic and environmental factors is needed to increase understanding of why some individuals get cancer from smoking, but others are spared, and to develop methods for reducing risk of tobacco-related cancers. A better understanding of the independent and interacting effects of inherited susceptibilities and tobacco-exposure variables could elucidate risk profiles and the biological mechanisms involved in the development of cancer. This knowledge could lead to the development of tailored approaches to prevention and treatment of tobacco-related cancers. Highly targeted chemopreventive agents or cancer therapies could be developed for use by individuals with particular genotypes. It will be particularly important to study the effects of susceptibility to tobacco-related cancers in women who have been understudied in previous research and in former smokers who appear to be at continued risk for cancer development. Chemopreventive agents can also be used to treat former smokers, who remain at increased risk for lung cancer for years following cessation because of persistent carcinogen effects at the cellular and genetic levels. Finally, studies of youth and young adults (and especially cohort studies) may lead to a better understanding of the process of nicotine addiction as well as genetic and environmental factors that predispose individuals to this problem.

- 9. Research should be conducted on expanded surveillance systems to monitor tobacco use behaviors, the implementation and fidelity of tobacco-related interventions, and other factors that influence tobacco use.**

Surveillance research is critical to an effective, comprehensive tobacco control research program and is an integral and necessary component of a comprehensive research portfolio. Today, tobacco surveillance consists primarily of examining

changes in tobacco use by analyzing questions added to national or state surveys and by estimating per capita tobacco consumption from federal or state excise tax receipts. While useful in highlighting changes in smoking behavior and prevalence, these data fall critically short of providing researchers, program evaluators, and policymakers with necessary information about why tobacco use changes occur (or fail to occur) and those factors that influence trends. A comprehensive and integrated program of surveillance research is needed to ensure consistency, frequency, and completeness of measurement. Information provided by such a system would facilitate efforts to understand biological, behavioral, and social influences that drive tobacco use among teenagers and adults. Also, as new, innovative interventions are developed and disseminated, surveillance mechanisms must monitor the implementation and quality of these interventions over time. By providing critical information needed to understand tobacco use behaviors and evaluate all aspects of tobacco control interventions in community settings, surveillance research facilitates a more comprehensive and effective tobacco research program at the state and national levels.

OTHER PRIORITY RESEARCH ISSUES

In addition to these highest priority tobacco research opportunities, the TRIG also made other recommendations. Research is needed concerning the influence of different tobacco products and alternative delivery devices/systems on initiation, nicotine addiction, and cessation of tobacco use. Investigation is also necessary to determine the optimal settings and mechanisms to deliver effective tobacco cessation treatments to culturally diverse and high-risk populations. Prevention research must focus upon development and evaluation of novel approaches for preventing tobacco use among youth at disproportionate risk.

CONCLUSION

The tobacco research opportunities identified by the Tobacco Research Implementation Group should be pursued through a variety of mechanisms. Most NCI-funded research must be supported through investigator-initiated research proposals. Every effort should be made to convey to the research community

the NCI's interest in this broad range of tobacco control research, including training. In addition, several strategically chosen initiatives should use set-aside funds to catalyze research in selected high priority areas. The transdisciplinary centers could use a mechanism developed for Specialized Programs of Research Excellence (SPORE). Cofunding by NIDA and the Robert Wood Johnson Foundation would be desirable. Since the proposed community studies would be relatively large and complex, they would benefit from cofunding from other institutions and organizations. It may be useful to consider special mechanisms, such as the use of supplements to augment existing youth cohort studies. Wherever possible, strategic funding partnerships should be pursued to facilitate a coordinated, comprehensive attack on the tobacco problem.

The nine unique opportunities that are outlined in this report constitute the highest priorities for advancing the science of tobacco control. They are made with a thorough understanding of recent advances in this diverse field. A comprehensive approach to tobacco control research must include each of the activities described above. The aggressive pursuit of these nine research opportunities will significantly advance tobacco control research and maximize the potential for reducing tobacco use and tobacco-related diseases. As the new millennium approaches, the NCI should make the commitment to catalyze the research needed to turn the tide on the tobacco epidemic.

Tobacco-related cancers exact an exorbitant toll on the Nation's health. Tobacco use is responsible for over 450,000 deaths and 170,000 cancer deaths each year in the United States—more than 30 percent of all cancer deaths. Worldwide, tobacco use causes an estimated 3 million deaths per year, and this number is expected to rise to 10 million deaths annually by the 2020s or early 2030s. Smoking, the most common form of tobacco use, is a known cause of cancer in eight major sites, many of which are among the most difficult to diagnose and treat. Smoking causes more than 85 percent of all deaths from lung cancer and over 50 percent of all deaths from cancers of the larynx, oral cavity, and esophagus. Further, smoking is a known cause of chronic obstructive lung disease, peripheral vascular disease, coronary heart disease, stroke, and many other serious diseases. Exposure to cigarette smoke in the environment also can cause lung cancer and

(both licit and illicit), homicides, murders, and AIDS. It is as though two fully loaded jumbo jets crashed every day of the year—with no survivors.

Using smokeless tobacco and smoking cigars also results in serious health problems. Smokeless tobacco is causally related to several forms of oral cancer, particularly cancers of the cheek and gum, and causes other noncancerous oral diseases. Cigar use causes cancers of the lung, larynx, esophagus, and oral cavity.

Tobacco-related deaths today reflect the cumulative outcome of tobacco use over decades. Both current smokers and former smokers are affected. Reductions in smoking prevalence over the past several decades provide some optimism for the future. Today, just under 25 percent of adults in the United States are cigarette smokers, including those who do not smoke daily (20 percent of the total). These figures are an improvement over

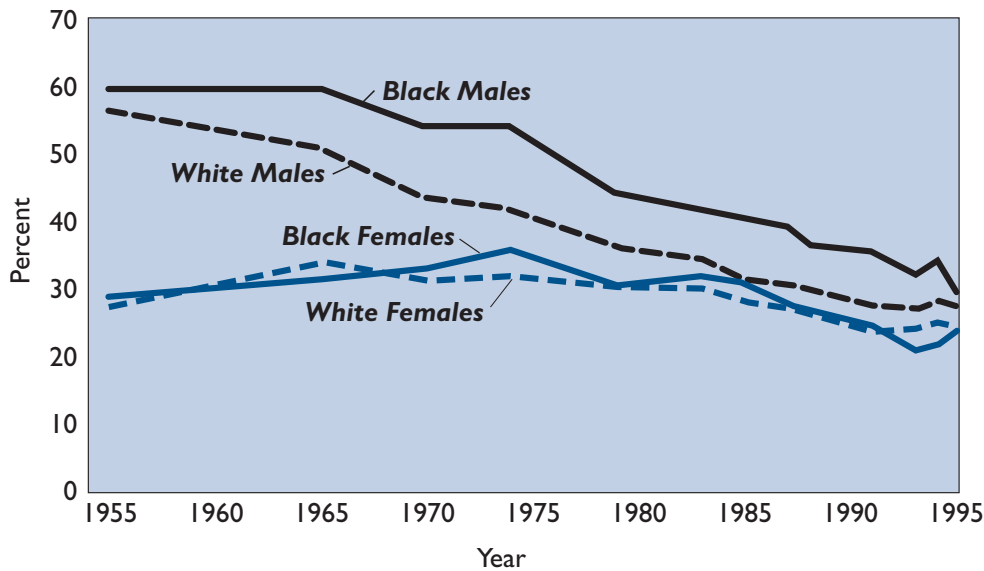
Estimated Cancer Deaths Caused by Cigarette Smoking in the United States, 1998

Site	Males	Females	Total
Lung	83,321	50,987	134,308
Esophagus	6,970	2,002	8,972
Pancreas	3,626	4,619	8,245
Oral Cavity	4,801	1,579	6,380
Bladder	3,679	1,402	5,081
Kidney	3,202	481	3,683
Larynx	2,706	769	3,475
Cervix		1,499	1,499
Total	108,305	63,338	171,643

respiratory symptoms. It is difficult to overstate the health burden of smoking; the annual death toll from smoking exceeds the combined annual death toll from all accidents, suicides, drug use

smoking prevalence rates in the middle part of this century, when nearly 60 percent of men and 30 percent of women smoked and most smoked every day. Nonetheless, the number of current

Prevalence of Cigarette Smoking Among Adults, 1955-1995



Source: 1955 Current Population Survey (CPS); National Health Interview Survey (NHIS) 1965-1995.

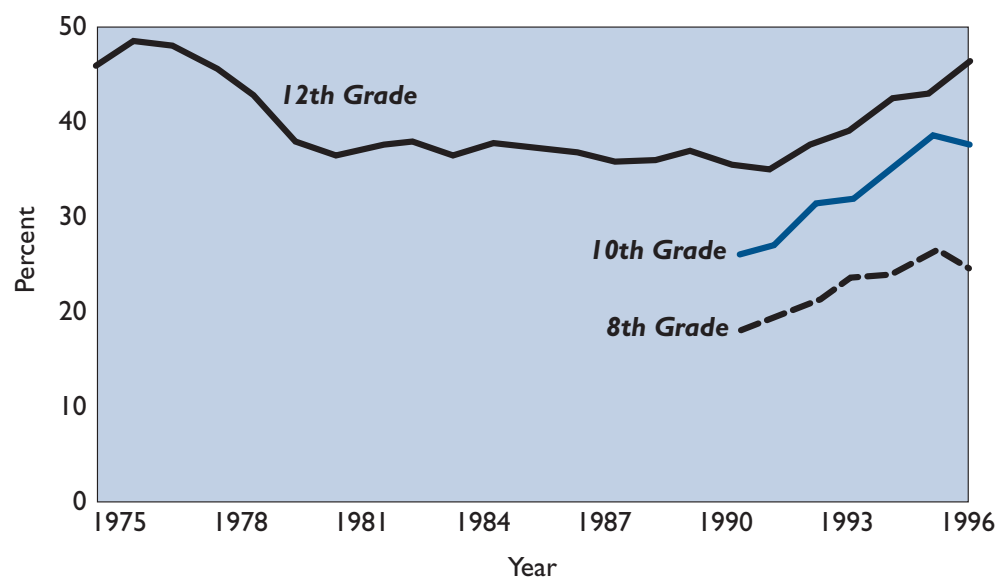
smokers, and thus future cancers, remains alarmingly high. Forty-six million adults in the United States alone currently smoke cigarettes, and millions more use other forms of tobacco. In contrast to the steady declines in smoking rates through the 1970s and 1980s, smoking among adults over the past few years appears to have leveled off. Moreover, rates of smoking are disproportionately high among certain population groups, such as African-American men.

Other areas of concern persist. Smoking among adolescents has been increasing since the early 1990s. A recent report from the CDC shows a 73 percent increase in teenage smoking from 1988 levels. More than 6,000 adolescents try their first cigarette and over 3,000 teens become regular smokers every day. These findings are consistent with

previous studies that suggest significant increases in smoking prevalence among adolescents in the U.S. since 1991. Overall, these data show that public health gains observed during the 1970s and 1980s are being reversed. Moreover, promising declines in smoking among black teens have reversed. In the early 1990s, fewer than 10 percent of black high school seniors reported smoking in the past 30 days, compared to over 30 percent of white teens.

Unfortunately, smoking among black teens has risen over 50 percent in just the past five years. These are alarming trends. Equally troubling is the increasing prevalence of smoking now being reported among younger teens. Should these patterns continue into adulthood, they will have a profound impact on future cancer rates and smoking-related diseases.

Prevalence of Current Cigarette Use Among 8th, 10th, and 12th Grade Students



Source: University of Michigan.

Trends in the use of other tobacco products, such as smokeless tobacco and cigars, are also of concern. The U.S. Department of Agriculture reports that consumption of moist snuff has surpassed chewing tobacco for the first time in U.S. history. Cigar use, which declined for a period of over 20 years, increased by nearly 50 percent between 1993 and 1997. Consumption of large cigars, which accounts for over two-thirds of all cigars in the U.S., increased by nearly 70 percent over the same time period. National and regional surveys of children have documented high rates of current cigar use among both boys and girls. Cigar use among adolescent males is two to three times higher than their use of smokeless tobacco and is approaching their rate of cigarette smoking. Cigar use also appears to be gaining in popularity among adolescent girls. Moreover, cigar use has gained acceptance among well-educated men and women 18-34 years, a group that had previously eschewed cigarettes. It is not known whether their use of cigars could serve as a gateway to use of other tobacco products.

THE NCI's TOBACCO RESEARCH PROGRAM

The NCI has played a vital and leading role in the battle against tobacco use. The NCI's leadership, commitment to and involvement in tobacco-related research dates back more than 40 years, and NCI research on smoking and tobacco has spanned a broad spectrum, from basic biology to epidemiology to prevention and treatment. The NCI's initial research efforts focused primarily on epidemiologic studies of the association between tobacco use and cancer and on the basic biology of tobacco-induced cancers. Later research identified hazardous elements in tobacco and tobacco smoke and sought ways of reducing exposure. The NCI's cancer control research in the past 15 years focused on why people smoke and the development of interventions to prevent and stop tobacco use. During most of the 1980s, the NCI's smoking research program emphasized interventions in three broad areas: those delivered through specific intervention channels (e.g., schools, worksites, mass media, health care settings, and community groups); interventions that targeted specific populations (e.g., minority and ethnic populations and women); and groups of tobacco users considered at high risk (e.g., poor smokers and heavy smokers).

This research provided a strong foundation of empirical information about tobacco control interventions. Behavioral models of tobacco use cessation were established; characteristics of successful school-based interventions to prevent or delay tobacco use initiation were defined; physician training and office protocols for patient smoking cessation programs were developed; and approaches for utilizing and enhancing self-help interventions were identified. Mass media interventions capable of reaching large numbers of individuals with prevention and cessation messages were developed and strategies for reaching minority, ethnic, and high-risk populations were tested. With this information as the cornerstone, the NCI launched two projects that sought to translate this knowledge about tobacco control interventions into widespread public health impact.

These two initiatives—the Community Intervention Trial for Smoking Cessation (COMMIT) and the American Stop Smoking Intervention Study for Cancer Prevention (ASSIST)—are important for their unique designs and because they remain two of the largest community-based smoking control efforts ever attempted. These initiatives are described in the Community and State Intervention Research section.

Concurrent with the implementation of these large-scale community-based tobacco control projects, sweeping societal changes in attitudes, public policy, and legal regulation of tobacco products have taken place. Government agencies, professional and voluntary organizations, and academic institutions joined to eliminate tobacco use and exposure to tobacco carcinogens. Public attitudes reflected decreasing acceptance of smoking as a social norm, and public policies restricted the locations where smoking was permitted and limited the access of minors to tobacco products. The U.S. Food and Drug Administration (FDA), with support from the President of the United States, asserted jurisdiction over tobacco products. States' attorneys general sued tobacco firms, and secret files from the tobacco industry and depositions from industry officials exposed the continued promotion of tobacco use by the tobacco industry in full knowledge of the myriad related health effects. These factors converged to create the current climate of societal readiness to tackle the formidable challenge of reducing the health burden of tobacco use.

During this time, spectacular advances also were made in understanding the molecular and genetic factors underlying the progression of a normal cell into a cancer cell. Research focusing on the role of tobacco as a trigger for the cell changes that lead to cancer has revealed that different tobacco products and methods of nicotine administration influence the type and quantity of exposure to cancer-inducing agents. Other tobacco product characteristics, such as burning temperatures, additives, and filter composition, have been found to alter these carcinogenic agents as well. Research also has identified three specific classes of agents in tobacco smoke that cause cancer: nitrosamines, aromatic amines, and polycyclic aromatic hydrocarbons. While all the specific sites of action of these tobacco carcinogens are not yet characterized, many of the molecular changes induced in different cancer sites (e.g., head and neck, lung) appear similar, suggesting a common mechanism of epithelial cell damage in these sites. These discoveries open the door to identifying precancerous lesions and biomarkers that may serve as predictors of cancer in these and other sites. Additionally, research on the molecular characteristics of tobacco-induced cancers has identified differences in lung cancer mutation characteristics. For example, lung cancers in women more commonly have estrogen and progesterone receptors, and these hormones stimulate cancer growth. Some epidemiologic studies also have provided evidence of differences in the proportions of specific types of lung cancer among men and women and possible differences in risk associated with cigarette smoking.

These significant advances over the past several decades in basic and applied research, as well as changes in public attitudes and policies, present an unprecedented opportunity to expand research to gain new insights that will significantly reduce the burden of death and disease caused by tobacco use. But while there is reason for optimism about the potential to exert a positive impact on the public health problem of tobacco use, the challenge is formidable. It is clear that

reducing the burden of tobacco use requires novel strategies, borne from new ways of thinking about old problems. A deliberate, focused plan is required and a renewed commitment to ending this public health threat is essential. It is imperative that the NCI focus its research agenda, identifying where research is most needed and how best to prioritize and achieve research objectives that will have the greatest impact on the problem.

THE NCI TOBACCO RESEARCH IMPLEMENTATION GROUP

To accomplish this goal, the Director of the NCI created the Tobacco Research Implementation Group (TRIG), which includes more than two dozen leading scientists and experts from within the NCI, the National Institute on Drug Abuse (NIDA), and the Office of Behavioral and Social Sciences Research (Office of the Director), and from the extramural research community, as well as representatives of major NCI review and advisory committees. The TRIG was charged with establishing the NCI's tobacco-related cancer research priorities for the next 5 to 7 years.

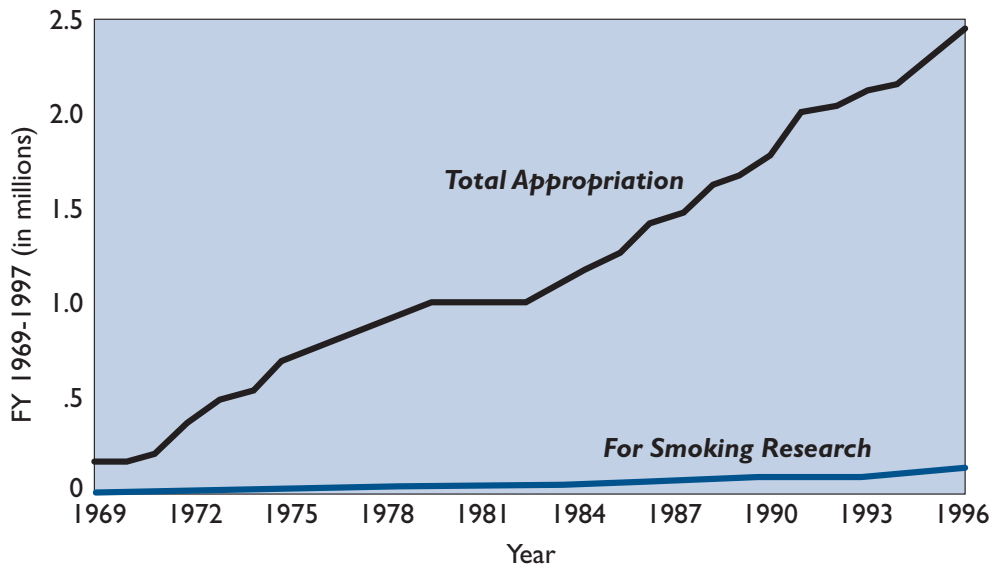
The TRIG began by reviewing the extensive recommendations of four earlier advisory groups.¹ Each of these excellent reports produced major recommendations for tobacco control research. While a number of the recommendations from these earlier review groups had already been partially or completely implemented, much remained to be done; no single previous report had considered the entire spectrum of tobacco control research, from basic biological research to dissemination research.²

The TRIG also analyzed the FY97 portfolio of tobacco-related research across NCI divisions. This analysis reviewed the balance of current research across topic areas and the distribution of funding across projects and by funding mechanism; it also identified emerging issues from research in progress. Research projects (intramural and extramural) were

1 Major reports reviewed included the report of the Behavioral Research in Cancer Control Meeting, published in *Preventive Medicine* in 1995, the Report of the National Cancer Institute Cancer Prevention Program Review Group (1997), the Report of the National Cancer Institute Cancer Control Review Group (1997), and *Taking Action To Reduce Tobacco Use*, a report of the National Cancer Policy Board of the Institute of Medicine (1998).

2 For example, a major recommendation to create a tobacco control research branch has been accomplished, and a branch chief has been appointed. An earlier recommendation that also is being implemented is the transfer of the American Stop Smoking Intervention Study (ASSIST) to the Centers for Disease Control and Prevention. In addition, new initiatives have been developed in biobehavioral research, genetic regulation of susceptibility to tobacco-related carcinogenesis, and the prevention of tobacco use among youth.

National Cancer Institute Total Budget and Amount Spent For Smoking Research – Fiscal Years 1969 through 1997



epidemiology, and chemoprevention. The definitions of these categories may be found at the beginning of each section of the report. More detailed presentation of the portfolio analysis is provided in the Appendix.

Epidemiology, treatment of tobacco addiction, and community and state intervention research each accounted for about 20 percent of the total number of tobacco projects funded by the NCI. This picture differed when assessed by the allocation of funding, with commu-

nity and state intervention research accounting for more than 40 percent of the FY97 funds for tobacco-related research. This category will be reduced as the ASSIST program is transferred from the NCI to the Centers for Disease Control and Prevention (CDC) in FY99. Research on the treatment of tobacco addiction accounted for 18 percent of the funds expended. When assessed either by the number of projects or the amount of funding, biobehavioral, prevention, and

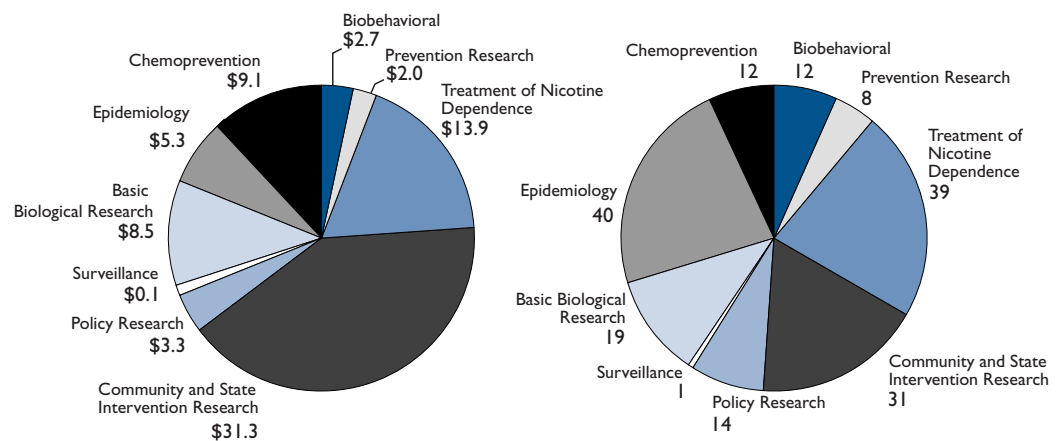
included if at least 10 percent of the project was related to tobacco. Projects focusing upon treatment of tobacco-related diseases (e.g., interventions with lung cancer patients) were excluded from portfolio analysis.

The NCI spent \$76.2 million on 175 tobacco-related research projects in FY97. This represents less than 3 percent of the NCI's budget. The disproportionate funding of tobacco research relative to the NCI's total research budget is remarkable given the contribution of tobacco to the total cancer burden (approximately 30 percent of all cancer deaths).

Projects were categorized into nine broad research areas, including biobehavior, prevention of nicotine use, treatment of nicotine addiction, state and community interventions, policy, surveillance, basic biology,

community and state intervention research accounting for more than 40 percent of the FY97 funds for tobacco-related research. This category will be reduced as the ASSIST program is transferred from the NCI to the Centers for Disease Control and Prevention (CDC) in FY99. Research on the treatment of tobacco addiction accounted for 18 percent of the funds expended. When assessed either by the number of projects or the amount of funding, biobehavioral, prevention, and

National Cancer Institute Research Portfolio – Funding Levels (in millions) and Total Number of Projects Funded in 1997



Total Funding Level = \$76.2

Total Projects = 176

policy research accounted for less than 10 percent of the tobacco portfolio. Surveillance was the most undersupported area in terms of tobacco-specific funding. Research grants (R01) and contracts (N01) represented the most frequently used funding mechanism, accounting for almost three-quarters of the tobacco research funding combined.

TRIG members generated research recommendations after reviewing the portfolio analysis. These proposed recommendations provided the foundation for subsequent discussion of research priorities and development of an initial draft of the Tobacco Research Implementation Plan (TRIP). The group then sought input from experts reflecting various research and public health perspectives. Several scientists were provided with the initial draft of the TRIP and invited to present their perspectives to the group.

Following this input, TRIG members narrowed and refined the list of research recommendations and, through a consensus-building process, identified and prioritized a core set of tobacco-related cancer research opportunities. These recommendations build on past research accomplishments, are consistent with the recommendations of previous advisory groups, address major gaps in knowledge, and have the potential for great impact on the cancer burden caused by tobacco.

The recommendations reflect research across scientific disciplines and levels of focus from the basic structure of the cell to the broad influence of society. Because nicotine addiction plays a critical role in the ongoing use of tobacco products, a better understanding of nicotine addiction is a vital first step toward preventing or stopping tobacco use. This report places a major emphasis on the factors that influence tobacco use and nicotine addiction. The Biobehavioral Model of Nicotine Addiction and Tobacco-Related Cancers provides a framework for conceptualizing the broad spectrum of research factors. Tobacco use and nicotine addiction arise from a complex interplay of social, psychological, and biological factors that interact with genetic vulnerabilities to nicotine addiction. Social influences are broad, including peer and family modeling, tobacco industry marketing, and media influences. Depressed or anxious mood and attention-deficit hyperactivity disorder (ADHD) are examples of psy-

Criteria for Prioritizing Research Recommendations

Recommendations should:

- Be research-focused
- Increase substantially our understanding of the process of tobacco addiction, initiation, and cessation
- Exert a major impact on the prevention of tobacco use
- Increase substantially the effectiveness of treatments for nicotine addiction
- Exert a major public health impact on population smoking rates
- Provide balance of long- and short-term investments
- Provide balance across categories of research

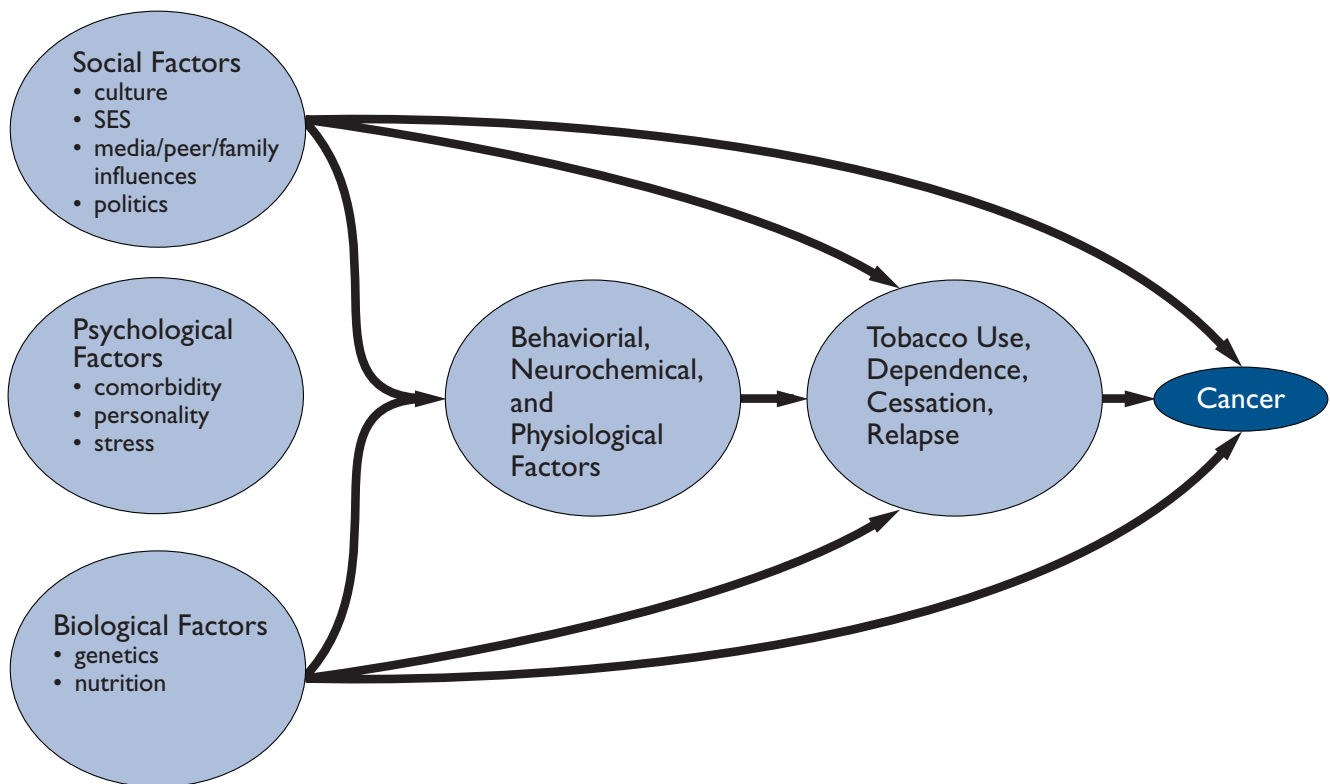
chological factors that affect smoking, from initiation to maintenance to cessation.

The effects of these three overarching determinants are mediated by behavioral, neurochemical, and physiological factors to influence tobacco use, dependence, cessation, and relapse in the individual. Not all individuals exposed to tobacco carcinogens develop cancer. This suggests that genetic and other biological factors have a modifying effect on tobacco-induced carcinogenesis. By addressing the behavioral endpoints identified in this model—tobacco use, addiction, cessation, and relapse—the NCI's research agenda has the potential to dramatically reduce tobacco-related cancers. The tobacco research agenda must be based on recognition of the complexity of tobacco use if we are to succeed in prevention and intervention targeting to children, adolescents, and adults.

Addiction and Tobacco-Related Cancers

Within the core set of recommendations, the TRIG identified nine unique, overarching research opportunities as the highest priorities, requiring immediate implementation. These opportunities cover the range of tobacco control research from basic biological and basic biobehavioral research to clinical intervention,

Biobehavioral Model of Nicotine Addiction and Tobacco-Related Cancers



Adapted from Anderson, Office of Behavioral and Social Sciences Research, 1998.

policy, epidemiology, surveillance research, and support for research infrastructure. The research priorities also emphasize the unique opportunities and challenges of tobacco initiation, use, addiction, and cessation among youth and populations at disproportionate risk.

The TRIG emphasized that transdisciplinary approaches and the formation of strategic partnerships in the implementation of this research agenda are critical for success. Moreover, the NCI must collaborate with partners in both the public and private sectors, such as NIDA, CDC, the American Cancer Society, and the Robert Wood Johnson Foundation. For example, NIDA has supported research on the fundamental neuroscience, biobehavioral, and genetic factors underlying addiction to drugs, including nicotine. This report will highlight where particularly fruitful collaborative activities with NIDA and other organizations can be initiated to enhance the NCI's support of research on nicotine addiction.

Each section of this report focuses on specific components of the Biobehavioral Model of Nicotine Addiction and Tobacco-Related Cancers, identifies outstanding opportunities and priorities in each area of research, and discusses the potential short- and long-term impact on tobacco-induced cancer that can be realized by pursuing this research.

It was the unanimous and fundamental conclusion of the Tobacco Research Implementation Group that an unequivocal commitment of the NCI to a comprehensive but focused program of research on tobacco use can help to reverse the existing epidemic of tobacco-related cancer.

Research infrastructure assures the availability of necessary human, financial, and technological resources, systems for collaboration, and mechanisms for information dissemination and feedback to provide a strong foundation upon which effective research may be designed and conducted.

INTRODUCTION

Infrastructure provides the foundation for research, much as a foundation supports a house. Adequate staff, laboratories, other core support, and training are all needed to assure the long-term stability and success of the research enterprise. Yet, as Bennet Bertenthal of the National Science Foundation observed in 1998, “most researchers rely on various forms of infrastructure that they take for granted.” Noting that “science is getting bigger, faster and more expensive,” Bertenthal argued that the social sciences are at an important juncture in how they prepare for the future. Consequently, investments in infrastructure are extremely important for the social sciences as well as for genetics, epidemiology, and the other sciences associated with the study of nicotine addiction. Achieving the tobacco research goals detailed in this report will require a major investment in such infrastructure.

The organization of research can have a major impact on its productivity and outcomes. Across a range of scientific disciplines, the ideal research model is based on transdisciplinary teams of scientists working in settings that facilitate collaboration and promote productivity. The complexity and interdisciplinary nature of the tobacco control research recommended in this report require such a critical mass of scientists working both independently and in collaboration with each other to accomplish these research objectives. A mix of scientists from different research areas, such as basic sci-

ence, clinical science, and population science, should work in close geographic proximity, or at least in intellectual proximity, to each other. The development of transdisciplinary research centers is the most effective way to facilitate such productive interactions between different types of scientists and more rapid exchange of research findings among basic, clinical, and population studies.

RECOMMENDATIONS

Transdisciplinary Tobacco Research Centers should be created to study the initiation of tobacco use, prevention of tobacco use, addiction to tobacco, and/or treatment of tobacco addiction and tobacco-related cancers.

The highest priority for the NCI's investment should be the creation of Transdisciplinary Tobacco Control Research Centers to investigate important questions about nicotine addiction and the prevention and treatment of tobacco use. These transdisciplinary centers should include strong basic research closely linked with epidemiology, biobehavioral, prevention, treatment, dissemination, and/or policy research. Such centers would embrace a range of disciplines and investigations and would provide the critical mass of expertise needed to advance tobacco control efforts through the pursuit of promising new research opportunities. The level of specialization in different aspects of tobacco research would vary across centers. However, the centers should focus thematically on areas, such as adolescent smoking and use of other tobacco prod-

ucts, where there are significant gaps in knowledge. The collective effort at a center could result in major advances in and the application of knowledge. For example, nicotine addiction centers could explore and reveal the neuropharmacologic and genetic bases of nicotine addiction, which would lead to improved, tailored prevention and treatment strategies for vulnerable population subgroups. Specialized tobacco prevention centers could explore precursors of initiation and assess whether and how prevention strategies work for different populations in different contexts, such as health care organizations, work sites, and communities. Other specialized centers could investigate psychosocial factors and identify why and how strategies based on such factors work in outreach efforts that are successful with unmotivated users. Such centers also could join with health departments and other organizations to explore research issues involved in successfully transferring proven interventions from research settings to communities. To ensure further cross-fertilization and maximize the impact of the innovative research that will be conducted at tobacco control centers, mechanisms would be developed to encourage intercenter communication and collaboration.

Centers will also be able to make important contributions to methodology. For example, they could serve as repositories for biospecimens needed for tobacco research. Centers would have the opportunity to develop new methodologies that would advance the ability to conduct tobacco research in specific areas, such as community dissemination and implementation. They also could take existing methodologies and measures from related fields and adapt them for use in tobacco control research. Finally, centers might develop ways to translate tobacco industry marketing strategies into effective antitobacco campaigns or to apply new information technologies to tailor antitobacco messages to individual motivational factors.

One of the most important functions of the tobacco research centers would be to contribute to the



development of the next generation of tobacco control researchers. The centers' critical mass of scientists conducting research across the spectrum of tobacco control would make it possible to train future tobacco research scientists who are knowledgeable about the need for and conduct of transdisciplinary research. Only in such a fertile environment of collaboration will tomorrow's scientists gain a true vision of transdisciplinary research.

While close geographic proximity is characteristic of transdisciplinary centers, the Internet has made it possible to establish virtual research centers. These "collaboratories" permit researchers from centers across the globe to conduct collaborative research. For example, collaboratories can enable researchers to simultaneously conduct similar experiments at different locations in the United States and in other countries using the same protocols. Such studies may be especially useful for the study of nicotine addiction, since different centers with access to unique populations and study conditions would have the potential to discover significant similarities and differences in the nicotine addiction process that could be applied to the development of prevention and treatment interventions. Scientists working at the different centers should be brought together to foster synergy. Moreover, academic attention should be paid to strategies for maximizing transdisciplinary collaboration within and between

centers. Novel approaches should be encouraged and supported.

The NCI should consider funding centers through the Specialized Programs of Research Excellence (SPORE) mechanism. These specialized centers support the full-range of research and development, from basic research to clinical and population research, and are ideally suited to facilitate the kind of transdisciplinary, bench-to-bedside research required to advance the science of tobacco control. The SPORE mechanism would provide the needed flexibility to change course when new discoveries are made and the opportunity for unique research interactions, both within a SPORE and across SPOREs. Three aspects of SPOREs are especially appropriate for enhancing the field of tobacco control research: the mandate for training and career development, the availability of developmental funds, and the provision of support for core resources.

OTHER INFRASTRUCTURE RECOMMENDATIONS

In addition to centers, the scope of the proposed research efforts detailed in this report also calls for transNIH initiatives, where possible, with funding from multiple institutes, including NIDA. In addition, partnerships should be developed with voluntary organizations (such as the American Cancer Society), foundations (such as the Robert Wood Johnson Foundation), and private industry (such as pharmaceutical companies).

Cohort studies should be expanded to identify determinants and health consequences of tobacco use in children and young adults. Such cohorts would permit research to track multiple behaviors and outcomes, such as smoking, alcohol use, drug use, and depression, over time. Long-term research with such cohorts could pinpoint the precise relationship of individual characteristics, such as “low self-esteem,” and behaviors, such as tobacco use, and the time sequence in which they occur. Such research also should investigate other individual and family factors or genetic and biological factors that contribute to tobacco use. Funding for these efforts should derive from multiple NIH institutes.

Training the next generation of tobacco control researchers is essential. The Transdisciplinary Tobacco

Control Research Centers represent an ideal model for training. However, more training opportunities are needed for the next generation of tobacco control investigators. The extramural community should be encouraged to apply for training grants and to develop programs that would use transdisciplinary groups of researchers to train scientists in tobacco research. In addition, young scientists should be encouraged to apply for Independent Scientist and Career Awards with a focus on tobacco control research. We also must consider other mechanisms to meet the urgent need to train investigators from minority and underserved populations. Training is absolutely critical if the science of tobacco control is to be advanced.

The rapid advancement of tobacco research requires the use of a variety of mechanisms. Possibilities include a mechanism like the B/START (Behavioral Science Track Awards for Rapid Transition), which was developed by NIDA. These awards are tailored for new investigators and could be used for quick-start research on new or novel research approaches and collection of pilot data in tobacco control research. Special exploratory or developmental initiatives should also be considered for pilot studies in tobacco control research, including the use of ethnographic methods.

Members of the TRIG were concerned about the upcoming changes in the NIH review process. They were emphatic that tobacco research needs fair peer review. They recommended that the NCI should be cautious about giving up review of tobacco research grants, especially those in high-priority areas. This is important if researchers in tobacco control are to have optimal opportunities to conduct research.

Much of the investment in tobacco research will be lost without adequate attention to the synthesis of research results and the dissemination of proven programs and techniques. The NCI should strengthen its capability in research synthesis and should regularly disseminate research results using both the peer-review literature and special monographs. Dissemination strategies should also utilize the Internet. Similarly, the impact of research investment is diminished if the programs developed through that research are not disseminated successfully to those who can apply them to tobacco control. The NCI should increase its commit-

ment to research dissemination by building a strong unit that focuses on the efficient and effective transfer of proven tobacco control programs and technical assistance to assure that these programs are implemented as designed. The goal of these efforts is to disseminate evidence-based strategies for tobacco control.

THE IMPACT OF BUILDING THE TOBACCO RESEARCH INFRASTRUCTURE

Few places in the United States now have the critical mass of scientists needed to optimize tobacco

control research. Therefore, these infrastructure initiatives could have a major impact on tobacco use and tobacco-related cancer. Changing the way research is conducted on a national level could accelerate the development of more effective tobacco control interventions for general and special populations, speed the transfer of these scientifically validated approaches to application in communities across the Nation, and create a core of new tobacco control researchers who can advance the science of tobacco control in the next century.



Basic biobehavioral research in tobacco control focuses on the interactions of biological, psychological, sociocultural, and other environmental processes in initiation of tobacco use, nicotine dependence, cessation, and relapse.

INTRODUCTION

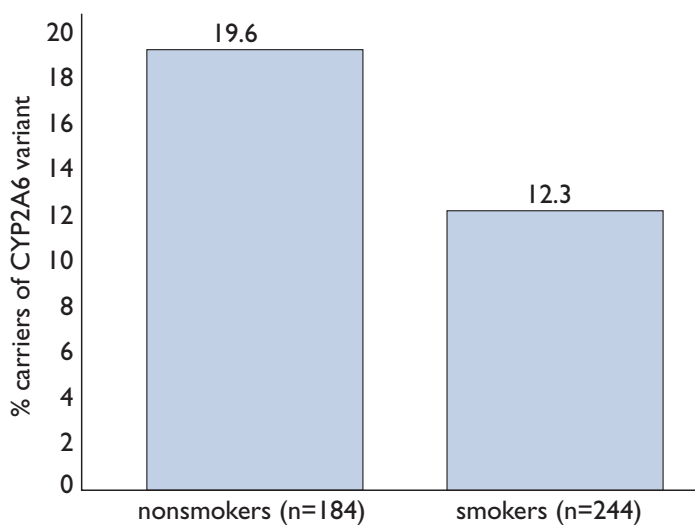
We still do not know why some people adopt or cease behaviors that increase cancer risk, such as tobacco use. Such gaps in fundamental knowledge highlight the need for basic biobehavioral (pre-intervention) research to elucidate the links between biological, behavioral, and environmental influences and cancer risk behaviors. This knowledge is essential to develop more effective tobacco prevention and cessation interventions, to understand the mechanisms by which such interventions succeed or fail, and to target interventions to people most likely to benefit from them.

We have made significant advances in our understanding of the psychosocial determinants of tobacco use. Many sociocultural, environmental, behavioral, and psychological factors are linked to cigarette smoking. These include: low income; use of tobacco by peers, parents, and other family members; poor academic performance and frequent school absences; and low-self esteem and depression. Further research is needed to explore the interdependencies of these factors. Significant gaps also exist in our understanding of the relationship between biology and behavior. The recent identification of genes that modify

nicotine metabolism and regulate the activity of chemicals in the brain that affect mood changes and feelings of pleasure triggered by nicotine provides unique opportunities for studying these links. Genes in the brain's reward pathways have been implicated in a variety of addictive behaviors, including tobacco and alcohol use. Increased understanding of the underlying neurobiology of nicotine addic-

Effect of CYP2A6 Gene Variant on Tobacco Dependence

Percentages of smokers and nonsmokers carrying one copy of the CYP2A6 gene variant. The variant reduces the efficiency of nicotine metabolism, resulting in a lower likelihood of smoking ($p < .04$).



Source: Pianezza et al., *Nature*, Vol. 393, 1998

tion, and of other biobehavioral factors in tobacco use, should lead to more effective, targeted approaches for tobacco prevention and smoking cessation.



RECOMMENDATIONS

Basic biobehavioral research should be conducted to understand the sociocultural, psychological, physiological, and genetic factors that influence the initiation of tobacco use, progression to nicotine addiction, and smoking cessation among children, adolescents, and adults.

Despite our increased knowledge about why people begin to use tobacco products and how they become addicted to nicotine, many important questions about tobacco use and cessation remain. For example, why are some children and adolescents susceptible to tobacco use, while others seem impervious to social influences, such as peer pressure, media glamorization of smoking, and tobacco industry marketing? Why do some children and adolescents smoke for only a short period of time, while others develop long-term nicotine dependence? Research is needed to examine the complex interplay between social influences, psychological factors, and genetic vulnerabilities. Laboratory studies could probe the genetic and biological bases of nicotine metabolism and/or the rewarding effects of nicotine at different stages of development (e.g., childhood, adolescence, and adulthood) in relation to tobacco use. How these factors relate to gender and ethnicity also should be studied.

Research to determine the critical thresholds for progression from occasional use of tobacco products to

nicotine addiction also would aid in identifying appropriate levels of intervention at different stages of tobacco use. Special attention should be given to the primary and interactive effects of developmental factors, psychological comorbid disorders (such as depression and attention deficit hyperactivity disorder [ADHD]), and tobacco product design and marketing influences on youth initiation of tobacco use and nicotine dependence. While recent NCI initiatives have stimulated studies to determine why youths begin and continue to use tobacco, we need more research on young adults ages 18 to 25, a group that has increased its use of a variety of tobacco products. Collaborative research with NIDA would be appropriate.

Additional pre-intervention research could consider the role of biological factors and their interaction with coexisting psychological disorders and sociocultural factors in smoking initiation, nicotine addiction, and tobacco use. Such research can enable us to learn more about how genetic factors that affect mood, behavior, and the metabolism of nicotine interact with coexisting sociocultural factors and psychological disorders to increase or reduce an individual's vulnerability to nicotine addiction. In addition, research is needed to explore and understand the brain as well as the bodily processes through which tobacco product design and genetic factors interact to influence initiation and cessation of tobacco use. For example, brain-imaging techniques could be used to study how genetic factors control the brain's response to nicotine use and withdrawal. Furthermore, research is needed into the basic neurobiological processes and mechanisms related to nicotine addiction. Research in animals and cellular models is needed in this area. The



findings from such research could contribute to the development of new medications to aid smoking cessation.

Research should be conducted to understand the influence of different tobacco products and alternative nicotine delivery devices/systems on initiation and cessation of tobacco use as well as nicotine addiction.

Different tobacco products and alternative nicotine delivery devices/systems contain different amounts of nicotine and deliver it in different ways to the body. These differences in the way nicotine is administered affect both its addictive and treatment potential and directly influence initiation of tobacco use, nicotine addiction, and cessation from tobacco use. Therefore, it is important to conduct biobehavioral research on individuals' responses to new nicotine delivery devices and tobacco products. Consideration should be given to whether the NCI should support harm reduction strategies. If so, the findings from biobehavioral research would provide an important and critical foundation.

THE IMPACT OF BIOBEHAVIORAL RESEARCH

Major research breakthroughs have made it possible to examine the biological bases of tobacco use and nicotine addiction, including the role of genetic factors and ethnicity in nicotine metabolism. In the short term, research in this area will help identify pre-existing biological vulnerabilities and determine how their interactions with sociocultural and psychological influences affect tobacco initiation, addiction, and cessation. In the long term, the findings from basic biobehavioral research will provide the scientific knowledge needed to develop more effective tobacco use prevention and cessation interventions, both behavioral and pharmacological, that are tailored to the unique needs of individuals. Increased understanding of the biobehavioral underpinnings of tobacco use and dependence also will be key to informing both public policy and public health practitioners about how to better target tobacco prevention and treatment policies and strategies for youth and adults.

Prevention research in tobacco control seeks to identify and test interventions to prevent the initiation of tobacco use and nicotine dependence, primarily among youth.

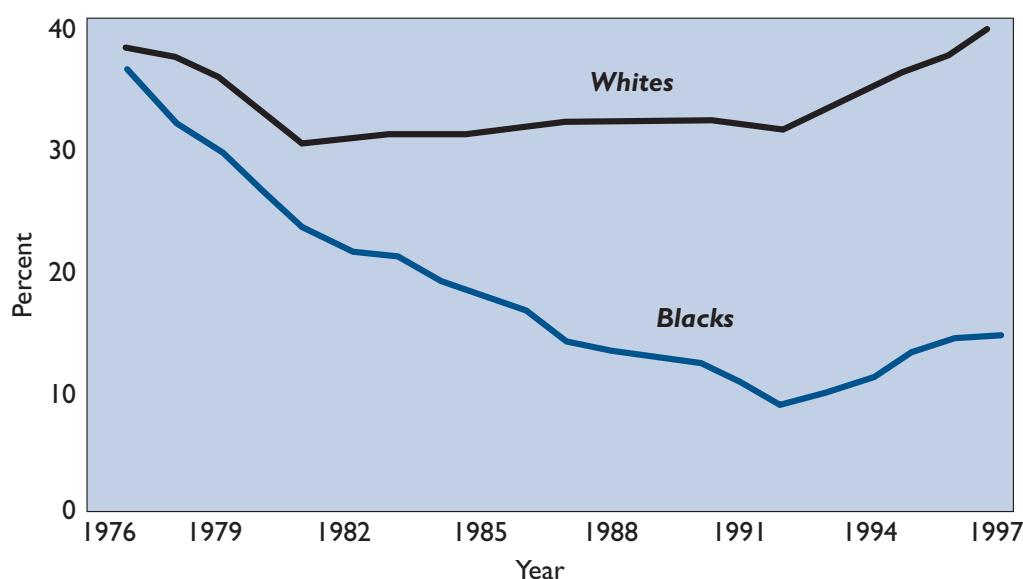
4. Prevention of Tobacco Use and Nicotine Addiction

INTRODUCTION

Researchers and educators have been striving since the 1960s to develop and implement effective tobacco prevention programs for youth. Most of these programs have been school-based interventions, although programs also have been directed at community-based settings, such as clubs, youth organizations, and components of the health care system. From the mid-1970s through 1991, these efforts appeared to “pay off” in a steady decline in rates of youths beginning to smoke. Among African-American youth, for example, smoking fell to a level approximately one-fourth that of white youth. Youth smoking initiation rates have been rising steadily since 1991 among African-American and white youth.

Past tobacco prevention research, much of it funded by the NCI and NIDA, has provided a solid foundation on which to build the more sophisticated interventions that are needed to address the changing mix of sociocultural and environmental factors that promote tobacco use among today’s youth. For example, investigators have demonstrated convincingly that school-based prevention programs that target social influences on smoking and provide youths with the skills to resist those influences can have a short-term impact on the initiation of tobacco use during the most vulnerable junior high school period, when experimentation with tobacco is most likely to occur. A few of these programs also have demonstrated a sustained prevention effect on tobacco use throughout high school. However,

Trends in Current Cigarette Use Among Black and White High School Seniors



Source: Monitoring the Future, University of Michigan.

the difficulties of moving these programs from the research setting to implementation in “real-world” community settings have been daunting. Therefore, while we need to support research to develop and refine tobacco prevention programs, we must simultaneously address societal and policy issues that influence the implementation and effectiveness of these programs. As discussed in a later section, such policy-related research issues include: establishing tobacco prevention as a priority in the educational curriculum; promoting environmental policies to ban tobacco use by students and teachers within and near schools; banning tobacco advertising in the vicinity of schools; and preventing minors’ access to tobacco products. It is important that youth programs provide an understanding of the biological basis of addiction. Basic biologists and biobehavioral researchers should interact with prevention scientists in designing programs.

tings, and how to tailor prevention materials appropriately for different populations. Markers of tobacco susceptibility in early childhood could be used to develop and test targeted prevention approaches for younger children. Prevention research might also focus on family interventions to deter youth from tobacco use. Other important target groups are young people who are not in school and those who have entered the workplace.

Prevention strategies are more likely to be effective if they are tailored for groups at high risk of initiating tobacco use and nicotine addiction. This includes children with attention deficit hyperactivity disorder (ADHD) and/or low academic achievement levels, depressed youth, substance-abusing youth, and “risk takers” with other health or lifestyle problem behaviors. Research on prevention programs for high-risk groups also should consider gender-specific issues, such as white female teens using cigarettes to prevent or control weight gain. Such research also should examine ethnic-specific issues, such as the apparently low smoking rates among Asian-American women and African-American girls or the very high rates of smoking among Native American children, both of which are linked to sociocultural variables. Research also is needed to develop special interventions for high-risk medical subgroups, such as young people with asthma or diabetes, pediatric cancer survivors, and children with elevated cardiovascular risk factors, for whom tobacco initiation can pose particularly damaging health consequences. Finally, we need research on prevention strategies to address individuals with a genetic susceptibility to nicotine addiction that may increase their likelihood of initiating tobacco use or moving from experimentation to regular, dependent smoking.

These research initiatives should be built on the findings from biobehavioral research about the factors influencing tobacco use and addiction, which are discussed in more detail in that section. Collaborative opportunities with the National Institute of Child Health and Human Development (NICHD) and NIDA would be appropriate in these areas.



RECOMMENDATIONS

Research should be conducted to develop and evaluate novel approaches to preventing tobacco use, especially among populations at disproportionate risk.

While school-based approaches that teach skills to resist social influences to smoke have had some success in preventing tobacco use among youths, major gaps remain in our understanding of the most critical elements of tobacco prevention interventions, their timing, how best to target high-risk subgroups and set-

OTHER RECOMMENDATIONS

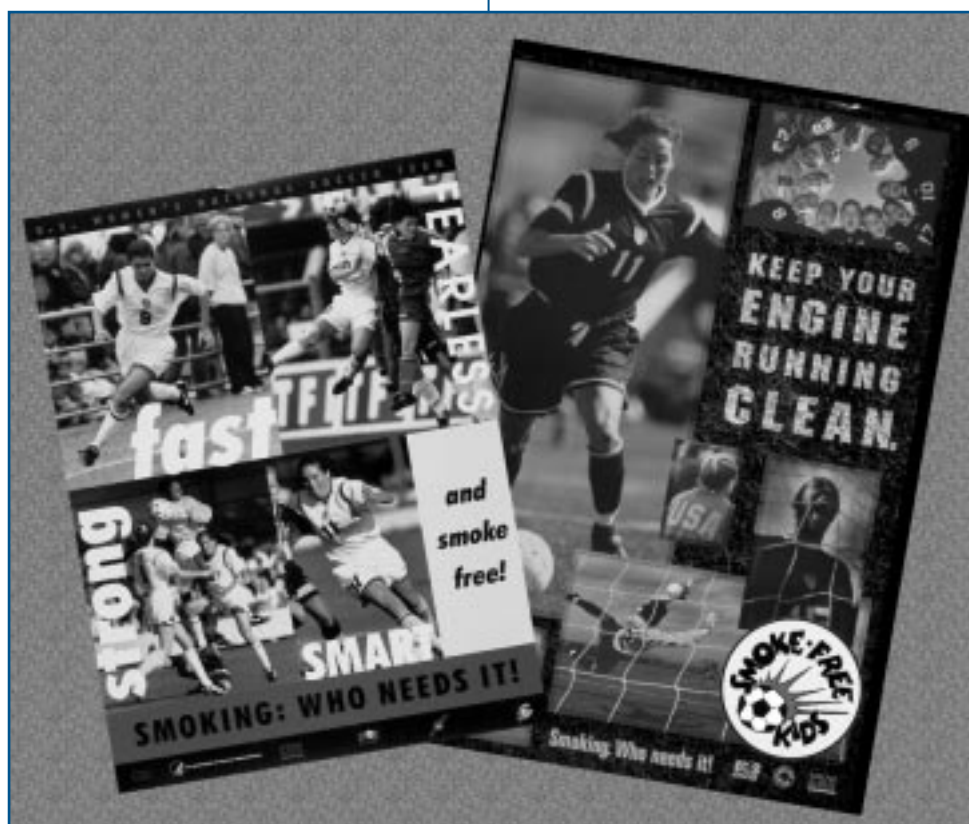
Prevention research should be conducted in conjunction with community and state intervention research, to explore the relative effectiveness and consequences of prevention interventions that employ single-risk versus multiple-risk strategies. Such research can determine if it is more effective to deliver a prevention intervention that focuses on tobacco use alone or to integrate tobacco prevention into a program that addresses other risk-taking behaviors, such as abusing alcohol and other drugs.

Research is needed to identify the best strategies for diffusion of effective youth prevention efforts through different channels of delivery, such as schools, health centers, and other community settings.

As discussed in more depth under Community and State Intervention Research, it will be critical to develop such diverse diffusion strategies to increase the impact of novel, nonschool-based approaches.

THE IMPACT OF PREVENTION RESEARCH

The continuing increase in the use of tobacco products by American youth during the 1990s constitutes both a pressing challenge and a unique opportunity to reduce the tobacco-related diseases in the next century. If we act now to develop and implement successful tobacco prevention interventions, we will avert a major upturn in tobacco-related cancers in the middle of the next century.



Smoke-Free Kids & Soccer is an innovative collaboration of the U.S. Department of Health and Human Services (DHHS), the U.S. Women's National Soccer Team, and U.S. Soccer. Participating DHHS agencies include the National Cancer Institute and the Centers for Disease Control and Prevention. This campaign promotes participation in soccer as a positive, healthy alternative to tobacco use; it offers free vibrant posters and tips to help teens model the success and smoke-free lifestyle of National Team members via web site: www.smokefree.gov.

Research focusing on the treatment of nicotine addiction seeks to identify, test, and effectively disseminate interventions to treat tobacco users who are addicted to nicotine.

5. Treatment of Nicotine Addiction

INTRODUCTION

Most people who use tobacco regularly are addicted to nicotine. In recent years, a wide variety of approaches to treating nicotine dependence have been developed, including pharmacological treatments, behavioral therapies, and advice from health care providers. Though these approaches have enabled many cigarette users to stop smoking, modest success rates and substantial relapse have limited their effectiveness. As a result, broadly effective treatments that meet the needs of the majority of current tobacco users who are dependent on nicotine continue to be elusive. However, new developments have

created opportunities for increased success in treating nicotine dependence. While these developments portend an increase in both the effectiveness and availability of nicotine addiction treatments, we still must answer many difficult questions to fully seize these opportunities to reduce tobacco use in the United States. For example, as new pharmaceutical products, including over-the-counter medications, are developed to treat nicotine addiction, we need to evaluate and maximize their effectiveness. We also need to learn whether harm-reduction strategies, which involve less exposure to nicotine and tobacco toxins, are an acceptable treatment alter-

Developments in the Treatment of Nicotine Addiction

- Recent data suggest that the great majority of tobacco users—as many as 80 percent—would like to stop smoking. Treatment research could have a substantial impact on the Nation’s public health by developing broadly effective and widely available therapeutic approaches to nicotine addiction.
- Increasing realization that adolescent tobacco users also need help in quitting has resulted in a number of clinical trials aimed at addressing treatment needs, methods, and services for this previously underserved group.
- Nicotine replacement products, such as nicotine gum and transdermal patches, can now be obtained over-the-counter. This may increase the success rate of the majority of tobacco users who prefer trying to quit on their own without the aid of a formal smoking cessation group or medical attention.
- Advances in genetics have begun to suggest how new treatments for nicotine dependence may be developed and targeted to those smokers who are most likely to benefit from them.
- Development of new medications, such as the nicotine aerosol spray, and the application of existing medications, such as the antidepressant bupropion, to the treatment of nicotine dependence, will widen the array of treatment choices available to nicotine-addicted patients and their health care providers.
- The Smoking Cessation Clinical Practice Guideline issued by the Agency for Health Care Policy and Research in 1996 has provided an effective, evidence-based treatment guideline that can be used by a variety of health care providers in a range of treatment settings.

native to abstinence and, if so, for whom these approaches are most appropriate. In addition, we need research to determine whether combination therapies, such as using two or more medications or combining behavioral therapies with pharmacologic treatment, are more effective than single-focus therapies. Finally, we must identify which subgroups of smokers are most and least likely to benefit from each approach.

FDA-Approved Pharmaceutical Agents	
Nicotine Replacement Agent	Trade Name
Nicotine transdermal patch	Nicoderm CQ
	Habitrol
	Prostep
	Nicotrol
Nicotine polacrilex (gum)	Nicorette
Nicotine nasal spray	Nicotrol NS
Nicotine oral inhaler	Nicotrol Inhaler
Non-nicotine agent	
Bupropion HCl tablet	Zyban

These questions can be answered by an organized, carefully planned program of research. Such a program interacts with other areas of tobacco research described in this report. For example, surveillance and epidemiology provide the up-to-date data on tobacco use behaviors needed to identify target groups and patient pools for treatment research. Biobehavioral and basic biological research provide information about psychosocial factors and genetic predispositions to nicotine addiction and tobacco-related cancers. They lay the groundwork for new treatments aimed at these factors. And, community and policy research help treatment research to increase access to treatment and widen dissemination of effective treatments. In addition, collaborative opportunities with pharmaceutical companies, NIDA, the National Heart, Lung, and Blood Institute (NHLBI), and other research institutes would be particularly appropriate in this area.

RECOMMENDATIONS

Research should be conducted concerning the treatment of nicotine addiction to find the best ways to tailor tobacco cessation interventions to specific sociocultural, psychological, physiological, and genetic subgroups.

Tobacco use either has declined at slower rates, remained level, or increased among a number of subgroups within the overall population, such as women, blue collar workers, low-income Americans, ethnic and racial minorities, and adolescents. These trends indicate that tobacco-induced cancers and other serious health problems will continue to increase unless we conduct research to evaluate whether unique treatments are needed for special populations. Such research can tell whether treatments need to be tailored for groups, such as pregnant smokers, smokers with comorbid mental disorders, African-American tobacco users, cigar smokers, and adolescent tobacco users, or whether generic treatment approaches are just as effective. Also, as addressed in the Basic Biobehavioral Research section, advances in genetics and pharmacology may make it possible to determine whether a smoker's genetic makeup can be used to predict response to various treatments for nicotine addiction. Answering this question would make it possible to match treatment to an individual's genetic makeup to increase its effectiveness.

Research should be conducted to determine the optimal settings and mechanisms to deliver effective tobacco cessation treatments to culturally diverse and high-risk populations.

The development of tailored therapies for culturally diverse and high-risk groups is only the first step in reducing tobacco use and nicotine addiction among these populations. It is equally important to ensure that these treatments make the transition from research laboratories to successful application in the community. This creates an urgent need for treatment research in conjunction with community and state intervention research and policy research to learn how best to deliver and implement effective treatments and to ensure that tobacco users from traditionally underserved populations have access to them. These wide-ranging questions should be addressed on a number of levels, including:

- managed care organizations (MCOs);
- the growing array of new communications technologies;
- training of health care providers; and
- strategies centered on the worksite and health care settings ranging from primary to rehabilitative care.

Innovative uses of the new digital media, for example, can be used to tailor smoking cessation programs based on information needs and preferences. Given limited health care resources, it is important to evaluate the relative cost-effectiveness of new and existing nicotine dependence treatments, as well as the effect of reimbursement policies on treatment delivery and utilization.

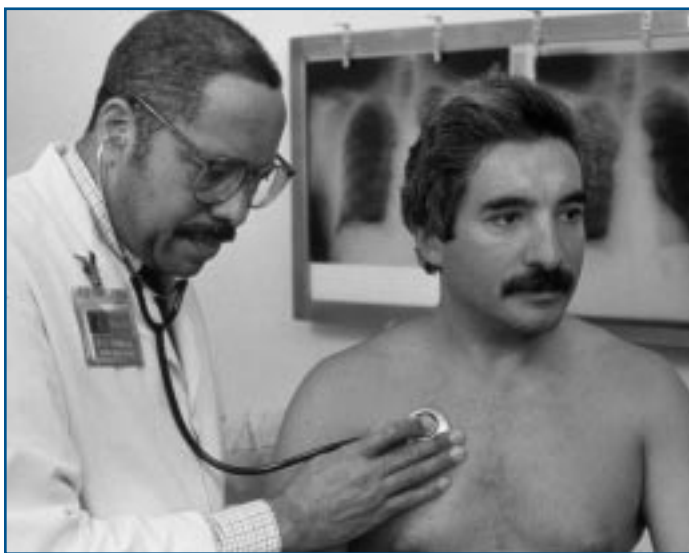
OTHER RECOMMENDATIONS

Research also is needed to assess the benefits and consequences of treatments designed to reduce harm from tobacco use. Such research should determine if approaches aimed at reducing exposure to nicotine and tobacco toxins, such as long-term nicotine maintenance through pharmacologic aids, are an acceptable alternative to abstinence for treatment-resistant tobacco users who are unable to quit.



THE IMPACT OF TREATMENT RESEARCH

The potential impact of improving delivery of existing treatments for nicotine dependence and developing new ones is enormous. With over 450,000 total deaths and 170,000 cancer deaths annually in the United States alone, the potential to reduce tobacco-related deaths and disease may be greater for nicotine addiction treatment than for any single medical treatment on the horizon. By improving our ability to understand nicotine addiction, developing better methods of treating it, and ensuring that those treatments are made widely available to all who wish to use them, including culturally diverse and high-risk groups, the treatment process can be made more effective and the toll of tobacco on our society can be significantly reduced.



Community research focuses on the impact of single and multiple interventions on the prevention and cessation of tobacco use among large groups of people. Community research examines various types of intervention strategies, such as educational programs, clinical services, media programs, and policy interventions in a wide range of settings, including schools, worksites, health care facilities, and community organizations.

INTRODUCTION

Ultimately, all tobacco control research should be applied at the state and community levels. Communities are the final “laboratories” where tobacco control interventions are tested to determine if and how they work in real-world settings. The need for such research on state and community interventions has never been greater. New tobacco control programs are underway in almost every state, and each program raises new research questions and opportunities to provide useful information that can improve the effectiveness of these interventions.

To seize this opportunity, community and state research must use a transdisciplinary approach that draws on, applies, and assess the impact of research from many different research areas discussed in this report. Ideally, community research uses the results of more basic biological, behavioral, and treatment research and links their findings to policy research to develop and evaluate community tobacco control programs. Community interventions frequently include a component that promotes public health policies through coalitions and the mass media. Community research also draws extensively on epidemiology and surveillance methods to obtain critical information needed to assess the impact of tobacco control interventions. In other cases, community research takes advantage of what are, in effect, large

“natural experiments” that occur when new programs or policies are implemented in a group of states or communities. State settlements with the tobacco industry are providing resources for tobacco control programs and new opportunities for natural experiments. The development of new measurement tools and surveillance systems will be needed to support this complex but vital research.

During the last 15 years, the NCI has conducted a program of community intervention research that has developed and tested a large number of cancer control interventions. Trials of individual interventions ultimately led to the Community Intervention Trial for Smoking Cessation (COMMIT), which tested the impact of multiple interventions in community settings on adult smoking cessation rates. The combined interventions significantly increased smoking cessation rates among adults who smoked less than 25 cigarettes per day but not among heavier smokers. If this rate of success was expanded nationally, it would generate an additional 1.2 million individuals annually who successfully stop smoking.

Currently, the NCI supports a much broader intervention program, the American Stop Smoking Intervention Study (ASSIST). Now in its final phase, ASSIST is testing the impact of a more comprehensive intervention on smoking rates among adults and youth in 17

states. Building on lessons learned from COMMIT, the intervention used in ASSIST states added a strong emphasis on public and private tobacco control policies. The evaluation of ASSIST now underway will detail the impact of the intervention on several different outcomes, including the prevalence of smoking and tobacco use. It also will describe the impact of different parts of the intervention on these outcome measures. A midpoint analysis has shown that cigarette consumption is significantly lower in ASSIST states than in other states. As a result, the Centers for Disease Control and Prevention will fund programs based on the ASSIST model in all 50 states beginning in 1999.

Research-based programs like COMMIT and ASSIST have illustrated the potential of community and state tobacco control interventions to change the societal influences on tobacco use and reduce the tobacco-related cancer burden. As states continue to expand the implementation of such programs, we must seize this opportunity to expand research on the community and state levels to increase understanding of the most effective approaches to achieving broad reductions in tobacco use.

RECOMMENDATIONS

Research should be conducted to improve community and state tobacco control programs and to increase their effectiveness for populations at disproportionate risk.

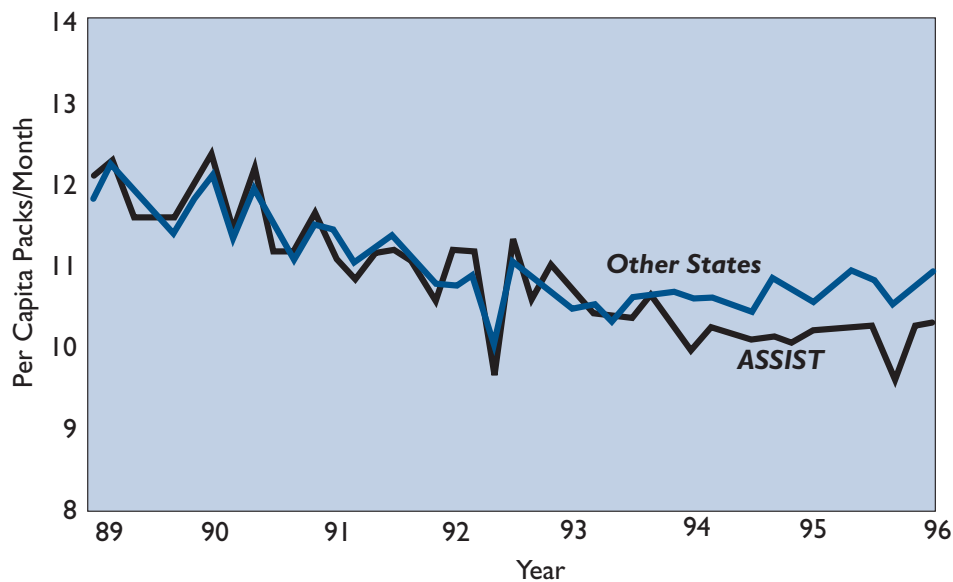
Although comprehensive state tobacco control programs have led to significant reductions in the tobacco use rates among very large populations, major questions remain about the relative importance of different components of these programs. Therefore, a high priority is to establish research protocols in state tobacco control programs to ascertain the impact of new and existing interventions and to determine how they and their individual components work to achieve their effects. This research should be an integral and ongoing part of state and local programs.

We also need to conduct intervention trials to develop, test, and refine tobacco control interventions on an ongoing basis. One of the most important components of such trials should be assessment of mass media interventions. Counter-advertising campaigns funded by state governments are highly visible and costly. Research in this area should document effective

components and guide future campaigns. Many other important research questions only can be addressed in communities and states that are conducting multiple interventions. For example, we need to conduct simultaneous testing of multiple interventions in different community settings to clarify the relative contribution of each intervention to reductions in tobacco use. We also need observational studies of interventions and policies whose implementation is beyond the control of the investigator to provide new information about how these initiatives influence tobacco-use behaviors. Such research will require the use of complex study designs that

Deseasonalized Per Capita Consumption

ASSIST states were consuming 7 percent fewer cigarettes per capita compared to other states in 1996.





**It's time
We made
smoking
history.**

Slogan for the Massachusetts Tobacco Control Program.

account for variation in the multiple parameters that are found in these very complex environments.

Special emphasis should be given to high-risk populations in developing and evaluating community and state tobacco-control programs. These populations include ethnic and racial minorities, adolescents, children, people with low educational levels, and blue-collar workers. Of particular concern is research to address the needs of low-income Americans, who have consistently higher rates of tobacco use than the general population. Ethnographic studies and survey research, economic and behavioral-economic studies, studies of targeted tobacco marketing, and biobehavioral research to clarify the basic mechanisms contributing to higher tobacco use and nicotine addiction among low-income Americans and other high-risk populations could help to generate more effective prevention and cessation strategies and tobacco control policies for these groups. Research in this area also must consider the features of the population that influence the delivery, receipt, and impact of a particular intervention.

Research should be conducted to identify mechanisms for optimal dissemination of proven prevention and treatment interventions at the community and state levels.

As prevention and treatment interventions are found to be effective for particular groups, larger-scale dissemination and diffusion trials should be conducted to evaluate the best approaches for applying these programs at the state and community levels. For example, we know that few Americans currently have access to the most effective school-based prevention programs or physician-initiated and self-help smoking cessation programs that follow the guidelines of the Agency for Health Care Policy Research (AHCPR). Research is needed to increase scientific knowledge about policies and strategies that increase dissemination and application of these and other effective tobacco-control interventions. One promising treatment dissemination strategy makes nicotine addiction treatments with different levels of intensity available to large populations. This

strategy uses a “stepped” approach to treatment and a matching of patients to appropriate therapies. It is inherently cost-effective because it assumes that people should be given the least intensive intervention that is effective.

Research is also needed to develop new strategies for accomplishing the systemic change needed to institutionalize effective tobacco control interventions. Examples of promising approaches in health care settings include implementing systems in medical offices, clinics, and hospitals to identify patients’ tobacco-use status; providing education and feedback to health care providers about tobacco cessation approaches; and providing reimbursement for smoking cessation treatment.

THE IMPACT OF COMMUNITY AND STATE INTERVENTION RESEARCH

The findings of community and state intervention research can have a tremendous impact on the tobacco control programs that are already underway in all 50 states as well as the new and expanding programs that are under development. The impact of existing programs on tobacco-use behaviors among large

populations already has been established. Expanding community and state research will increase our understanding of how to change societal influences on tobacco use, increase the effectiveness of these programs, and contribute to the development of the next generation of both targeted and broadly applicable tobacco-control programs. Thus, research on these intervention programs, which includes much of the policy research described in the next section, is likely to have an enormous impact on the rapid reduction of tobacco-use rates and subsequent tobacco-related cancers.

Policy research examines the impact of policy and environmental interventions on the prevention or cessation of tobacco use.

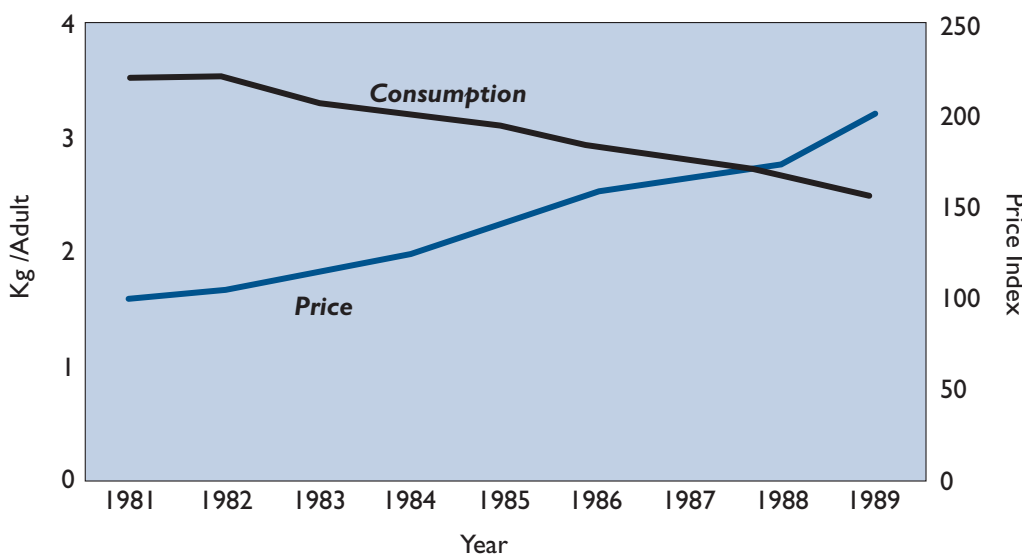
INTRODUCTION

Public and private policy changes are critical to the success of tobacco control because of their potential to create a social, policy, media, and economic environment conducive to reducing tobacco use and exposure among children, youths, and adults. Such an environment can reduce tobacco use among large populations.

Policy research should focus on understanding the complex relationships that link the social context, the public health agenda, tobacco use, and individual behavior change. Determining these relationships will inform policymakers and tobacco-control program planners about those policies and programs that are most likely to be effective. As described in the Community and State Research section of this report, decreases

in tobacco use have resulted from policies that increase the price of tobacco, restrict its marketing, and restrict where it can be used. It is clear, for example, that tobacco price and tax increases affect youth and adult smoking patterns. It is less clear what effect price increases have on intentions to start or quit smoking, or how gradual, small price increases compare to lump-sum, large increases in terms of their impact on tobacco consumption or choice of brands. We also need to clarify the extent to which counter-advertising campaigns, retailer compliance checks, or school-based prevention programs heighten the public health impact of tobacco price increases. Taken together, such research will help determine the relative impact on the use of tobacco among youths of policies that increase prices and those that reduce tobacco advertising and promotion.

Tobacco Consumption and Price in Canada



Source: Kaiserman and Rogers, Am J Public Health 1991;81:902-4.

We also need policy research to provide science-based answers to a number of other questions. How, for example, does tobacco marketing interact with biobehavioral factors (e.g., culture, social influences, and personality) to influence youth susceptibility to tobacco use? Research should also focus upon how price increases and youth access laws affect different segments of the population. The effect of product design, including amount of nicotine and mode of delivery, upon nicotine use and dependence among users may also be evaluated. Finally, the relative costs and benefits of mandating Medicaid coverage for nicotine addiction treatment is worthy of inquiry. Policymakers and tobacco control program planners need answers to these questions. Furthermore, the potential to link policy research to research on the state and community interventions as described below provides a unique opportunity to maximize the impact on tobacco use from both lines of research.

RECOMMENDATIONS

Research should be conducted to understand the impact of tobacco policies, including taxation and pricing, clean indoor air policies, marketing restrictions, youth access restrictions, and tobacco product and nicotine replacement regulation.

Research to evaluate the impact of individual and combined policy and environmental interventions is needed. Much can be learned about controlling tobacco use through studies that evaluate the multitude of “natural experiments” occurring as a result of existing and expanding state and local tobacco control programs described in the previous section. For instance, policy research could evaluate the impact of naturally occurring differences in the price of cigarettes and other tobacco products in different communities, the success of efforts to curb youth tobacco advertising/promotion, and the effects of variations in school-based tobacco control policies and sanctions. Such research also should examine the extent of enforcement of youth access laws and whether such policies should penalize youth or retailers or both.

We need research on policies to improve Americans’ access to effective nicotine addiction treatment aids and tobacco cessation interventions. This research should examine and assess the impact of

treatment reimbursement policies on tobacco use, disincentives for tobacco use, system changes to promote routine tobacco cessation intervention in primary health care settings, and managed care tobacco performance accountability measures. Policy research also is needed to determine the optimal allocation of treatment resources for the greatest population impact. The NCI’s new research network of managed care organizations provides an important opportunity to examine alternative access-enhancing strategies.

Most past policy research relied upon cross-sectional analyses, which are limited in their usefulness. High priority should be placed on conducting prospective, long-term policy research that can demonstrate cause-effect relationships and indicate the impact of various policies on transitions in tobacco-use patterns over time. Mechanisms for “quick strike” or “rapid response” studies should be included to allow investigators to seize opportunities to evaluate natural policy experiments. Furthermore, methodologies for assessing the implementation and impact of these interventions should be expanded and refined.

Research to inform policymakers about the design and marketing of tobacco and nicotine-replacement products represents another important avenue for

An issue that hits close to home

Brewers crack down on smoking

Locke to sign teen tobacco measure

BOSTON SETS AN EXAMPLE: A smoking ban will work in Portland, too

research. To improve future regulation of such products, the NCI should consider funding research on harm-reduction strategies aimed at both youth and adult smokers. For youth, research could examine the impact of product design, including level of nicotine and mode of delivery on nicotine use and dependence. Research could examine the effects of long-term nicotine maintenance, alternative nicotine delivery devices, and reduction in tobacco toxins for highly addicted adult smokers. These studies could evaluate the biological, behavioral, social, and economic consequences, both intended and unintended, of modifying and substituting different tobacco products. It should be made clear that studying these strategies does not represent an endorsement of them.

Research on harm-reduction approaches should also include investigations of the behavioral and health impacts of policies and interventions designed to reduce environmental and occupational exposures to environmental tobacco smoke (ETS). This also is referred to as second-hand smoke or passive smoking. Basic biological research on the extent of the role ETS plays in tobacco-related lung cancer can play an important role in forming such policies.



The rapid global increase in the consumption of tobacco products has accelerated the need for coordinated international research efforts to reduce the morbidity and mortality associated with this global pandemic. The NCI can take the lead in research to examine cross-national differences in tobacco-control policies as well as learn from effective foreign tobacco-control policies. International research can help clarify the impact of advertising restrictions and excise taxes on tobacco use. Tobacco products, as well as social, cultural, and environmental factors, vary from country to country. Consequently, international research can look at important questions concerning tobacco control in the design, packaging, and marketing of tobacco products that cannot be studied in the United States alone.

A vital investment in international tobacco control research would be to increase the surveillance capacity of countries to monitor tobacco use, tobacco-control policy development, and tobacco-control efforts. The NCI could also make a significant contribution by providing training opportunities to international physicians and policy researchers to promote tobacco control in their countries.

THE IMPACT OF POLICY RESEARCH

Policy research, especially in combination with the state and community research discussed in the previous section, has the potential to affect the most wide-reaching interventions currently used in tobacco control. Effective public and private policies can reduce tobacco use among populations of entire states and nations. The research proposed in this section can make tobacco control policies more effective and point the way to the next generation of more powerful programs and policies for preventing tobacco use and nicotine addiction.

Basic biological research in tobacco-related carcinogenesis focuses on identifying genetic and epigenetic events that contribute to cancer and what can be done to prevent these cancers from occurring.

INTRODUCTION

We now know that a series of changes in gene function and activities that control cell growth and behavior transform normal cells into cancer. The components of tobacco smoke clearly cause genetic and other changes that lead to cancer. Because of this, tobacco use causes more than 30 percent of all cancer deaths and as much as 90 percent of all lung cancers. Basic biological research, which is enhanced by sophisticated new genetic and biochemical research techniques, is changing our understanding of carcinogenesis. It is critical that basic scientists formulate new hypotheses about carcinogenesis that include the role of tobacco and the route of exposure (active smoking, passive exposure, smokeless tobacco products). Moreover, experiments using the latest research tools, such as genetically engineered animal and cell lines, must include tobacco carcinogens.

Understanding the complex characteristics of tobacco products is necessary if we are to learn how tobacco causes cancer. The burning of tobacco products leads to the production of over 3,800 chemicals, including known human mutagens and carcinogens. Although cancer-causing chemicals have been found in tobacco-smoke vapor, the majority of chemicals that lead to mutations and cancer reside in tobacco smoke particulates.

Limited information is available about the molecular mechanisms of damage caused by tobacco smoke within specific organs. Even less is known

Partial List of Harmful Tobacco Smoke Components

*2-naphthylamine**

*4-amminobiphenyl**

Acetic acid

Acetone

Ammonia

*Benzene**

Carbon dioxide

Carbon monoxide

Cholesterol

Formaldehyde

Methyl chloride

*Nickel**

Nicotine

*Polonium-210**

***Known human carcinogen**

about why tobacco smoke components target particular genes. Research to determine whether harmful tissue changes in one organ predict similar changes in others could lead to new ways to detect, diagnose, and treat cancer in its earliest stages for individual patients. In addition, basic biological research can lead to important insights about why some people may be especially vulnerable to harm from tobacco. For example, research may explain why women might be more susceptible to tobacco-related cancers than men, and why lung cancer risk for former smokers remains higher than for individuals who have never smoked (although much less than current smokers).

RECOMMENDATIONS

Basic biological research should be conducted to identify and validate biomarkers of tobacco exposure and tobacco-induced cellular events as they relate to the different stages of carcinogenesis.

Expanding research is essential to identify, validate, and increase the availability of biological markers. Such research can provide the tools to determine the amount and type of carcinogens in individuals exposed to tobacco products. Examples of biological markers include carcinogen-macromolecular adducts, assays to measure enzymes involved in critical cellular processes, methods to detect DNA damage and decreased DNA repair, RNA-based methods to identify changes in expression, genetic variations that increase vulnerability or resistance to cancer-causing chemicals, and metabolites of procarcinogens or cancer-causing agents.

The development of new biomarkers is dependent on the basic biological research of tobacco carcinogenesis. An understanding of the effects within, and by, cancer susceptibility genes will lead to the identification of genes that should be targeted for biomarker



development. Similarly, research into the stages of carcinogenesis will be important for identifying biomarkers that can mark cancer progression. Basic biological research on tobacco smoke should focus on specific tumor-enhancing or prevention strategies, such as the role of dietary (e.g., antioxidants), environmental (e.g., radon, air pollution) and occupational (e.g., asbestos, metals) factors. Smoked, and smokeless tobacco, filtered and unfiltered cigarettes, and high- and low-nicotine tobacco all result in exposure to different



types and amounts of carcinogens. Yet, little research has been done to specify and determine the amount of these carcinogens and to assess the changes in the profile of the carcinogens over time. Further, the effects of the burning temperatures (pyrolysis)

on the most commonly used tobacco additives have not been investigated to any degree. Other areas that have not been studied adequately are how tobacco smoke components interact with each other and what synergies might exist. The development of biomarkers that can measure these effects and differences can provide a critical understanding of why we see variations in cancer incidence, what has caused changes in lung cancer histology over the last 40 years, and why there may be differences in risk between gender or races.

THE IMPACT OF BASIC BIOLOGICAL RESEARCH

The development of biomarkers for cancer risk can lead to the development of early detection methods and perhaps provide information about tumor responses to treatment. If development and validation of biological markers will allow testing, then we can test different prevention strategies by assessing changes in specific markers. In summary, if we gain a better understanding of human metabolic pathways through which the chemicals in tobacco cause their cancer-causing changes and identify the critical steps in those pathways that lead to increased susceptibility to tobacco-related cancer, then we will be better able to identify individuals at greatest risk for tobacco-related diseases and devise prevention strategies for them.

Epidemiologic research examines and assesses relationships between biologic/genetic factors, environment, tobacco use, and cancer in humans.

INTRODUCTION

Recent advances in molecular biology have catalyzed molecular epidemiology. This approach, which tests biological hypotheses about disease in the laboratory through studies in human populations, is being applied by epidemiologists to understand the molecular keys to cancer. In particular, improved technologies to describe the role of genes have increased our ability to define disease risk in terms of genetic traits and provided new insights about how particular genes interact with environmental exposures.

The relative roles and magnitude of the effects of inherited susceptibility and exposure to carcinogens can be very different for familial compared to common cancers. Genetic epidemiology seeks to identify the genes that cause cancers in families, often cancers that are found in syndromes that are uncommon in the general population. Molecular epidemiology seeks to identify the genes that contribute to cancer in the general population.

While the basic role of tobacco in causing cancer is firmly established,

Gender Issues

Women started smoking later in this century than men, so the lung cancer epidemic was initially a male phenomenon. However, female lung cancer death rates have increased over 550 percent since 1950, and lung cancer is now the leading cause of cancer death in women in the United States. Today, lung cancer accounts for one in every four female cancer deaths, making it a very significant women's health issue. Following diagnosis, survival is poor (relative 5-year survival rate for women with lung cancer is only 16 percent, and most die within 2 years of diagnosis). Thus, it is generally agreed that attention needs to be focused on smoking prevention and cessation efforts to prevent the disease from developing in the first place. The vast majority of lung cancer cases in women, as in men, are known to be caused by smoking, but important research questions relevant to tobacco and cancer remain: Do similar factors influence girls and boys to initiate smoking or to decide to remain nonsmokers? Are there gender differences in susceptibility to nicotine? Does the same amount of smoking affect women and men differently in terms of lung cancer risk? Are there gender differences in the effect of smoking on risk of specific histologic types of lung cancer? Would cessation programs tailored to concerns expressed more often by women than men who smoke (such as fear of weight gain) increase the proportion of female smokers who quit? The answers to these and other questions will help us to better understand tobacco carcinogenesis and to develop effective tobacco control programs.

many important questions remain. For example, why do some individuals, smokers and nonsmokers alike, get cancer while others are spared? We need to learn more about cancer in persons who have successfully quit smoking. While the risk of cancer decreases substantially when smokers quit, it never drops to the level of nonsmokers. Unraveling these questions is becoming more important as more people quit. Former smokers, who remain at increased risk for lung cancer for years following cessation because of persistent carcinogen effects at the cellular and genetic levels, are candidates for prevention through chemopreventive agents. Are certain segments of the population, such as women and African-Americans, more vulnerable to tobacco-related cancer and nicotine addiction? New epidemiological studies will allow us to take genetic data obtained from laboratory probes and identify genetic and other biological factors that may increase vulnerability to tobacco-related cancer in these groups. This knowledge could contribute to more rational cancer prevention and treatment strategies for vulnerable individuals.

RECOMMENDATIONS

Research should be conducted to understand genetic and environmental interactions in susceptibility to tobacco-related cancers in order to identify subgroups at risk.

Continued study of the relationship between genetic and environmental factors is needed to increase understanding of the risk of tobacco-related cancers for specific populations. Some data suggest that there are differences in the risk of tobacco-related cancers between men and women. This might be due to differences in smoking practices or to differences in innate biological mechanisms. Men's and women's lung cancer mutation characteristics also differ. For example, the p53 tumor suppressor gene, which serves many important cellular functions, is more commonly mutated in men, but the type of mutations observed in women is more strongly associated with exposure to the components of tobacco smoke. Women have higher levels than men of estrogen and related hormones, and lung cancers in women more commonly have estrogen and progesterone receptors that are stimulated by these hormones. These receptors may have a special proliferation trigger that increases women's risks for certain types of lung cancer. Despite these

observed gender differences in lung cancer biology, it has been difficult to compare the lung cancer risks of men and women smokers, and study results have been inconsistent.

Epidemiological studies are needed to establish definitively if there is a difference in tobacco-related cancer risks for men and women and the genetic and other biological determinants of such a difference. Similar studies are needed to identify whether genetic and other biological factors are responsible for different lung cancer risks across races and ethnic groups.



Why do some people get cancer from smoking while others with long-term histories of heavy smoking never suffer smoking-related cancers? Answers to this question may arise from studies to characterize the independent and

interacting effects of the large number of variations in genes governing the activation and detoxification of tobacco carcinogens as well as continued study of the interplay between genetic and environmental factors.

Studies of how diet and potential chemopreventive strategies influence the risk of tobacco-related cancers in people with genetic susceptibilities to cancer from tobacco exposure also are needed. Approaches to reducing the cancer risks of people who have successfully stopped smoking are of special importance. Studies also are needed to determine how smoking alters various types of tissues in former smokers to help explain why they remain more likely to develop cancer than people who have never smoked.

Large-scale epidemiologic studies, both case-control and cohort studies, may provide the most definitive answers to these and other questions. However,

smaller-scale pilot studies also are needed to characterize and validate individual biological markers of genetic susceptibility to tobacco-induced cancer. Such work will provide critical information on how the genetic makeup of individuals or groups is modified by environmental factors, such as tobacco exposure, thereby leading to the development of new genetic tests that can then be validated in larger studies.

THE IMPACT OF EPIDEMIOLOGIC RESEARCH

A better understanding of the independent and interacting effects of inherited susceptibilities and tobacco-exposure variables could elucidate risk profiles and the biological mechanisms involved in the development of cancer. Ultimately, this knowledge could lead to the development of tailored approaches to prevention and treatment of tobacco-related cancers in high-risk populations. Finally, studies of youth and young adults, especially cohort studies, may lead to a better understanding of the process of nicotine addiction, as well as genetic and environmental factors that predispose individuals to such addiction.

Surveillance research in tobacco control should monitor and evaluate trends in tobacco use and related cancer risk factors, health services, and policy and environmental interventions to determine the influence of these factors on trends in cancer incidence, morbidity, mortality, and survival.

INTRODUCTION

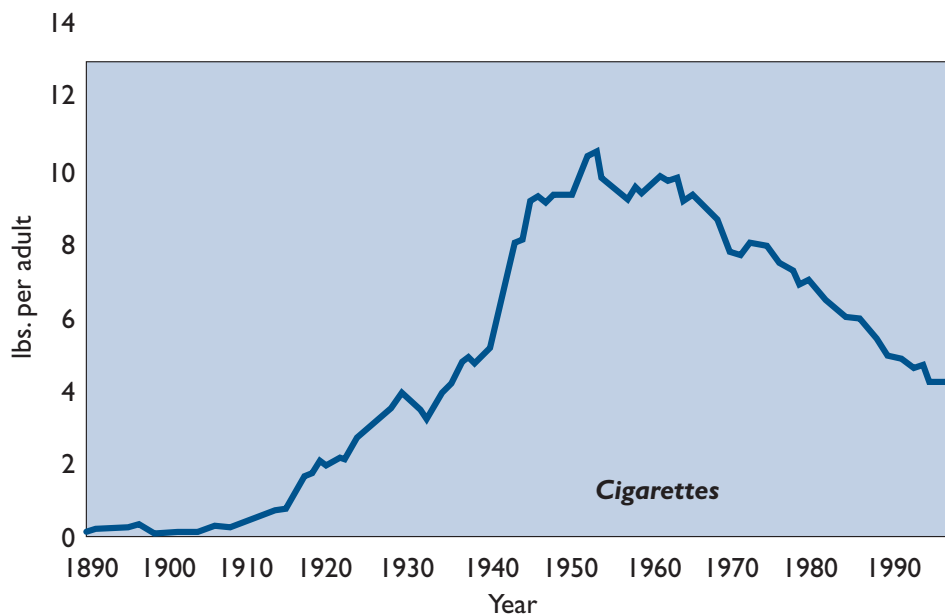
A comprehensive and integrated program of surveillance research is an essential component of a complete tobacco control research portfolio, and must address a wide spectrum of planning, implementation, and evaluation needs. Researchers, policymakers, health care planners, and community organizers require data on the use of tobacco products, changes in tobacco use, and the factors that influence such behaviors in order to plan, develop, and implement more effective tobacco control interventions and policies.

Ideally, a tobacco surveillance system should systematically monitor and analyze tobacco-use behaviors and changes

in those behaviors in relation to a variety of social and environmental influences. A well-designed, integrated approach to data collection and analysis should go beyond conducting surveys about current tobacco use and how use changes over time. It also must assess how social and environmental factors interact with tobacco control initiatives and tobacco industry activities to influence tobacco use in various populations.

Today's rapidly shifting societal attitudes toward tobacco use, along with new state and community legislative and policy initiatives, have created a unique opportunity to establish a tobacco surveillance system. Such a system should monitor the impact of these influences on tobacco use

Trends in Per Capita Tobacco Consumption, United States 1890-1997



Source: 1955 CPS; NHIS 1965-1995.

and provide the critical information tobacco control efforts need to succeed.

RECOMMENDATIONS

Research should be conducted on expanded surveillance systems to monitor tobacco use behaviors, the implementation and fidelity of tobacco-related interventions, and other factors that influence tobacco use.

Tobacco surveillance currently consists primarily of (1) routinely measuring tobacco use (current, former, never) using questions added to existing national or state surveys, (2) intermittently administering comprehensive, specialized tobacco surveys, and (3) compiling tobacco sales data from federal or state excise tax receipts. Federal surveys that are conducted regularly measure current smoking status for a given population at a given point in time. While this information is important and should continue to be collected, national surveys should expand to follow individuals over time to assess the determinants of and changes in smoking behavior longitudinally. Such cohort surveys would enable researchers to assess population trends, and are critical for both evaluating interventions and understanding why changes in tobacco use did or did not occur and what factors are influencing trends at the national, state, or local level. Two national surveys (the Adult Use of Tobacco Survey and the Teenage Attitudes and Practices Survey) have provided detailed information about adult and teenage tobacco use behavior. However, they have not been conducted frequently enough to meet the needs of researchers, policymakers, and public health planners.

New surveillance measures should delineate the biological, behavioral, and social influences underlying tobacco use. Special surveys and oversampling should be used, where needed, to collect data on teenagers, low-income adults, and other high-risk groups. Findings can be used to evaluate existing tobacco-control approaches and refine or design new ones where needed. For youths, monitoring and analyzing the social and environmental factors that lead to tobacco experimentation and subsequent addiction are needed to develop more effective tobacco-use prevention approaches. Data on attitudes and beliefs about low tar and nicotine tobacco products and dose-response effects and beliefs about nicotine addiction that result from using these products are needed to develop tar-

geted behavioral and pharmacological approaches for all tobacco users. Additionally, expanded data on attitudes and beliefs about “smoke-free” accommodations and workplaces are needed to assess public opinions about tobacco policy initiatives and whether these policies reduce tobacco use in the population.

As tobacco-control initiatives increasingly move to the state and local levels, we need to expand capabilities to monitor the dissemination, quality, and outcomes of those efforts. This includes continuing to track state and local tobacco control legislation and evaluating whether this effort needs to be expanded. The NCI should continue to fund Tobacco Use Supplements to the Current Population Survey (CPS), conducted by the Census Bureau, to track tobacco issues, such as prevalence, policies, and other measures, for the individual states. The CPS tobacco use questionnaire should be modified to incorporate new measures of tobacco-use behaviors and new supplements should be commissioned to cover new and emerging areas of importance. The NCI should build on its leadership in maintaining the State Cancer Legislative Database (SCLD) and continue to define and track measures of state-level tobacco policy implementation. Ultimately, the NCI should assess the most appropriate location for the SCLD within the NCI. Moreover, there should be discussion of how to integrate the NCI and CDC legislative databases for maximum efficiency and cost-effectiveness.

The comprehensive and integrated program of surveillance research required to serve the needs of a broad range of organizations and researchers must ensure the consistency of data measured over time and completeness of measurement. Research collaboration is needed to develop a common set of basic core measures to allow comparisons of local, state, and national surveys. The collaboration should include researchers and activists working at these levels. Furthermore, standard definitions of what constitutes a “smoker” and the age range of teenagers for measurement purposes needs to be agreed upon and remain consistent over time in order to permit accurate tracking of trends in tobacco-use behaviors.

The fidelity of tobacco-related interventions to their original design needs to be monitored when interventions are translated beyond their original

research settings. Technical assistance to help modify interventions to adapt them to the new research settings should also be available. One of the greatest barriers to evaluating tobacco control interventions has been the absence of any ongoing monitoring of how these strategies are being applied (process evaluation). Hundreds of research papers have been published documenting the effectiveness (or lack thereof) of various interventions in controlled settings. However, when these interventions are moved from a research environment to the community, monitoring and evaluation often ceases or is insufficient. For example, while comprehensive school health programs that include tobacco prevention reduce youth smoking, it is commonplace to find that schools are not adhering to the program as it was originally designed and implemented only 3 to 5 years after a recommended curriculum is adopted. Comprehensive surveillance mechanisms are critical to evaluate both the processes and the outcomes of interventions directed at special populations. Cost-effectiveness of these programs should also be analyzed and data should be collected for that purpose.

While it is not economically feasible, practical, or necessary to monitor all tobacco industry activities, the tobacco-control surveillance systems should be

expanded to document and track industry counteractivities and their possible effect on program success. Newly released tobacco industry documents are expected to provide information to help guide this effort. Surveillance should track such tobacco industry strategies as new advertising campaigns, themes, promotions, and legislative lobbying efforts as well as changes in product packaging, design, pricing and positioning.

OTHER SURVEILLANCE RECOMMENDATIONS

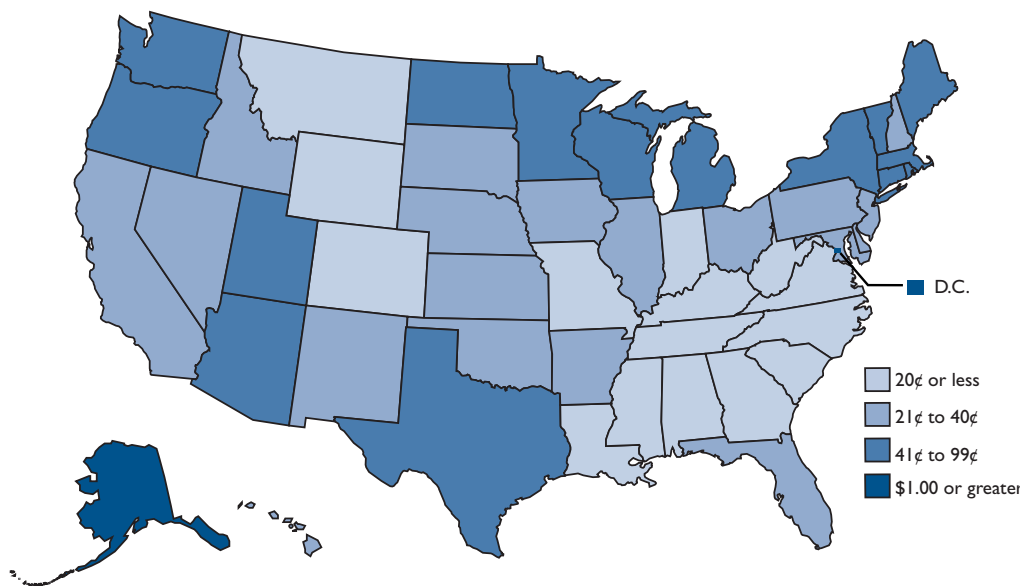
It is important to regularly synthesize tobacco control research findings. For example, resources should be committed to summarizing what we have learned from interventions directed at low-income and minority smokers. Syntheses of research findings in major areas of tobacco control are an important part of surveillance and build the base of scientific knowledge that is needed to advance tobacco-control efforts. Such information is needed for both practitioners and researchers. This has rarely been done in the past.

THE IMPACT OF SURVEILLANCE RESEARCH

Surveillance research is a necessary and integral component of a complete tobacco research portfolio.

Much of the research recommended in this report could not be carried out without a comprehensive surveillance system. By providing the critical information needed to understand tobacco-use behaviors and evaluate all aspects of tobacco-control interventions in community settings, a comprehensive, coordinated, and specialized tobacco-control surveillance research program would promote and enable development of a more comprehensive, stronger, lasting, and effective tobacco-control program.

Excise Tax Rate Per Pack of Cigarettes: Sample State Cancer Legislative Database Data



Tobacco-related cancers exact an enormous toll in the United States and worldwide. The NCI's commitment to tobacco-related research should be commensurate with the health burden caused by tobacco use. There is now an unprecedented opportunity to accelerate groundbreaking research that can prevent cancer associated with tobacco use. This report reflects the consensus of leading scientists and experts regarding tobacco-related research priorities. It embodies a comprehensive set of research opportunities with nine overarching research priorities. These opportunities cover the range of tobacco control research from basic biological and basic biobehavioral research to clinical, policy, epidemiologic, and surveillance research, as well as support for research infrastructure. The research priorities presented in this report also emphasize the unique opportunities and challenges of tobacco initiation, use, addiction, and cessation among youth and populations at disproportionate risk. It was the unanimous and fundamental conclusion of the Tobacco Research Implementation Group that an unequivocal commitment of the NCI to a comprehensive, focused program of research on tobacco use can help to reverse the epidemic of tobacco-related cancers.

**The National Cancer Institute
Tobacco Research Implementation Plan
Board of Scientific Advisors (BSA) Review of Special
Initiatives for Fiscal Years 1999 and 2000**

Initiative	Date to BSA
Transdisciplinary research centers	11/98
State and community research	11/98
Research on the treatment of nicotine addiction	1999/2000
Expanded surveillance research	1999/2000
Epidemiologic studies	1999/2000
Basic biobehavioral research	1999/2000

INTRODUCTION

The National Cancer Institute (NCI) established the Tobacco Research Implementation Group (TRIG) in 1998 to assist the Institute in formulating a Tobacco Research Implementation Plan (TRIP). The TRIG, consisting of NCI and non-NCI scientists, was established to examine the NCI's extramural research portfolio in tobacco and identify priorities for tobacco-related research for the next 5-7 years.

METHODS

An initial analysis of the Fiscal Year 1997 NCI research portfolio of tobacco-related research was prepared by the NCI members of the TRIG. This initial analysis organized the FY97 research portfolio into eight research categories, and within these primary categories, into a varying number of subcategories. Following deliberation by the full TRIG, a ninth category was added to the analysis. Research categories are presented in the following section. Research on the treatment of tobacco-related diseases, such as lung cancer, was specifically excluded from this analysis.

The first step in the analysis was to identify all intramural and extramural research and training grants and contracts that received funding in FY97 and addressed tobacco-related issues. Searching the NCI's Research Analysis and Evaluation Branch (RAEB) database of grants and contracts identified all NCI extramural research projects. All projects that were coded as tobacco-related and were active in FY97 were identified for the analysis. Training grants and intramural research projects were identified

by reviewing internal grant files and tracking databases. Only research projects involving greater than 10 percent relevance to tobacco were included in the analysis. Only the portion of the research budget reflecting the relative percent of the project that focused on tobacco issues was included in financial calculations. Projects that did not have an associated budget, such as those completing research under a no-cost extension, were excluded from the analysis. The RAEB search was compared to a search of the NIH CRISP database to ensure that all projects had been identified.

Once the projects to be included in the analysis had been identified, a single reviewer categorized all projects. Each project was assigned to only one category based on the primary hypothesis of study. Area experts then reviewed these category assignments. Discrepancies were resolved across reviewers and appropriate refinements to category definitions were made.

The categories used for the analysis represent research in the current portfolio and may not represent all of the important issues that might or should be addressed in the future. The NCI portfolio primarily includes tobacco-related issues as they relate to cancer. Additional research addressing the basic biology of drug dependence and tobacco-related heart disease are addressed by other NIH institutes, such as the National Institute of Drug Abuse (NIDA) and the National Heart Lung and Blood Institute (NHLBI), and these are not included in this analysis.

TOBACCO RESEARCH CATEGORIES

Each tobacco research project was assigned to one of nine tobacco research categories and associated sub-categories. These categories and the criteria for assignment include:

Basic Biobehavioral Research

Research studies that assess basic principles of behavior, including basic laboratory research as well as research directed at individuals, and seeking to develop and test behavioral models of action.

Behavioral/Biological Associations – Studies to assess the basic relationships between biological and behavioral factors and/or their potential relationship to tobacco-use prevention and cessation interventions.

Behavioral Mechanisms – Studies to identify behavioral and social factors that influence tobacco-use behaviors and studies to develop and test specific interventions aimed at changing tobacco-related behaviors.

Prevention Research

Studies to develop and test interventions that are designed to prevent the initiation of tobacco use among individuals.

Treatment of Nicotine Dependence

Research studies that assess the clinical treatment of individuals for nicotine dependence. The specific focus of treatment interventions is the individual in clinical and physician-based settings.

Pharmacological Treatments – Studies to identify and test pharmacological interventions, such as nicotine replacement, specifically for the treatment of physiological addiction to nicotine.

Behavioral Treatments – Studies to develop and test behavioral interventions specifically for the treatment of physiological addiction to nicotine that involve health care providers as well as studies directed at behavioral interventions among health care providers and in medical practice settings.

Self-help Treatments – Studies to develop and test interventions directed at individuals that do not involve face-to-face interaction with a health care provider or tobacco control counselor, such as self-help and telephone counseling.

Combined Pharmacological/Behavioral Treatments – Studies to identify and test combined pharmacological and behavioral interventions, such as the combined use of nicotine replacement and biofeedback, specifically for the treatment of physiological addiction to nicotine.

Community and State Intervention Research

Research studies that test group and population-based interventions and the dissemination of group and population-based interventions to prevent and reduce tobacco use.

Prevention Research – Studies to test and implement interventions among groups of individuals that are designed to prevent the initiation of tobacco use.

Cessation Research – Studies to test and implement interventions among groups of individuals that are designed to stop current use of tobacco.

Combined Prevention/Cessation Research – Studies to test and implement interventions among groups of individuals that are designed to both prevent the initiation of tobacco use and stop current tobacco use.

Policy Research

Research studies that assess the effect of policies, including worksite, community, state and Federal policies, on tobacco initiation and use.

Basic Biological Research

Laboratory-based research studies that assess the effects of tobacco and tobacco products on cell biology and cellular mechanisms of action, including the role of tobacco and tobacco byproducts in the initiation and promotion of cancer and the biological and health effects of exposures to tobacco.

Genetics – Studies that seek to identify genes that are related to the tobacco-induced carcinogenic process or that can conceivably be related to cancer risk associated with tobacco use. These include the identification of genetic susceptibility genes associated with tobacco-induced carcinogenesis or tobacco addiction. They do not include those genes being studied in the context of an epidemiological investigation.

Carcinogenesis – Studies to assess the role of tobacco and tobacco byproducts in DNA damage, carcinogen metabolism, and carcinogenesis and/or studies seeking to identify biomarkers as indicators of DNA damage or carcinogenesis.

Animal Models – Studies that seek to identify or that use animals as models of the biologic and/or carcinogenic effects of tobacco and tobacco byproducts.

Epidemiology

Population-based research studies that assess associations between tobacco use, behavioral and biological factors, and cancer.

Descriptive Epidemiology – Population and patient-based studies that describe trends and associations between risk factors, tobacco, and cancer.

Molecular Epidemiology – Population and patient-based studies that assess trends and associations between molecular and genetic factors, tobacco, and cancer.

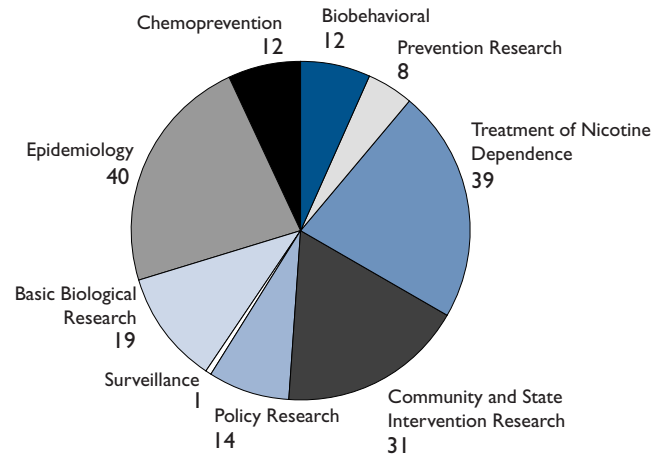
Surveillance

Research studies that assess trends in tobacco-related risk factors, behaviors and health services to determine changes over time and the influence of these trends on cancer incidence, morbidity, mortality and survival.

Chemoprevention

Studies that assess the administration of specific chemicals and/or dietary modifications to reverse or suppress the carcinogenic effects of tobacco and prevent the development of invasive cancer.

Number of Projects by Research Category



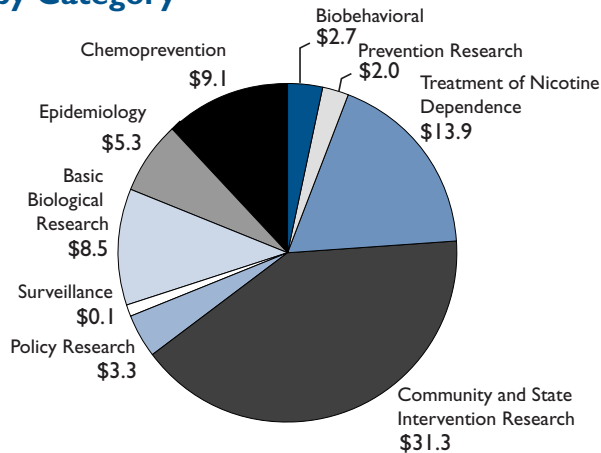
RESULTS

The tobacco research portfolio analysis revealed support for a wide spectrum of tobacco-related research. The NCI supported 176 research projects across both intramural and extramural divisions, excluding projects with 10 percent or less relevance to tobacco. The total FY97 annual budget for tobacco-related research was \$76.2 million.

As shown in the figure above, epidemiology, treatment of tobacco addiction, and community and state intervention research accounted for the largest number of research projects, about 20 percent each of the tobacco research portfolio funded by the NCI. In contrast, only one tobacco-related surveillance project was funded in FY97.

This picture differed when assessed by the allocation of funding. Community and state intervention research accounted for more than 40 percent of the FY97 funds for tobacco-related research. Research on the treatment of tobacco addiction, which represented the next largest allocation of funds, accounted for 18 percent of the funds expended. This proportion was roughly comparable to the proportion of projects addressing treatment of nicotine dependence. When assessed either by the number of projects or the amount of funding, biobehavioral, prevention and policy research each accounted for less than 10 percent of the tobacco portfolio. Tobacco-related surveillance was the most under supported area of tobacco research in 1997.

Amount of Funding for Tobacco Research by Category



The tobacco research portfolio also was evaluated in terms of the funding mechanisms used to support tobacco research. Fifteen different types of funding mechanisms were used to support tobacco research. The most frequently used funding mechanism was the R01 research grant; 48 percent of the tobacco-related research projects were supported by R01s. This mechanism also accounted for a large proportion of the total tobacco funding, with 36 percent of tobacco-related research dollars being provided to investigators through the R01 mechanism. Thirty-five percent of funds supported research through contracts (N01). These two mechanisms (R01 and N01) combined accounted for almost 70 percent of the tobacco research funding.

CONCLUSIONS

The tobacco research portfolio analysis revealed support for a broad spectrum of tobacco-related research. Proportional to tobacco's cancer burden, however, tobacco research reflects a disproportionately small portion of the NCI

budget. While tobacco use accounts for almost 30 percent of cancer deaths, the total annual budget for tobacco-related research represents only 3 percent of the NCI budget.

This analysis reflects current tobacco research priorities. Current research priorities focus on community and state interventions, treatment of nicotine addiction and epidemiological investigations. Biobehavioral, prevention and policy research on the other hand, appear under-emphasized, and tobacco surveillance research receives almost no attention.

The analysis provides a clear picture of current tobacco research across topic areas and the distribution of funding across projects and mechanisms. It provides a strong foundation from which research priorities for the next 5–7 years can be established.

Number of Tobacco Research Projects by Funding Mechanism

