Tobacco Control Research Priorities for the Next Decade:

Working Group Recommendations for 2016 - 2025

Report to the NCI Board of Scientific Advisors

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Introduction

Background

After a century of tobacco-caused cancer morbidity and mortality in the United States, the elimination of tobacco use and its unequaled harms is now within our grasp. Achieving this goal will require significant scientific progress, including advances led by the National Cancer Institute's (NCI) Tobacco Control Research Branch. New and innovative research is necessary to confront – both directly and swiftly - the remaining factors that are responsible for the continued use of tobacco in America. These factors include a changing population of users, evolving patterns of initiation and use, new and modified tobacco products, and a complex and changing policy environment. This report highlights key tobacco control research priorities for the next decade that will advance progress towards our national goal of ending the tobacco epidemic. NCI's Tobacco Control Research Branch has tremendous potential to contribute substantially to that goal.

Tobacco and Cancer

For more than half a century, cigarette smoking has been the leading cause of cancer mortality in the United States. As reported in the American Cancer Society's Cancer Facts and Figures[1], about 171,000 of the estimated 589,430 cancer deaths in the U.S. in 2015, including almost all deaths from lung cancer, will be caused by tobacco smoking, our nation's leading cause of cancer mortality. Eliminating smoking in America would, over time, eliminate almost one-third of all cancer deaths. Additionally, the 2014 Surgeon General's Report summarized the health consequences of persistent smoking for individuals diagnosed with cancer (i.e., increased toxicity and poor cancer treatment response, increased risk for disease recurrence and second primary cancers, increased all cause and cancer specific mortality)[2]. There is no other single public health action that can have such a substantial impact on reducing cancer morbidity and mortality in our country.

The Changing Epidemiology of Tobacco Use in the U.S.

Rates of smoking in the United States have fallen dramatically over the last 50 years. In the late 1950s and early 1960s, smoking prevalence peaked in the U.S., with about 43% of all adults smoking. Today, smoking prevalence is down substantially, to approximately 17% of the adult population. Several notable advances in tobacco control have contributed to this decline, including: communications regarding the health effects of smoking following the landmark 1964 Surgeon General's Report; efforts to prevent children from initiating tobacco use; the engagement of healthcare providers and systems in tobacco cessation efforts, including the development and dissemination of evidence-based clinical practice treatment guidelines to help current smokers to quit; expanded insurance coverage for tobacco dependence treatments resulting from the Affordable Care Act, Medicaid coverage mandates, and other legislative and regulatory requirements; changes in social norms that have decreased the acceptability of smoking; policy interventions including excise tax increases and clean indoor air policies; increased knowledge of the product development and marketing practices of tobacco companies through public disclosure of industry documents and analyses; and restrictions placed on the tobacco industry's marketing and promotional tactics including the Master Settlement Agreement between the State Attorneys General and tobacco companies in 1998.

Facilitating much of this progress has been a robust set of scientific advances that arose from research funded by the NCI's Tobacco Control Research Branch, and others. Yet, more than 40 million individuals in the United States still report that they currently smoke. As a result, tobacco use continues to kill almost half a million Americans each year, highlighting the urgent need for research advances to further reduce smoking prevalence in this country. Achieving the goal of eliminating tobacco use and its harms requires new science and its effective translation.

The demographic and psychosocial characteristics of tobacco users have also changed markedly over the last 50 years, with tobacco use moving from an equal opportunity killer to one concentrated within subpopulations of our society. This evolution has created an epidemiologic imperative requiring the development of science-based prevention, treatment, and policy interventions for high risk groups who have been left behind – groups that disproportionately bear the burdens of cancer and other health consequences of continued tobacco use. The poor, those with the least education, those with mental health and substance abuse comorbidities, the LGBT community, members of the military and veterans, and certain racial and ethnic groups smoke at significantly higher rates and/or experience markedly higher rates of tobacco-caused illness and death. Finally, the tobacco product landscape and patterns of use have also changed over the last 50 years, with the evolution of poly-tobacco use and the emergence of new classes of tobacco products including electronic nicotine delivery systems (ENDS) such as e-cigarettes and e-cigars, and so-called modified risk products.

The grim statistics regarding continued tobacco use reveal that half of all smokers alive today (about 20 million Americans) will die prematurely of a disease directly caused by their smoking if they do not quit. If we are to end the tobacco epidemic in the United States, we must focus increased attention on populations left behind.

The Working Group on Tobacco Control Research Priorities for the Next Decade

In 2015, Dr. Doug Lowy, Acting Director of the National Cancer Institute (NCI), established the Tobacco Control Research Priorities Working Group to recommend research priorities for the NCI's Tobacco Control Research Branch for the next 10 years (from 2016 to 2025). The charge to this working group was to identify and highlight tobacco control research priorities that NCI is particularly well positioned to address over the next decade, emphasizing priorities that have the greatest potential to help end the tobacco epidemic and the cancers it causes. The working group was asked to exclude two areas of research that will be addressed by NCI apart from this report - international tobacco control research efforts and regulatory tobacco control research that might be addressed by the Food and Drug Administration's Center for Tobacco Products.

The working group met in-person on two occasions as they prepared their report and finalized their work collaboratively and electronically. In an effort to ensure that the recommendations would complement research efforts by other agencies and groups, the working group invited other public and non-profit research funders and tobacco control stakeholders including the National Institute on Drug Abuse, the Food and Drug Administration, the Centers for Disease Control and Prevention Office on Smoking and Health, the Truth Initiative (formerly the American Legacy Foundation), and the Campaign for Tobacco Free Kids, to report on their areas of focus for current and future tobacco control research funding.

The working group identified seven priority areas (Table 1) with great potential to further the goal of eliminating tobacco use and its harms, particularly cancer harms. These seven research priority areas were designed to be broad, with some overlap across them. All seven were viewed by the working group as equally important; their ordering does not reflect any judgments regarding their importance or priority. The working group recognized that these recommendations would serve as just one component of a larger review by NCI of research priority initiatives of the Tobacco Control Research Branch for the next decade.

In addition to the seven priority topics, the working group identified cross-cutting research infrastructure needs that would help to accelerate research progress. These included: a) the potential development of a clinical trials network or infrastructure to facilitate innovative, collaborative research efforts; and, b) suggestions to overcome key barriers to research success such as the need to enhance recruitment of special populations; the need for more rapid funding mechanisms to support important, emergent research initiatives in a timely manner such as research directed at evaluating the impact of novel product, policy, and regulatory changes; and the need to encourage more pragmatic and innovative methods in study design. A clinical trials network, in which cross-institutional agreements could be reached to help facilitate study start-up, cross-site IRB agreements, and shared recruitment efforts could help ensure success of trials when larger and more diverse participant samples are needed.

Summary

Eliminating tobacco use and its harms from the United States is now an achievable goal. But realizing that goal requires new scientific advances. NCI and its Tobacco Control Research Branch are central to developing the requisite science. The Tobacco Control Research Branch has a long history of supporting seminal scientific work that has advanced tobacco control, including advances in behavioral science relevant to tobacco use; treatment development and delivery; policy, system, and environmental changes; and public health interventions. The Branch is eminently well positioned to support future advances. This report is designed to aid the Tobacco Control Research Branch as it develops its research priorities for the next decade.

Table 1: Seven Tobacco Control Research Priorities

1 Optimize intervention effectiveness by increasing the reach, demand, quality, dissemination, implementation, and sustainability of tobacco use treatment

2 Reduce adolescent and young adult tobacco use

3 Address disparities in tobacco use and its harms

4 Understand the complexity of current tobacco products, patterns of use, and associated health-related outcomes

5 Develop novel behavioral interventions for tobacco use

6 Use a chronic disease approach to address smoking behavior across all its developmental phases, including studies of motivation and precessation, cessation and adherence, and relapse and recovery

7 Identify innovative policy and macro-environmental approaches that further reduce tobacco use

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Overview

Since the publication of the first Surgeon General's Report over 50 years ago, substantial progress has been made in reducing the prevalence of cigarette smoking and its resulting harms. Yet, much remains to be done: more than 40 million Americans continue to smoke; almost 500,000 deaths each year are directly attributable to smoking; and, tobacco use remains responsible for one-third of all cancer deaths in the US. The tobacco product landscape, characteristics of tobacco users, and the macro-environmental influences on tobacco use have all changed dramatically over recent years. These changes create new challenges and opportunities if we are to achieve the promise of the 50th Anniversary Surgeon General's Report – to end the tobacco epidemic and its resultant harms. The National Cancer Institute and its Tobacco Control Research Branch is uniquely positioned to advance this national goal. The next decade provides an opportunity to address remaining key research gaps and priorities by:

1. *Optimizing intervention effectiveness.* Intervention impact can be improved through research that addresses ways to increase the reach, demand, quality, dissemination, implementation and sustainability of evidence-based tobacco use treatment.

2. *Reducing adolescent and young adult tobacco use.* Adolescents and young adults face a heightened developmental vulnerability to tobacco use initiation and dependence. Their vulnerability is also likely affected by societal changes and changes in the tobacco product landscape, the types of tobacco products that are available and policies related to them. Research is needed that informs and reflects such changes, that improves our understanding of the heightened vulnerabilities of these populations, and that yields strategies for preventing their development of tobacco use and dependence.

3. *Addressing disparities in tobacco use and its harms.* Disparities in tobacco use prevalence and its harms have increased dramatically over the last 50 years, with tobacco use and its effects now concentrated in specific subgroups of tobacco users. Research is needed that more directly targets and improves treatment reach and effectiveness among populations with high prevalence and/or intensity of use or who suffer disparate outcomes from tobacco use.

4. *Understanding the complexity of current tobacco products, patterns of use, and associated health-related outcomes.* Significant changes have occurred both in the tobacco product landscape and in patterns of tobacco use over the last decade including: wide-scale marketing and use of non-cigarette tobacco products; reductions in the heaviness and frequency of cigarette smoking among many users; and, marked increases in users reporting use of more than one tobacco product (i.e., poly-tobacco product use). Little is known about the implications of these changes, and few interventions have addressed the complexity of these products and patterns. Research is needed to better understand these changing tobacco use products and patterns, their short and long-term effects on cancer and other health risks, and how they impact the broader goal of eliminating tobacco use and its harms.

5. *Developing novel behavioral interventions for tobacco use.* Treatment effectiveness may be accelerated by: a) developing novel behavioral targets and approaches to cessation and b) using more innovative research methods that enable more efficient and informative study (e.g.: screening of treatment components, evaluation of delivery algorithms and strategies, investigation of mechanisms of treatment effects).

6. *Using a chronic disease approach to address smoking across all of its developmental phases.* To date, most treatment research has focused on the relatively small proportion of smokers who are ready to quit and engage in treatment at a particular point in time. To engage more smokers in effective treatment and further reduce smoking prevalence, novel approaches are needed that recognize the many transitions of tobacco use, including research that addresses all phases of cessation from motivation through relapse and post-relapse recovery.

7. *Identifying innovative policy approaches that further reduce tobacco use.* Multiple tobacco control policy approaches (e.g., tax increases, clean indoor air policies) have been shown to reduce tobacco use at the population level. However, innovative policy and environmental approaches are needed, especially ones that are integrated with and complement existing resources such as prevention or cessation resources (e.g., via healthcare systems; state, federal, and private health insurance coverage expansions; quit-lines; community resources). Research is needed to identify innovative local, state, federal, and private sector policy approaches that will advance the goal of eliminating tobacco use and its resultant harms, as well as effective strategies to more completely disseminate these approaches.

Optimize Intervention Effectiveness by Increasing the Reach, Demand, Quality, Dissemination, Implementation, and Sustainability of Tobacco Use Treatment

There is a consensus that evidence-based smoking treatments have yielded disappointingly low rates of tobacco abstinence when they are used in real world settings[3]. While the science of tobacco use treatment has advanced substantially over the past few decades[4], the bulk of this research has been conducted in efficacy contexts, often with populations that do not reflect the current demographics of tobacco users. As health systems and researchers have endeavored to translate the medication and counseling treatments validated in efficacy research into real world settings and populations (e.g., primary care), they have found that these treatments have shown disappointing impact due to reduced effectiveness, low rates of patient demand, limited reach, variable treatment fidelity and other dissemination and implementation challenges[5]. Thus, there is a clear need to optimize interventions and intervention delivery strategies that enhance the effectiveness and reach of tobacco interventions so that they produce larger reductions in population-based rates of tobacco cessation.

Evidence-based treatments often fail to reach their full potential because of incomplete translation at multiple points along the treatment delivery continuum; research is needed to address this incomplete translation[6]. Knowledge gaps include the need for improved methods for: a) extending or offering evidence-based tobacco use treatments to broader, higher prevalence populations (e.g., low socioeconomic status [SES] populations, individuals with mental health/substance abuse diagnoses); b) increasing smoker demand for evidence-based treatments (identifying and addressing treatment engagement barriers such as limited access to treatments, smokers' concerns about the effectiveness/safety of pharmacotherapy, or doubts about their ability to quit); c) expanding the reach of effective treatments (the proportion of a target population that receives treatment); d) improving treatment delivery, implementation, and sustainability (e.g., increasing the offer of both combination pharmacotherapy and behavioral approaches; extending treatment duration; improving implementation); e) "institutionalizing" or creating system-wide integration of evidence-based treatments into healthcare; f) expanding the context of treatment and treatment delivery mechanisms beyond those available via traditional healthcare settings, including into nontraditional settings where populations with a higher prevalence of tobacco users can be found; and, g) leveraging technological advances (e.g., electronic health records [EHR], eHealth, mHealth) as means of expanding the population-wide reach of evidence-based treatments. Improving the successful translation of evidence-based treatment (i.e., its reach, demand, and quality) at all points along the delivery continuum may substantially increase population quit rates.

Research needed to address these knowledge gaps includes:

1. Evidence-based treatments for tobacco use exist, yet their uptake by smokers has been modest. What innovative health system and population-wide approaches can increase both the *demand for (by smokers and systems) and reach of* existing evidence-based treatments?

2. Health systems have failed to adopt, integrate, and sustain the delivery of evidence-based tobacco use treatments. What models of care *will improve the implementation quality and*

sustainability of evidence-based tobacco use treatment across the various components of multi-level health systems (e.g., organizational, provider team and provider type, individual clinician)? What are effective strategies to improve provider adherence to clinical practice guidelines? Can patient navigators or tobacco treatment specialists enhance treatment use and effects?

3. How can *an expanded array of healthcare settings* that often serve populations with high smoking prevalence and tobacco smoke exposure rates (e.g., urgent care centers, emergency departments, mental health and substance abuse treatment centers, cancer care settings, lung cancer screening sites, dental practices, pharmacies) be configured to spur demand for effective tobacco use treatment, and also expand its reach and adoption?

4. How can *community-based non-healthcare infrastructures* that serve populations with high smoking prevalence and tobacco smoke exposure (e.g., food banks, employment agencies, homeless shelters, community agencies serving the poor, 211/311 call-in centers, Women, Infants, and Children (WIC) clinics, Head Start Centers, casinos) be used to disseminate evidence-based smoking treatments effectively. In particular, what implementation, support resources, and treatments are appropriate and effective in such venues?

5. How can we improve the *interoperability* of smoking cessation resources (i.e., communication across different treatment delivery entities) to enhance their impact and reach, with a goal of providing more consistent, clinically-effective, and cost-effective evidence-based tobacco interventions (e.g., across different: clinics and healthcare systems; EHR systems; quit line vendors; pharmacies; community mental health/substance abuse centers; and, eHealth and mHealth platforms)?

6. How can new *legislative and regulatory mandates* (e.g., provisions of the Affordable Care Act, Meaningful Use requirements, and Joint Commission Hospital Tobacco Cessation measures) be used to increase the rates of delivery of tobacco use treatment in healthcare settings (e.g., both via incentives and penalties)?

7. How can mobile and emerging technology (eHealth, mHealth, social media, short message service (SMS), interactive voice recording [IVR], virtual social networks) strategies and resources be used to increase the demand and reach of evidence-based treatments in the general population, and amongst higher prevalence populations (e.g., lower income, lower educated individuals) in particular?

8. Meaningful Use legislation (2009 Health Information Technology for Economic and Clinical Health [HITECH] Act) has led to the rapid, widespread adoption of electronic health record (EHR) technology across healthcare systems nationwide. How can *EHR advances* (e.g., systematic collection of patient information) and capacities (e.g., smoker registries, patient accessible portals) be used to increase the demand for, recruitment into, and reach of, tobacco use interventions?

9. Cost-effectiveness and cost-per-quit of tobacco use treatment have not been extensively examined in real world settings. How can *advanced economic analysis* of tobacco use interventions guide the selection and implementation of treatment, accounting for various factors including effectiveness, demand, and reach? How can 'big data' address these goals?

Research Priority 2

Reduce Adolescent and Young Adult Tobacco Use

The prevalence of cigarette smoking among adolescents has declined significantly over the last few years; 9.2% of high school students reported using cigarettes in the past 30 days in 2014 compared to 15.5% in 2011[7]. However, the percentage of high school students using *any* tobacco product in the past month remains high (24.6% in 2014[7]), reflecting the increasing diversity of tobacco product use among adolescents. In addition, a growing percentage of young adults initiate tobacco use after age 18 and escalate that use both in frequency and intensity during the young adult years[2]. Adolescent and young adult tobacco use is further complicated by the variety of tobacco use patterns, including intermittent, non-daily use, lower intensity use and poly-tobacco use (the use of multiple tobacco products)[2]. The probability of developing nicotine dependence and tobacco-related diseases increases with younger initiation and longer use[2]. These findings highlight the need for new approaches to reduce tobacco use during adolescence and the young adult years.

Traditional approaches to both prevention and cessation may have limited fit and reach for current adolescent and young adult tobacco users, given their nontraditional tobacco use patterns as well as the changing demographics of users. Adolescents who smoke, for example, may be more socially disadvantaged (lower socioeconomic backgrounds) than in previous decades and the social stigmatization of cigarette smoking may isolate these youth more[8]. In addition, given the later age of initiation of tobacco use, prevention approaches that go beyond traditional school-based programming are needed. Few tobacco prevention and cessation interventions have addressed multiple product use or the variety of tobacco products used (including hookah, cigars, e-cigarettes, etc.). Tobacco cessation among both adolescents and young adults continues to be challenging, given that most adolescents and young adults want to quit without formal assistance, and relatively few use evidence-based approaches[9]. In addition, compared to adults, rates of cessation among adolescents are low[10]. In addition, compared to the adult evidence base, there are comparatively few well-designed and well-powered cessation trials for adolescent smokers, and an especially scant evidence-base for pharmacotherapy with adolescents[11].

Research is needed to expand traditional prevention and cessation approaches and venues to address these new patterns of tobacco use among adolescents and young adults and to further improve success rates. In addition, research gaps exist about how the rapidly changing tobacco product landscape, as well as current marketing and mass media messages, influence adolescent and young adult tobacco use. Reducing tobacco use during these key developmental periods will help to prevent the development of tobacco dependence and enhance long-term abstinence.

Research needed to address these knowledge gaps includes:

1. The development of innovative interventions that target tobacco users after their initial trials with tobacco and while they are at low, occasional levels of use. What novel interventions can be used to reduce tobacco use, considering the diversity of tobacco products, in adolescent and young adult beginning smokers, while they are using tobacco at low frequency and intensity? What are effective approaches for reducing tobacco use escalation among initial or early users? Do "stealth" interventions (i.e., those that target other behaviors but also may affect tobacco

use, such as physical activity or mood regulation) reduce tobacco use in adolescents and young adults?

2. Success rates need to be improved for adolescent cessation treatments, and treatments need to reach more disadvantaged youth. What innovative approaches, beyond cognitive-behavioral group-based treatments, can improve cessation rates among adolescent smokers? For example, can targeting non-tobacco related mechanisms, such as executive cognitive skills training or positive affect enhancement, increase success rates? How can evidence-based interventions be delivered to adolescents cost-effectively, especially those who may be more socioeconomically disadvantaged, to improve access and reach?

3. Rates of uptake of cessation interventions continue to be low for young adult smokers, especially among non-daily smokers and light smokers. What approaches can be used to increase young adult smokers' motivation to use and access evidence-based treatments? How can social media platforms best be used to decrease the appeal, discourage the use, and encourage the cessation of tobacco products among adolescents and young adults?

4. An increasing proportion of adolescent and young adult tobacco use is of non-cigarette tobacco products (e.g., hookah, little cigars). What interventions discourage experimentation/initiation and increase cessation of these tobacco products among adolescents and young adults?

5. Tobacco use among adolescents and young adults is often concurrent with marijuana use. How do concurrent patterns of marijuana and tobacco use, considering their temporal ordering and contingency (e.g., simultaneous use such as blunts, sequential but temporally related use) and types of tobacco products, influence patterns of tobacco use, including tobacco cessation and reduction? How do state policy changes and variability in marijuana legalization status affect adolescent tobacco use?

6. Social and mobile media hold promise for reaching adolescents and young adults for tobacco prevention and cessation efforts. How can social media platforms best be used to decrease the appeal, discourage the use, and encourage the cessation of tobacco products among adolescents and young adults? How does exposure to, and active engagement with, social media and tobacco-related messages and context influence tobacco-related attitudes, cognitions, and behaviors among adolescents and young adults? How can gamification principles be used to improve intervention efficacy with adolescents and young adults?

7. Several states and localities are considering raising the minimum age of purchase of tobacco products. How does the implementation of such policies influence patterns of use, attitudes about tobacco, and social norms related to tobacco use among adolescents and young adults?

8. Family norms and behaviors remain a primary influence on adolescent tobacco use. Yet parental approaches to helping reduce adolescents' risk for tobacco use are not well understood, particularly during the transitional period from adolescence to young adulthood. What intergenerational factors increase or reduce the risk of tobacco use? How can more parents become tobacco free themselves and, regardless of their own tobacco use status, be

more effective at reducing the risk of tobacco use among their adolescent and young adult children?

Research Priority 3

Address Disparities in Tobacco Use and Its Harms

Rates of tobacco use and its resultant morbidity and mortality are disproportionately distributed among several subpopulation groups within the U.S. While the most significant disparities are observed among smokers of low socioeconomic status and those with comorbid mental health or substance abuse diagnoses[2,12], inequities are also pervasive in other populations including racial/ethnic minorities, individuals with physical disabilities, LGBT, veterans/military[12], and criminal justice populations[12-16]. The harms of tobacco use within these vulnerable populations are often heightened by their decreased access to tobacco treatment and/or their poorer treatment response[17,18], and their exposure to other health related risk factors. Reasons for tobacco-related health disparities may vary by subpopulation groups[19].

Despite a large and growing body of evidence that has identified inequalities in tobacco use rates and outcomes, relatively little is known about how to best address these disparities, including the need to evaluate innovative treatment methods for targeting and tailoring interventions for vulnerable individuals and communities[20]. In addition, there is a need to identify and implement tobacco control policies that reduce or eliminate tobacco-related inequalities. Research targets include: innovative strategies that reach vulnerable populations with high tobacco prevalence; provision of interventions in novel settings that serve large numbers of vulnerable individuals (e.g., community, health care, and social service environments); greater insight into population-specific differences in tobacco use and motivations; greater knowledge regarding barriers to resources for tobacco reduction and cessation (e.g., built environmental factors); and increased knowledge regarding the effects of policy approaches to increase intervention reach and effectiveness that are targeted for such vulnerable populations. Novel approaches to addressing the multiple contributors to tobacco-related disparities are likely to be needed in order to realize substantial breakthroughs in this area.

Research needed to address these knowledge gaps includes:

1. What strategies can increase the uptake of evidence-based treatments in vulnerable populations? What theoretical frameworks, including novel approaches from a broad variety of disciplines, can be used to guide the development of evidence-based interventions to enhance their accessibility, appeal, and uptake in vulnerable populations? What is the most effective intensity of tobacco cessation interventions for various vulnerable populations? What population-specific leverage points might enhance intervention accessibility, appeal, and uptake? Attention to barriers to treatment, including beliefs, resources, and motivational barriers, is of particular importance.

2. What theoretical approaches can help guide the development and testing of novel, multi-level interventions (e.g., clinical, policy, community) to reduce the use of tobacco products in vulnerable populations?

3. Does the targeting and tailoring of interventions for tobacco prevention and cessation for vulnerable populations enhance their effectiveness, and if so, what are the most important factors on which to base tailoring?

4. How do health insurance tobacco cessation coverage policies, including Medicaid policies, influence access to and utilization of evidence-based tobacco dependence treatments by disparate populations?

5. What subgroup features, including nature of tobacco use, are useful in understanding disparities in tobacco use initiation, prevalence and cessation outcomes in vulnerable populations? How do contextual and social factors influence tobacco use and cessation in populations with tobacco-related health disparities?

6. How can social media and social network interventions be used to reduce tobacco use in vulnerable subpopulations?

7. What is the role of the built environment (e.g., tobacco outlet density point-of-sale tobacco advertising) in promoting the use of tobacco products in low SES and other vulnerable communities? What interventions might mitigate the effects of the built environment in promoting tobacco use initiation and undermining cessation efforts?

8. What is the validity and utility of measures used to assess tobacco use and dependence, screening, use behaviors, and motivation in disparate populations? Do subpopulation differences in cognitions and attitudes, types of tobacco product use, or patterns of tobacco use behavior account for differences in validity and utility of measures?

Research Priority 4

Understand the Complexity of Current Tobacco Products, Patterns of Use, and Associated Health-Related Outcomes

Patterns of tobacco use have changed considerably over time. For much of the 20th century, cigarette smoking was primarily defined as a daily pattern of use. However, in the early 1990s, non-daily cigarette smoking emerged as a stable pattern of use, and the proportion of non-daily cigarette smokers increased. By 2013, nearly 1 in 4 current cigarette smokers were non-daily users. The proportion of daily smokers who report that they are light smokers (defined as smoking fewer than 5 to 10 cigarettes per day) has also increased markedly over the last few decades[2]. Furthermore, in the context of declining cigarette use, consumption of other tobacco products, including moist snuff, cigars, and pipe/roll-your-own tobacco has increased over the past decade[2,21,22]. New and emerging tobacco products, like hookah and electronic cigarettes, have also diffused rapidly in the U.S. Finally, poly-tobacco use (i.e., current use of more than one tobacco product) is increasingly common in the U.S., particularly among adolescents and young adults. Preliminary data from the Population Assessment of Tobacco and Health (PATH) study suggest that approximately 40% of adolescent (12-17 years old) and adult tobacco users currently use more than one tobacco product[23].

The 50th anniversary edition of the first Surgeon General's Report clearly highlighted the increasing complexity of modern tobacco use behaviors, like intermittent cigarette smoking, use of non-cigarette tobacco products, and concurrent use of multiple tobacco products. Moreover, today's tobacco marketplace is more diverse than ever, with a wide array of products available to consumers. We know relatively little about the social, behavioral, and environmental factors that influence emerging patterns of tobacco use. Despite recognition of these changing patterns, there are limited data to inform treatment, communication, and policy strategies related to these newer patterns. Reducing tobacco-caused morbidity and mortality including reducing the rates of tobacco-caused cancer will require increased attention to these changing patterns of tobacco use.

Research needed to address these knowledge gaps includes:

1. What are the most common transition patterns among poly-tobacco users and the poly-use behaviors (e.g., mix of product use, heaviness of use of the different products) associated with cessation or continued tobacco use? Is poly-tobacco use a step toward quitting combustible tobacco, a barrier to cessation, and/or a stable behavior pattern? What are the determinants of these different outcomes? Under what conditions might non-cigarette tobacco products be a barrier to tobacco cessation and for whom? Under what conditions might non-cigarette tobacco products be used to help tobacco users quit combusted tobacco products and for whom?

2. What is the impact, if any, of non-cigarette tobacco products on youth initiation trajectories?

3. The concept of tobacco and nicotine dependence is not well understood and assessed for non-cigarette and poly-tobacco users. Methodological advances and innovative approaches are needed to quantify dependence among different forms of tobacco users and poly-tobacco users. What defines dependence for non-cigarette tobacco users and poly-tobacco users and how can this be measured? To what extent can a single dependence measure be used? Or, are product-specific measures required?

4. Many adverse health outcomes from tobacco use may take many years to develop. What surrogate measures or biomarkers can provide timely assessment of the potential health risks from emerging patterns of different forms of tobacco use? Which patterns of tobacco use are most likely to lead to harm? What are the cancer outcomes and other health-related consequences of poly-tobacco use?

5. Few data exist on the generalizability of evidence-based tobacco treatment for complex patterns of tobacco use and how tobacco treatment may need to be adapted to address emerging patterns of tobacco use. What are the best screening questions to use in clinical settings to identify non-cigarette and poly-tobacco use? How can non-cigarette and poly-tobacco users be motivated to reduce all tobacco use? Which pharmacologic treatments, if any, are best for non-daily smokers, light smokers, non-cigarette tobacco users and/or poly-tobacco users?

6.   How do policy level factors at the local, state, and national levels (e.g., taxation, smoke-free air, minimum legal age of sale laws, as well as variation in marijuana legal status) influence patterns of non-cigarette and poly-tobacco use? To what extent do policies that address one product, affect use patterns, or attitudes about, other tobacco products, and are these positive or negative effects? What are evidence-based policy approaches for emerging tobacco products?

7.   Marketing practices and characteristics of the retail environment need to be better understood in terms of their impact on non-cigarette and poly-tobacco use and attitudes. How is tobacco product marketing, including point of sale activities and co-marketing of brand names, related to attitudes and use patterns with regard to different types of tobacco products and poly-tobacco use?

8.   How do tobacco industry marketing and promotion tactics affect attitudes, patterns of use, and social norms regarding tobacco product use among both adolescents and adults?

9.   Tobacco related communications come from a variety of sources, including the tobacco industry, the news media, social media, public health agencies and organizations, and practitioners. How does communication and information about the relative harm of different tobacco products influence non-cigarette and poly-tobacco use patterns? How do different communication strategies affect how different tobacco products are used for cessation purposes? Are there unintended consequences of different communication strategies?

Research Priority 5

Develop Novel Behavioral Interventions for Tobacco Use

Behavioral and counseling treatments are a key component of tobacco cessation interventions for all smokers with demonstrated evidence both alone and in combination with pharmacotherapy. Moreover, such treatments are currently the *only* recommended approaches for treating tobacco use among certain subgroups of users (i.e., youth, pregnant women, smokeless tobacco users, and light and non-daily smokers)[24]. Although the need is great, there have been few scientific advances in behavioral treatment for tobacco use over the last two decades. The identification of promising behavioral interventions is likely to be guided by a number of factors including: a) strong integration of well-established and more novel theoretical approaches, drawing from a variety of fields (e.g., behavioral economics[25,26], family systems theory, affective science); and b) a careful consideration and testing of treatment mediators and moderators at each phase of the tobacco cessation process (e.g., cessation, relapse, and recycling).

A key scientific goal is to increase both access to, and the effectiveness of, behavioral tobacco cessation treatments for the general population of tobacco users and for high-risk populations. Approaches could include tailoring behavioral approaches based on smokers' interest and prior success in quitting, contextual factors (e.g., pregnancy, mental health status, social network smoking and other social determinants such as environmental stressors), and available resources. Researchers should explore innovative delivery mechanisms (e.g., social networks) and venues in order to attract a broader

range of smokers into treatment, including online communities, low income housing, and other social environments with a high prevalence of smokers. Innovative research approaches such as sequential or adaptive designs[27], factorial designs[28], and pragmatic research methods should be used to examine more systematically individual behavioral treatment components, and combinations of such components, to determine their effects in real world contexts. In addition, studies should identify the mechanisms of action of promising behavioral treatment components and assess their cost-effectiveness.

Research needed to address these knowledge gaps includes:

1. "Just in time" and "real-time" interventions offer flexibility and tailoring to test individually-responsive behavioral approaches. Examples include, cued interventions in response to changes in mood, behavior, or tobacco related cues. What "just-in-time" interventions can be implemented effectively and efficiently to reduce tobacco use and to aid cessation?

2. Treatment algorithms and adaptive designs are showing promise for personalizing treatments as primary and/or adjunctive treatment strategies with great potential relevance for advancing behavioral treatments. Such decision rules require additional research that provides better data on dose-response relations with regard to intervention in smokers with different characteristics (e.g., dependence level, motivation). How can adaptive and efficient research designs be used to test hypothesized mediators and moderators of treatment components to develop more tailored and efficient behavioral intervention packages?

3. Combination pharmacotherapy treatments are an increasingly recognized approach for cessation. How can individual and combination behavioral treatment components be optimized (e.g., goal setting, withdrawal exposure, behavioral rehearsal, scheduled reduced smoking, mindfulness, commitment contracts) to maximize treatment effectiveness? In particular, how can we optimize behavioral treatments so that they best complement and synergize with medication treatments, and so that their effects are preserved when applied in real world settings and populations?

4. With the recognition that much of health care occurs outside of the clinical setting, eHealth and mHealth technology has great potential to increase research and engagement. How can eHealth and mHealth advances be utilized to design, test, and disseminate novel behavioral interventions for tobacco use that yield high clinical effectiveness at lowest cost?

5. Intra-treatment support (i.e., offered within the clinical encounter) has shown evidence for enhancing abstinence and is recommended[24]. The evidence for extra-treatment tobacco cessation social support (i.e., outside of the clinical encounter in existing or created social networks) is mixed. Needed is an understanding of under what conditions social support can enhance cessation engagement, abstinence, and relapse prevention. How can social support processes and social networks be used to increase treatment engagement, tobacco cessation, and long-term maintenance?

6. Theoretical frameworks are important for understanding the conditions and mechanisms by which behavior occurs and can be changed. What novel, theory-based psychological, social, and behavioral targets can be effectively and efficiently manipulated to enhance smoking

cessation treatment outcomes? For example, recent conceptual approaches emphasizing a transdiagnostic emotional vulnerability model of smoking[29] may provide new treatment insights, and integrative models of behavior change, such as the Capability-Opportunity-Motivation-Behavior model[30], may provide a more systematic framework for identifying intervention functions and translation into specific behavior change techniques.

Research Priority 6

Use a Chronic Disease Approach to Address Smoking Behavior Across All Its Developmental Phases, Including Studies of Motivation and Precessation, Cessation and Adherence, and Relapse and Recovery

Over the past decade, there has been growing recognition that tobacco use could be better understood and treated if it were conceptualized as a chronic disease that requires long-term treatment rather than as an acute illness[27,31-33]. Fully embracing this conceptualization could promote recognition of critical and related components of a continuum of care for smokers and, in turn, encourage research targeted at phases of this continuum as well as studies designed to address multiple aspects of this continuum simultaneously[32-34]. For instance, while upwards of 70% of smokers indicate a desire to quit smoking, only a small fraction of these individuals use evidence-based treatments for tobacco dependence[35]. Likewise, while numerous smokers take the important step of using evidence-based treatments, approximately two-thirds of these smokers will be unsuccessful in their attempt, with relapse strongly predicted by poor rates of treatment adherence. Even among the fraction of smokers who complete treatment successfully, many will ultimately succumb to relapse.

Considerable evidence indicates that motivation to quit smoking and maintain abstinence can change rapidly[36-38]. There is a critical need to engage smokers in evidence-based treatments that can capitalize on these natural shifts in motivation in a manner that facilitates re-engagement in treatment when motivation to maintain abstinence declines or in response to smoking relapse. Furthermore, the vast majority of evidence-based tobacco treatments emphasize the achievement of initial abstinence and the prevention of relapse over a relatively short period of time. Given strong empirical data indicating that tobacco use is a chronic, relapsing disorder, treatments designed to enhance recovery from a lapse or relapse, and to facilitate the long-term maintenance of abstinence, are critically needed. It is clear that novel and relevant research is needed to systematically and comprehensively develop a greater understanding of efficacious and effective approaches to treating tobacco dependence across the chronic disease continuum. The value of such approaches will be enhanced by their ease of use, ready access, dissemination potential, and cost-effectiveness.

Research needed to address these knowledge gaps includes:

1. What theoretical frameworks can be used to identify new targets to promote utilization of evidence-based treatments for tobacco dependence?

2. What theoretical frameworks can be used to help *unmotivated or ambivalent smokers* overcome barriers to treatment seeking, including barriers that may address significant life

challenges that interfere with quitting? What conceptual models and novel theoretical approaches can be used to develop interventions to increase motivation to quit, including studies of mechanisms that underlie the transition from unmotivated smoker to abstinence?

3. What innovative interventions, including novel behavioral and communication approaches, can effectively enhance motivation to use evidence-based treatments among *unmotivated or ambivalent smokers*, including sequential treatment strategies, or personalized strategies that match treatments to an individual's level of motivation or other intrapersonal features?

4. How can diverse settings be used to reach and engage unmotivated or ambivalent smokers in evidence-based treatment?

5. How can large systems or organizations, such as healthcare systems, insurance companies, or mass media be used to increase utilization of evidence-based treatments for nicotine dependence among *unmotivated or ambivalent smokers*?

6. What theoretical frameworks, including approaches from diverse disciplines, can be used to develop treatments that *increase or maintain high levels of sustained cessation and high levels of treatment adherence?* Such frameworks and the resulting research and treatments, should identify key mechanisms that produce such effects, and identify barriers to long-term cessation and treatment adherence.

7. What are effective interventions to promote the maintenance of abstinence from tobacco use and treatment adherence, including the use of personalized interventions? How can personalized treatments best be delivered?

8. What novel technologies and innovative treatment delivery models can be used to *reduce relapse, promote relapse recovery, and promote treatment adherence*? The technologies could include the use of mobile technologies, social media, mHealth and EHR resources, and the innovative delivery models could include stepped-care or sequential models and personalized matching algorithms.

9. What are innovative, effective motivational and treatment delivery strategies that can be used to re-engage smokers in treatment following relapse? Research should explore whether these approaches apply to sustained engagement for the entire chronic care continuum from precessation to cessation to relapse and relapse recovery[39].

Research Priority 7

Identify Innovative Policy and Macro-Environmental Approaches to Further Reduce Tobacco Use

Tobacco control policies have contributed powerfully to the reduced rates of tobacco use over the last half century. These policy changes have included raising tobacco product excise taxes, implementing

clean indoor air laws, restricting tobacco product marketing, executing media counter-marketing campaigns, and funding tobacco control programs. However, these policies have not been implemented consistently, and we need to understand better how to maximize the impact of both existing and new policy approaches designed to reduce the burden of tobacco use at the local, state, and federal levels.

The tobacco product landscape and patterns of tobacco use have also changed substantially over the past two decades, potentially requiring new policy approaches to confront this changing environment. In particular, the recent marketing and increased use of electronic nicotine delivery systems (e-cigarettes or ENDS) along with other products (e.g., filtered cigars and cigarillos, smokeless tobacco) have transformed overall tobacco use patterns. Although all states currently levy some level of excise

taxes on cigarettes, there is great variability in the rates of taxation, particularly for non-cigarette tobacco products, and very few states currently tax ENDS. Similarly, while about half the adult population live in states that comprehensively restrict use of combustible tobacco products in indoor environments, few states have been added to this list over the past few years, and the rising popularity of ENDS has created new regulatory challenges for states and localities. We know little about how the changing tobacco product environment and behavioral patterns of use interact with existing policies and what the overall effect of such policies will be on population level tobacco use and harm. Moreover, emerging policies regulating the sales and marketing of tobacco products at the point of sale are rapidly gaining traction at the local and state level, providing new research opportunities to assess their impact. Overall, research is needed to understand better the impact of tobacco control policies designed to influence non-combustible tobacco product use and the potential consequences of such policies on overall tobacco use patterns.

Finally, changing social norms regarding tobacco use over the last decade have facilitated additional policy actions such as raising the age for the legal sale of tobacco products as well as establishing smoke-free outdoor locations, campuses, and multi-unit housing. Currently most states ban tobacco sales to individuals under age 18, but more jurisdictions are considering raising the minimum age of sale to age 21, creating new research opportunities[40]. Taken together, policies have the potential to transform tobacco control efforts and to bring about additional reductions in tobacco use. However, research is needed to determine which approaches and combinations of approaches would be most effective.

Research needed to address these knowledge gaps includes:

1. What communication strategies and messages are most effective for promoting tobacco use prevention and cessation within the context of emerging tobacco policy initiatives (e.g., smokefree public housing, raising minimum age for sale of tobacco). How can these messages be best delivered and tailored to be sensitive to local contexts and challenges (e.g., difficulties and barriers to many individuals in public housing to access and benefit from cessation treatments)?

2. What novel communication approaches and messages may be effective in helping to reduce the *attractiveness* of the broad array of tobacco products and *motivations* for their use?

3. How do tobacco industry messaging, marketing, and promotion efforts affect tobacco use behavioral patterns, social norms, and attitudes across age groups?

4. How do tobacco industry tactics affect local, state, federal, and private sector tobacco control policy initiatives and their implementation?

5. Effective tobacco control policies (e.g., taxation, clean indoor air ordinances) have been unevenly implemented with varying outcomes. What factors optimize adoption and implementation of effective tobacco control policies at the local and state level, and what strategies can help maximize these effects?

6. How can simulation modeling best be used to project the impact of integrating tobacco control interventions and policies? How can simulation modeling best be used to estimate the impact of potential new policies or extensions of existing policies (e.g., taxing non-cigarette tobacco products) on varying tobacco use behaviors (e.g., initiation, cessation), combinations of products, as well as on economic outcomes?

7. What is the effect of non-governmental actions (e.g., pharmacies deciding to stop selling tobacco products) on tobacco use behaviors and attitudes, at both the individual and population level? How can the public health impact of such policies be enhanced or promoted?

8. What types of incentive systems can be used to encourage tobacco cessation? For example, the Affordable Care Act includes provisions that allow health insurers to charge a premium based on tobacco use status but individuals trying to quit are exempt from such premiums. How are these types of financial incentives best adopted and implemented to achieve the public health goal of reducing tobacco use? Can other financial incentives (e.g., store coupons, transportation vouchers, direct financial payments) be effectively paired with cessation interventions?

9. What are the impacts of new counter-marketing approaches, such as new point-of-sale policies, banning tobacco coupons or restricting price promotions?

10. How can clean indoor air policies and tobacco free policies best be implemented to encourage cessation? How can the introduction of these policies in new venues (e.g., multi-unit housing, campuses, mental health treatment facilities) best be combined with cessation approaches?

11. Given the strong relationship between higher tobacco prices and lower consumption, what are the most effective policy approaches to raising tobacco product prices across the array of tobacco products, including smokeless tobacco, little cigars and cigarillos, and electronic nicotine delivery system products?

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