Prospects for Tobacco Control Research

Structuring, Developing, and Advancing Scientific Research in Tobacco Control

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INTRODUCTION

Tobacco is the leading cause of at least 12 different types of cancer and is one of the leading causes of preventable disease and death in both the United States and France. In the United States, an estimated 618,000 people were expected to die from cancer in 2025—20% of them from lung cancer.[1] In France in 2018, an estimated 157,400 people died of cancer—21% of them from lung cancer.[2] Research into tobacco use remains a key focus for both the U.S. National Cancer Institute (NCI) and the French National Cancer Institute (INCa).

Rates of tobacco use have fallen in the United States and globally over the past two decades, with 2022 data showing about one in five adults worldwide use tobacco compared to one in three adults in 2000.[3] Yet, tobacco use remains particularly high in France, which has one of the highest tobacco use rates in Europe.[4] In 2022, 31.8% of the French population aged 15–85 years reported currently smoking, and 24.5% reported smoking daily.[5] Among French 17-year-olds, daily smoking rates decreased from 2017 to 2022: 25.1% and 15.6% respectively.[5,6] In comparison, the prevalence of tobacco use in the United States is lower than in France, but many areas require further public health progress. In 2021, an estimated 46 million U.S. adults (18.7%) reported currently using any tobacco product, including cigarettes (11.5%), e-cigarettes and other electronic nicotine delivery systems[a] (4.5%), cigars (3.5%), and pipes/hookah (0.9%).[7] Although the rate of combusted tobacco (e.g., cigarettes, cigars, and pipes/hookah) usage remains unchanged, rising only slightly from usage in 2019 by 14% of adults, data from the Behavioral Risk Factor Surveillance System (BRFSS) show that e-cigarette usage among U.S. adults increased from 2.8% in 2017 to 4.5% in 2021, with slight declines in young adults aged 18–20, which may be partially attributable to the implementation of "Tobacco-21"[b] laws in states across the country.[8] In 2019, almost one quarter of adults (older than 18 years) who used e-cigarettes reported they had never smoked combustible cigarettes, and more than 56% of 18–24 year olds who used e-cigarettes reported they had never smoked a combustible cigarette.[9]Additionally, in 2022, e-cigarettes were the most used tobacco product among young adults aged 18–24.[10] Since 2014, e-cigarettes have been the most commonly used tobacco product among youth, and in 2023, 10% of high school students reported currently using e-cigarettes, with 25% of users reporting daily use.[10] This changing tobacco product landscape and use of emerging products by youth and young adults presents unique challenges and considerations for tobacco control that are relevant to both the United States and France.

Another major challenge for both countries concerns people with the lowest social and economic classifications; prevalence of tobacco use in the lowest income group in France rose from 30% to 33% in a 1-year period, 2019–2020. While in the U.S. the prevalence of current cigarette smoking has decreased across all income groups from 2019-2023, in 2023, individuals below the poverty line reported higher cigarette smoking rates—19.4% of those below the poverty line (95%CI: 17.6, 21.3) compared to 10.8% of all individuals surveyed (95%CI: 10.4, 11.3).[11]

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[a] Electronic cigarettes, also called Electronic Nicotine Delivery Systems (ENDS) and vapes, refers to a class of products that are battery powered and heat a liquid into an aerosol for inhalation. The liquid typically contains nicotine, solvents such as propylene glycol, glycerin, and other chemicals, and the heating process forms toxicants, including carcinogens.

[b] Tobacco 21 is a national campaign taking a local approach to raising the tobacco sales age from 18 to 21 years. Established in 1996, Tobacco 21 and the Preventing Tobacco Addiction Foundation strive to reduce smoking and tobacco use through a preventive effort locally and on the state level all over the United States and in American territories, such as Guam. Source: https://tobacco21.org/what-is-tobacco-21/

Research into the perceptions of combustible tobacco products and e-cigarettes is improving our understanding of the motivations behind their use. [6,12] With respect to e-cigarettes, the 2021 Cancer Barometer survey reported that 7 of 10 French adults perceived that e-cigarettes were harmful to their health and were concerned about the potential links to cancer, although they held the belief that e-cigarettes were less harmful compared to combustible cigarettes. [5,13] In contrast, according to data from the 2019 Health Information National Trends Survey (Cycle 5), 34.5% of U.S. adults reported that they believed e-cigarettes were equally as harmful as cigarettes. [7,14]

The United States and France are actively collaborating to shape a joint research plan aimed at mitigating the morbidity and mortality associated with tobacco use and are defining research priorities. Strategic documents in the field of tobacco control can guide these efforts. One example is from Cochrane's Tobacco Addiction Group, [15,16] which published a report identifying 183 unanswered research questions in the field of tobacco use and tobacco cessation and 8 priority research areas:

- E-cigarettes
- Addressing inequalities subpopulation differences
- Mental health and substance abuse
- Initiating quitting attempts
- Population-level interventions
- Pregnancy
- Young people
- Cessation treatment delivery

Some research questions identified in these studies require the tailoring of evidence-based tobacco prevention and cessation interventions for specific groups and the increased reach, effectiveness, delivery, and engagement of interventions. Applied to tobacco control, prevention and cessation intervention research involves a wide range of participants, knowledge, and contexts. In addition, there are methodological issues relating to co-construction, evaluation, and transferability to other populations both within and outside the U.S., encompassing a whole-person approach that contributes to reducing differences in health outcomes. [17-19]

Population-level tobacco prevention and cessation interventions are an effective tool to address tobacco-related public health challenges. In fact, interventions are defined as an organized set of actions designed to correct or improve a problematic situation in a given area. [16] Applied to tobacco control, intervention research involves a wide range of actors, methodologies, and contexts, all of which need to be understood to be able to propose effective and transferrable interventions. Despite their specific contexts, the United States and France have common public health and scientific challenges regarding tobacco. As such, this research strategic document focuses on the heterogeneity of three domains identified by NCI and INCa that each capture a series of populations of high scientific priority. Although they operate within distinct and unique contexts, both the United States and France embrace a proactive approach to tobacco control, addressing similar challenges and striving to diminish differences in tobacco use rates within and across countries. Given their significance, they fall within the scope of a holistic, cross-cutting, multi-disciplinary approach, and are aimed at developing knowledge and generating more probative data.

1. *Tobacco Use and Co-Occurring Behaviors:* The challenge is to expand and improve upon the evidence base that addresses tobacco use and co-occurring health behaviors, to design novel

approaches to cessation interventions, and to generate a paradigm shift in how existing interventions have been implemented at a population level.

2. *Multiple Tobacco Product (MTP) Use:* The challenge is to understand the patterns of MTP use and the gaps in research regarding these more complex use patterns, as well as to measure motivation for use, use behaviors, and health impact. Of particular interest are smoking cessation interventions among people who smoke and use other tobacco products and the gaps in research on how to intervene with people who report using MTPs to facilitate complete tobacco cessation.

3. *Populations Disproportionally Impacted by Tobacco Use:* The challenge is to foster research on smoking prevention and cessation interventions for populations disproportionately burdened by commercial tobacco use (e.g., people living in rural areas) by targeting, adapting, and creating novel individual- and population-level interventions.

There is inherent overlap among the three domains, but sub-topics are predominantly centered within one domain, directing attention to specific challenges pertaining to each area; however, certain topics may tap into more than one domain. This work also involves implementation science and intervention research as a basis for moving away from designing individual interventions—and toward population-level implementation efforts—through the consideration of scientific impact and its integration into future tobacco control research.

PURPOSE

The purpose of this work coordinated by NCI and INCa is to propose a general research framework defining three areas of scientific priority for the prevention and cessation of tobacco use, through the three cross-cutting domains previously outlined. Particular attention is focused on populations who are disproportionately burdened by tobacco use, through a lens that also encompasses the cancer continuum, with a goal of reducing disparate health outcomes.

Devised, designed and developed with researchers, this document is aimed at research funding organizations and the tobacco control research community, and provides a guide for informing and structuring research priorities in tobacco control.

METHODS

To achieve these objectives, INCa and NCI developed an innovative, collaborative approach. The main steps were as follows:

- **Phase 1: Creating an international expert consortium.** Based on an analysis of the international scientific literature and ongoing U.S. and European research projects (notably funded by NCI and INCa), INCa and NCI identified researchers and grantees with expertise in each of the three domains. Each domain focused on three main questions, which enabled the production of different deliverables:

  o **What do we know** in these research areas?
  o **What are the gaps** in our knowledge for each of these areas?
  o **How can we advance science** in areas where gaps are identified?

- **Phase 2: Drafting a white paper.** Based on a systematic review of U.S. and European scientific literature, INCa and NCI drafted a white paper describing the current scientific knowledge and state of science in the three domains.

- **Phase 3: Opportunities for consortium dialogue.**
  - *Virtual meeting*: In **February 2022**, 30 U.S. and European researchers attended a virtual meeting. The aim was to assess the research and development needs in the three domains. This meeting provided an opportunity to launch a group dynamic and identify the initial similarities and specificities between the United States and Europe, in particular France, and identify the area of expertise of each of the participants.
  - *Two-day workshop*: In **November 2022**, INCa and NCI organized a 2-day workshop attended by more than 40 U.S. and European researchers specializing in smoking prevention, cessation, and tobacco control policy. The participants presented their research, discussed gaps in knowledge, and identified research priorities in the three domains. In sub-group sessions, workshop participants brainstormed ways to address identified knowledge and research gaps.
  - *Webinar*: In **February 2023**, workshop participants attended a post-workshop webinar to discuss additional gaps in knowledge and prioritized previously identified gaps. This final meeting facilitated the drafting of this research plan.

This document summarizes the discussions and contributions from experts during the different phases and proposes new avenues for research. It is not intended to reflect the worldwide state of tobacco control, but rather, serves as a practical tool for outlining future opportunities for scientific advancement. This document can also be used to inform funding agencies and the general tobacco control research community and provide guidance for institutions that support tobacco control research.

SOME CONTEXT
- In the United States, 28.5% of cancer deaths are attributable to tobacco use or secondhand smoke exposure and 4.1% of cancer deaths are attributable to alcohol use. [20] In France, 13% of all deaths are tobacco-related and 7% are alcohol related. [21,22]
- Tobacco and alcohol co-use can have a multiplicative effect on the risk of developing cancer, particularly upper aerodigestive cancers. [23]
- In the United States, 29.1% of adults who smoke cigarettes, also reported using cannabis in the past 12 months. [24] In France, 8.5% of those aged 15–64 years reportedly use at least 2 substances among tobacco, alcohol, and cannabis, [22] and 4.4% of French 17-year-olds co-use tobacco and cannabis. [25]
- Cannabis is illegal in many European countries; it continues to be illegal at a federal level in the United States, although many states have legalized and decriminalized its use.

BACKGROUND: WHAT DO WE KNOW?

The intersection of tobacco use and co-occurring health behaviors (including use of multiple substances, such as tobacco and alcohol) has particular importance in tobacco control interventions. There are complex interactions between these behaviors and comorbidities, and evidence has shown that tobacco use in combination with other substance use disorders (SUDs)—including alcohol, cannabis, and opioids—worsens health effects. [15,26]

Research points to a specific benefit of tobacco use treatment on abstinence and recovery from SUDs, and smoking cessation interventions provided during treatment for other SUDs have been associated with a 25% increased likelihood of long-term abstinence from alcohol and illicit drugs. However, significant research gaps remain regarding the optimal timing of treatment and the choice between a multi-substance treatment approach and a prioritization to treat non-tobacco SUDs. Even in effective programs, tobacco cessation rates are low, and certain barriers to implementation persist for those with co-occurring behaviors.

Current national tobacco use surveillance systems are limited in their ability to capture the junction of tobacco use with co-occurring behaviors and comorbidities. These surveillance systems typically focus on monitoring the prevalence of tobacco use at a general population level, capture trends in patterns of consumption, and examine associated demographic factors. However, they may not provide comprehensive data on the complex interactions among tobacco use and co-occurring behaviors. Global tobacco use surveys (e.g., Global Adult Tobacco Survey or Global Youth Tobacco Survey) do not routinely collect data on alcohol, cannabis, or other drug use. Where such surveys exist, they may use unharmonized definitions or measures for these behaviors. In addition, the tobacco product marketplace and the context for alcohol, cannabis, and other drugs are in constant flux. Thus, expanding existing surveillance efforts that can incorporate the rapid monitoring of tobacco use for more timely information, plus more comprehensive measures on co-use of tobacco with other substances (given the rapid shift of the tobacco product marketplace and the delay of national tobacco use surveys to yield timely results), can increase our understanding of rapid variations in use patterns.

KEY ELEMENTS: WHAT ARE THE GAPS?

Developing and Optimizing Cessation Interventions to Treat Tobacco and Co-Occurring Substance Use

More research is needed that examines co-occurring behaviors in the framework of cessation interventions. A crucial approach involves integrating prevention interventions into cessation efforts by developing programs that address various substances simultaneously rather than target one product at a time; existing evidence has highlighted that relapse in one substance often triggers relapse in another. Health communication and implementation plans that address the co-use of substances should be maintained as integral components of these efforts.

Traditionally, providers have focused on clients maintaining cessation for one substance at a time during treatment, rather than concurrently treating the use of all substances, [27] despite research that indicates treating both tobacco and other substance use concurrently can support successful outcomes for both substances. [27] This prevailing norm has been perpetuated by health care staff misperceptions and the lack of implementation and enforcement of smoking bans/policies. These factors contribute to the continued acceptance of smoking within the context of cessation efforts for substances other than tobacco.

This research plan emphasizes the importance of treating the whole person, including increasing the use of evidence-based treatments; arriving at affordable, scalable, effective interventions to reach and help target populations; and addressing barriers to implementing tobacco treatments in health care settings. Recognizing that the co-use of substances has become the norm rather than the exception, practitioners should design the interventions to integrate co-use from the outset, and funders should frame funding opportunities in a cross-disciplinary manner across outcomes to focus on treating the whole person, as it can be challenging for funding agencies to think outside their own institutional priorities. In addition, emphasizing the whole person can allow for the role of a geospatial framework that includes other factors influencing related aspects of public health, such as the built environment (e.g., the geographical location of tobacco, cannabis, or alcohol retailers). Other innovative ideas of a whole-person focus can include incorporating novel aspects of personalized medicine, including AI in tailored interventions to more precisely interact with clients, identifying new biomarkers of multiple substance use, and tailoring electronic health record (EHR) systems (for example, an EHR system can be designed more efficiently to include time-saving incentives for providers to refer patients to interventions. This effort could involve streamlining the referral process with fewer screen clicks while adding more steps if the referring provider does not initiate the referral).

Tobacco Use and Co-Occurring Behaviors
Tobacco and Alcohol

Individually, tobacco and alcohol use are estimated to cause approximately 29% and 5.5%, respectively, of cancer deaths in the United States. [28,29] In addition, the concurrent use of tobacco and alcohol can multiplicatively and synergistically affect the risk of cancers in the upper aero-digestive tract. [30-32] Given the synergistic impact on the genesis of some cancers, both NCI and INCa are invested in reducing tobacco and alcohol co-use. More mechanistic evidence is essential to understanding the roles played by both substances, including their reinforcing effects, by stimulating nicotinic acetylcholine receptors and by amplifying dopamine release. Exploring, for example, how smoking can mitigate alcohol withdrawal/hangover effects and can contribute to substance dependence can elucidate the influence of one substance on the other.

A limiting step in advancing research specific to tobacco and alcohol co-use results from the need for more research into the contribution of sex (as a biological variable) to better understand the mechanisms,

determinants and correlates of alcohol and tobacco co-use. This would also potentially inform advances in treatment interventions. In addition, cessation interventions should consider co-occurring mental health disorders and should integrate any specific mental health needs concurrently with alcohol and tobacco treatment.

Some promising avenues for joint tobacco and alcohol cessation treatment include novel therapeutics for alcohol and tobacco dependence. Currently, very few integrated treatment options are available for individuals who smoke and have alcohol use disorder. Research using oral naltrexone for alcohol use disorder in the context of smoking cessation treatment (provision of nicotine replacement therapy) has also demonstrated that treating both SUDs jointly yields reduction in drinking.[33] Other research using contingency management has demonstrated that the incentive structure can be escalated the longer that former smokers maintain abstinence, and contingency management can be paired with another treatment, such as varenicline, with crossover effects.[34] Further research is needed to explore the future of an integrated mobile health (mHealth) cessation treatment to reduce the use of both substances.

Tobacco and Cannabis

Although the scientific research on the relationship between cannabis use and tobacco use is not well characterized, the current literature suggests that cannabis use is rising in the United States, more than one-third of people who use tobacco also use cannabis, and as much as three-quarters of cannabis users use tobacco.[35] In Europe, cannabis is illegal in many countries, and it remains illegal federally in the United States, although multiple states have legalized and decriminalized cannabis use. Understanding how the legality of substances plays a role in co-use behavior will be essential as the cannabis landscape continues to evolve. In addition, utilizing available surveillance data to better distinguish cannabis and tobacco co-use and their changes over time is important.

Recent research has suggested that people who use cannabis are more likely to start smoking cigarettes, continue smoking cigarettes (instead of attempting to quit), and relapse back to cigarette smoking once they have quit.[36] Similar to tobacco and alcohol, more mechanistic evidence is needed to understand the roles played by both substances, particularly if cannabis adversely affects tobacco cessation. Exploring the role of combined cessation or continued cannabis use during tobacco cessation is essential to developing effective cessation treatments.

Additional questions remain in cannabis harm reduction, including the appropriate treatment and a better understanding of the role of cannabis use in cancer risk with and without tobacco co-use.

SUMMARY

- Tobacco use often co-occurs with other substance use disorders (SUDs), such as alcohol and cannabis, leading to worsened health outcomes and increased relapse rates.
- Smoking cessation interventions during SUD treatment can enhance long-term abstinence from other substances by 25%, yet significant gaps in research on optimal treatment timing and approaches remain.
- Current national tobacco surveillance systems fail to capture the complexities of co-use behaviors and comorbidities, necessitating enhanced monitoring efforts to understand trends and inform policy.
- There is a need for research on simultaneous treatment of co-occurring substance use, moving beyond a single-substance focus to address the interconnectedness of behaviors for better outcomes.
- Existing treatments for tobacco and alcohol use are limited, and novel integrated approaches, including contingency management and mHealth solutions, require further exploration.

DOMAIN 2: MULTIPLE TOBACCO PRODUCT USE

SOME CONTEXT
- In the United States, 30% of high school students who report using any tobacco product use more than 1 tobacco product concurrently; [37] among higher-education students, this figure is 50%.[38]
- Among U.S. adults who currently use tobacco, 17.3% report using 2 or more tobacco products. [7]
- In France, in 2021, 7.5% of those aged 15–75 years reported regular e-cigarette use. Of these users, 10% were people who do not currently smoke cigarettes. [13] In 2022, 2.6% of those aged 15–75 years reported having tried heated tobacco products. [5]
- In Europe, there is an increase in the use of tobacco products other than cigarettes, but with significant disparities across countries; 14.5% of young Europeans concurrently use combustible cigarettes and e-cigarettes. [39]

BACKGROUND: WHAT DO WE KNOW?

With the proliferation of novel tobacco products on the market, use of MTPs (defined as concurrent use of products from different categories, such as cigarettes and e-cigarettes) appears to be increasingly common, particularly among adolescents and young adults. Before the widespread marketing of e-cigarettes, MTP use had already been noted as a distinct phenomenon regarding the use of cigarettes along with smokeless tobacco, cigars, hookah, and other products. Apart from adolescents and young adults, MTP use is also typically higher among non-daily tobacco users and has important implications for transitions into adult tobacco use. [40] MTP use represents a distinct set of behaviors from single product use and can reflect a variety of responses to social and physical cues, such as serving as a means to reduce smoking without complete cessation, to circumventing smokefree policies, or to maintaining the "authenticity" of conventional cigarette smoking. [41] Moreover, there are a wide range of MTP use patterns, which makes monitoring more complex. Studies have also suggested that health risks may be higher and cessation lower among MTP users compared with single product users. [42,43]

In the United States, nearly 30% of high school students who reported current tobacco use used 2 or more tobacco products, [37] and, according to another representative survey, more than 50% of tobacco-using college students use more than 1 tobacco product concurrently. [38] Additionally, more than half of people who report non-daily smoking also report using other tobacco products within the past 30 days. [44] Among current adult tobacco users, 17.3% reported using 2 or more tobacco products. [45] In Europe, there has been a similar rise in the use of non-cigarette tobacco products (e.g., heated tobacco, e-cigarettes) and MTP use. [46] Among young people, the prevalence of the combined use of conventional cigarettes and e-cigarettes has been estimated at 14.5%.[39] Data have also shown that tobacco product transitions, including adding and switching products, are common in Europe. [47] Data from the French Cancer Barometer 2021—a survey from a representative sample of the French population (n = 4,938)—indicated that 7.5% of respondents regularly used e-cigarettes, and 10% of people who never smoked had already tried e-cigarettes. [48] However, prevalence of e-cigarettes and MTP use varies widely between countries in Europe, and some countries may not have appropriate surveillance for capturing emerging trends.

Understanding Multiple Tobacco Product Use Behaviors and Identifying Metrics for Common Use

A fundamental research question to understand MTP patterns of use entails recognizing how to accurately measure the various combinations of tobacco product use behaviors that constitute MTP use. The determinants of MTP use patterns are complex, emanating from commercial, environmental, interpersonal, and

intrapersonal factors. [49] A better understanding of 1) the sub-populations of people who smoke who are also more likely to engage in MTP use patterns and 2) key factors determining the use behavior would have important implications for both the prevention of initiation and cessation approaches. It is particularly crucial to understand how these determinants differ among groups that experience disproportionate burden from tobacco use and how to address these disparities. Additionally, while several studies have suggested that people who use MTPs have greater dependence and more difficulty quitting tobacco use, there is limited understanding of the ways that different use patterns (e.g., daily/non-daily cigarette smoking with daily/non-daily e-cigarette use; weekly cigarette smoking and weekly e-cigarette use) contribute to substance dependence and adverse health outcomes as well as the ways in which MTP use affects different aspects of tobacco use spectrum, such as escalation, cessation, transitions between products, simultaneous use, and relapse.

A key prerequisite for advancing the monitoring and understanding of MTP use is to develop consistent definitions for tobacco products and a taxonomy of categories of different products (particularly non-cigarette products). A tobacco product taxonomy that groups different tobacco products into categories of products could enable analyses by category instead of analyses only at the level of individual product combinations (e.g., should nicotine pouches be considered alongside other emerging nicotine delivery devices or with smokeless tobacco products?). Moreover, it is important to acknowledge that there is utility in measuring each product in a systematic and comparable way (e.g., same item stem, same time anchor, same frequency of use assessment) so that multiple use patterns can be understood through an analysis of combinations of items. Another advantage of working to develop agreed-upon definitions of tobacco products is that those definitions can also help ensure that researchers clearly distinguish between cannabis and tobacco use when assessing smoking or e-cigarette use behavior. Respondents may not always know that researchers want them to think only about their tobacco or nicotine product use, and they may also confuse products (e.g., heated tobacco products and vaping devices). However, it is important to acknowledge the importance of taking specific terms used and the context of tobacco use within a specific country, while balancing the need to ask the questions similarly enough so that the data may be comparable across countries.

There continues to be a growing and rapid diversification of the tobacco product marketplace, with new products or changing product designs emerging from the industry on a near-constant basis, requiring the need for rapidity and nimbleness in the surveillance of the marketplace and use behaviors. This surveillance should include effective monitoring of the marketing of these products, and it is an important piece in determining policies and product regulation for the protection of public health. This complex and rapidly changing marketplace may differ by country, where certain products are available only in certain countries or are introduced at different times, which underscores the importance of sharing data across countries and of developing new structures by which to accomplish such data-sharing and data analysis collaborations. Innovative rapid surveillance and data-sharing could maximize the research and public health community effectiveness and could increase informed policy and regulatory decision-making.

KEY ELEMENTS: WHAT ARE THE GAPS?

Ultimately, the primary goal of improving our understanding of MTP use patterns is to support development and dissemination of effective interventions, which ultimately supports complete tobacco cessation and reduces tobacco-caused morbidity and mortality. However, it is important to acknowledge that there are varying perspectives both within the United States and internationally on whether and how potentially less harmful products (e.g., e-cigarettes) may be used as a substitute for or a bridge to quitting the most harmful combusted products. This effort has implications for how researchers frame their research questions pertaining

to MTP use. Additionally, this is further support for countries to prioritize the surveillance of their products as well as their marketing and multiple use patterns, which can determine whether the products are advancing harm reduction or exacerbating harm or otherwise stalling progress in reducing the morbidity and mortality from tobacco use. In addition, this knowledge can be used to understand how to effectively conduct counter-marketing.

We provide several recommendations to advance future research priorities. We need to better understand how to measure frequency and intensity of use (i.e., dosage) with respect to the newer tobacco products and the multiple use of products, as that knowledge would be an important factor in determining total exposure for disease risk and outcomes. At a minimum, it is recommended to assess each product used in the past 30 days and the number of times used per day; conduct formative research to understand the reasons behind why each product is used concurrently, as there may be different motivations for using each product, which would help identify important intervention targets and suitable intervention approaches; and include in studies measures of the reasons for the use of each product used. Another key research need is learning how to conceptualize and measure nicotine dependence in the context of MTP use, to understand the relationship between dependence or product use maintenance and the cessation of the various products used. Studies should provide multiple assessment points for symptoms at different times via both self-report and objective methods (e.g., biomarker measures, ecological momentary assessment, or biometric technologies). These symptoms can include substance dependence, mental health, other health behaviors associated with tobacco use, respiratory, cardiovascular, gastrointestinal, oral, and effects on maternal and fetal health (pre-natal and post-natal).

The use of a variety of study designs is important in understanding the implications of MTP use patterns—observational (especially longitudinal designs), experimental, and simulation models. There is a need for rigorous, largely powered observational longitudinal studies to help understand the effects of MTP use (e.g., whether e-cigarettes have a population-level effect in helping people quit smoking and/or encouraging dual use, especially sustained dual use). Two advantages of this type of study include the extent to which it can elucidate the trajectories of different products over time and the temporality and relationships of how the different products are used over time. An adequately powered study would also allow for capturing variations in MTP use trajectories in different sub-populations, especially in those who experience greater adverse tobacco-related health outcomes. Building consortia for these studies across countries would help us understand what contextual factors (e.g., social, geographical) promote the use of one product over another. Simulation modeling studies may be particularly useful in understanding a potential policy effect, especially whether a policy could unintentionally exacerbate differences in health outcomes. In addition, incorporating the symptom-reporting and biomarker data into observational, longitudinal, and experimental studies would help to understand the health impact of MTP use, including use by different subpopulations. Lastly, we need to balance the use of

existing data versus the investment in collecting new data (e.g., longitudinal cohorts), as there are a lot of extant data that we could leverage to explore these research questions as well.

SUMMARY

- Concurrent use of MTP, especially among adolescents and young adults, is on the rise, influenced by the availability of e-cigarettes and other emerging products.
- MTP users face greater health risks and difficulties in cessation compared to single product users, necessitating a deeper understanding of MTP behaviors and their health impacts.
- MTP behaviors are shaped by a variety of factors, including social cues and personal motivations, complicating the measurement and analysis of tobacco use patterns.
- Developing clear definitions and taxonomies for different tobacco products is essential for effective research and data comparison, particularly regarding emerging products.
- There is a need for studies on usage frequency, motivations for concurrent use, and measures of nicotine dependence to inform effective interventions and enhance public health outcomes.
- Enhancing international data-sharing and collaboration on tobacco use research can help identify trends, understand health disparities, and inform regulatory decisions to improve public health outcomes.

DOMAIN 3: POPULATIONS DISPROPORTIONALLY IMPACTED BY TOBACCO USE

SOME CONTEXT

- Data from the United State in 2022 showed that 17.1% of people who had a high school degree were cigarette users compared to 5.3% of people who had a college degree or higher. The prevalence of smoking was highest among those whose annual household income was considered low income (18.3%) compared to middle income (12.3%) and high income (6.7%).[50]
- Data from France in 2022 showed that 33.6% of the people who smoke were from the lowest income levels. The prevalence of tobacco use for those without education or an educational level below high school was 30.8%.[5]
- The prevalence of cigarette smoking among people with mental health conditions is approximately two times greater than that of the general population. [51]
- People living with HIV who smoke have a higher prevalence of tobacco use than the general population. They also have a higher risk of developing lung cancer, pneumonia, and cardiovascular disease. [52]

BACKGROUND: WHAT DO WE KNOW?

Although tobacco use has declined in both the United States and France over the past several decades, these declines have not been distributed equitably across these populations. Some subgroups remain at increased risk for tobacco use and related health consequences, and this imbalance has produced substantial differences in health outcomes. It is well documented that populations with less social and economic resources have higher rates of tobacco use. Additionally, differences in tobacco use patterns among persons with mental health conditions are significant; the prevalence of cigarette smoking among persons with mental health conditions is about twice that of the general population. [53] This difference is even higher for persons with serious mental illness or those who have been in SUD treatment in the past year. Tobacco use disproportionally impacts some population subgroups such as low intensity/frequency cigarette smokers, pregnant woman with lower socio-economic status level, and populations who live in rural areas and certain remote geographical areas, resulting in adverse health outcomes. These differences may be exacerbated by lack of access to effective interventions and exposure to other adverse conditions.

There is an opportunity to advance research on tobacco prevention and cessation interventions for these priority populations by targeting, adapting, and creating novel individual and population-level interventions for these individuals and communities. Although there has been a growing effort to *identify* populations disproportionately impacted by tobacco use, there remains a persistent gap in research to *address* these differences. For example, social support is associated with increased quitting success among U.S. smokers across certain racial and ethnic populations and could be integrated into cessation interventions. Some research finds that there are barriers and challenges due to adverse social and environmental conditions associated with smoking initiation and progression among adolescents in some race and ethnic minority groups, but significant knowledge gaps remain. Finally, the role of adjustment to local norms (e.g., neighborhood and place) in smoking cessation interventions remains a poorly understood area of research and is important for developing more effective interventions.

Although this research plan focuses on a set of examples of populations disproportionately burdened by tobacco use, we recognize there are also additional important populations with unique patterns of use where additional research and funding are warranted.

Enhancing the Reach and Delivery of Tobacco Cessation Interventions and Expanding the Engagement of Disproportionally Burdened Populations

We identify overarching areas outlined in a comprehensive approach to understand and address the science of tobacco cessation and prevention interventions, with a focus on the lived experiences of individuals who smoke. People may have membership in multiple population subgroups that are disproportionately affected by tobacco, and so may experience several risk factors at once, compounding their disproportionate risks. This research document emphasizes the importance of surveillance, global collaboration, implementation science, and innovative strategies as foci for future research opportunities.

The group described the importance of a greater understanding of the lived experiences of individuals who smoke as a critical component for developing effective cessation interventions. Research should delve into the nuances of these experiences, exploring intra- and inter-group factors influencing populations disproportionately burdened by tobacco use. Apart from quantitative research methods, qualitative research methods should be integrated to capture the complexity of perspectives. Developing reliable metrics to measure a person's lived experience is essential, and qualitative and mixed-methods approaches can help capture the multifaceted dimensions of individuals' experiences with tobacco use. This effort would include the creation of standardized tools to assess the impact of interventions on the lived experiences of different populations. We recognize that the multi-layered effects of multiple risk factors can synergistically compound differences and it is imperative to consider the lived experiences of people who smoke. Research efforts should explore the interconnectedness of various factors contributing to differences in tobacco use burden, such as race, sex, social and economic status, and other subpopulation characteristics.

As discussed in Domain 1, surveillance plays a key role in understanding the U.S. and global landscape of tobacco use. Efforts should be made to harmonize data collection within the U.S. and across countries, allowing for a comprehensive analysis of measures. Common data elements should be implemented to facilitate data aggregation and comparison across studies. Promoting better collaboration also includes components such as establishing an open-access database for effective interventions; this database should not only contain intervention outcomes but should also provide contextual information about the populations studied. The identification of levers to scale up successful interventions is crucial for a positive impact on health outcomes.

The role of implementation science is central to advancing cessation interventions among populations burdened by tobacco use. Future efforts should shift the focus of research from designing interventions solely for knowledge acquisition to designing them for dissemination and implementation in traditionally underserved populations. Interventions should be developed to ensure that they are not only effective but are also feasible for implementation. Moreover, implementation science principles and frameworks should guide the design of interventions to ensure real-world applicability.

Methods to improve engagement with and uptake of tobacco cessation interventions—considering that cessation interventions can be delivered through unconventional channels—can focus on reaching people "where they are" instead of solely relying on traditional health care providers to prescribe and deliver interventions, as well as leveraging community health workers as vital intermediaries in disseminating interventions to various populations. Developing best practices for sharing research results with participants and other stakeholders should be prioritized, including ensuring that results are accessible, relevant, appropriate and actionable, to foster a collaborative and participatory approach.

We also acknowledge the challenge of overcoming funding barriers, which includes addressing misconceptions about the benefits of qualitative methods, including the perceptions that these are less rigorous than quantitative methods. Instead, funders should advocate for the inclusion of qualitative methods, and investigators should highlight these methods as a unique contribution to understanding complex phenomena. In addition, funded research should prioritize the development of strategies to increase the reach of interventions while minimizing financial and logistical barriers for study participants.

In addition to traditional modes of cessation treatment, research should explore the role of mHealth in interventions. Considering that most of the population have access to smart phones, research should continue to explore and expand on the potential of mHealth interventions to reach a broader pool of individuals. This can include:

- Investigating optimal strategies for connecting individuals with mHealth interventions, ensuring accessibility and long-term engagement on cessation
- Examining ways to personalize and tailor mHealth interventions to individual needs and evaluating the effectiveness of incorporating cessation pharmacotherapy and medication adherence support within mHealth platforms
- Initiating research on engagement strategies within mHealth interventions and exploring the ways that process outcomes can be key indicators of success in addition to traditional effectiveness outcomes
- Challenging existing frameworks for examining individuals' experiences within treatments and considering novel approaches to understanding the subjective experiences of participants in cessation interventions.

KEY ELEMENTS: WHAT ARE THE GAPS?

Persons of Lower Social and-Economic Status Who Smoke

The persistent challenge of addressing the disproportionate impact of tobacco use by specific populations requires a comprehensive approach that delves into the complexities faced by these populations, particularly those with a lower social and economic status. Recognizing the intricacies of terminology, historical context, and the commercial determinants of health, this research document aims to summarize the contextual factors contributing to differences tobacco use to inform tailored interventions that address the unique challenges faced by these populations. The group described the importance of recognizing the continued challenges faced by lower social and economic status groups in quitting smoking, exacerbated by pressing concerns such as homelessness, economic and employment stressors, and limited access to substance use care. Evidence shows that lower social and economic status groups have a harder time quitting. Experts underscored the prioritization of needs within these populations, exploring ways to integrate tobacco cessation interventions effectively. In addition, there was discussion on understanding how the juncture of social determinants and structural influences affect tobacco use behaviors to inform tailored tobacco control interventions; investigating the mechanisms contributing to social and economic challenges in smoking, including exploring the early origins of barriers and challenges, such as maternal and familial smoking; and assessing the impact of exposure to violence and the availability of tobacco products as research gaps that can inform targeted interventions. The group also discussed terminology and system-centric perspectives and acknowledged the sensitivity of terminology when describing priority populations. They recognized that labels, such as "hard-to-reach," may not resonate with individuals facing socio-economic challenges, as it often conceals the fact that vulnerability is a

result of social and institutional challenges. Therefore, shifting toward language that respects the dignity and agency of these populations and destigmatizes them was a recommended approach.

When examining the stability of smoking prevalence differences over time in the United States, gaps between sub-populations remain unchanged, especially in relation to differing education levels in the population. (For example, the prevalence of cigarette use among adults aged 25+ with less than a high school education (21.6% in 2019, 20.0% in 2023) and those with some college education (16.0% in 2019, 13.7% in 2023) remained relatively unchanged, with differences of 1.6% and 2.3%, respectively.[11] Efforts to reduce the overall prevalence of smoking among adults have not adequately addressed persistent differences, particularly in geographical areas with lower educational levels, in rural communities, and among African American and American Indian/Alaska Native, and/or Hispanic individuals. There is also a continued gap in research investigating the role of price promotions in driving cigarette purchases, as a tobacco prevention area. We underscore the presence of commercial determinants of health, and the strategies and approaches employed by the tobacco industry that contribute to differences in smoking patterns. Understanding the impact of commercial determinants of health on tobacco-use–burdened populations, considering industry marketing tactics, accessibility, and industry influence, remains an area requiring further research.

We recognize the historical context and perspectives both from the United States and France (as well as other countries) where smoking rates have decreased, but subpopulation differences in several domains persist. For example, in France, the smoking prevalence among adults is around 30%, and 1 in 4 adults smoke daily.[54] In addition, we highlight the influence of historical factors that can contribute to the lack of tobacco prevention and cessation progress in certain populations, as reflected by specific tobacco retailer density patterns and tobacco industry activities, which shape current tobacco use behaviors.

The discussion also focused on political history and structural influences—acknowledging and addressing the factors that have shaped the social and-economic landscape and have influenced tobacco use behaviors. Regarding areas for tailoring tobacco control interventions, we emphasize the importance of developing interventions that recognize the unique challenges faced by populations experiencing disadvantages. This may be adapting tobacco control strategies to address the multi-layered effects of social and institutional influences; emphasizing the need for improving relevance to all populations, and community engagement in the design and implementation of interventions; and supporting social changes and evaluating their impact on subgroup differences.

Tobacco Use Among Populations with Mental Health Disorders

One-quarter of adults with serious mental illness have a co-occurring SUD, most commonly tobacco use, and 40% of those who use substances of any kind will be diagnosed with mental health conditions, most notably depression and anxiety.[51] In the United States, the rates of tobacco use among populations with mental health disorders are around three times higher than in the general population, and these populations have greater difficulty quitting and greater cessation treatment resistance, leading to worsened health outcomes.[55,56] That difficulty is rooted in multiple social determinants of tobacco use—reduced access to cessation interventions, institutional and social challenges, everyday stressors, neighborhood characteristics, and targeted marketing. In addition, moderators of this association include sensation-seeking and interpersonal factors, such as peer tobacco use, which is particularly apparent in young adults (those ages 18–24). Furthermore, young adults with more depressive symptoms report using a greater number of tobacco products but only when they have more peers who use tobacco.[57] Therefore, a greater focus of interventions among young adult populations with

mental health disorders could be beneficial for this group, as depression is the most commonly occurring mental health disorders and peaks during young adulthood. [58] Therefore, young adulthood could serve as the best time for prevention interventions or to stop the escalation of tobacco use.

Another important factor in the relationship between mental health disorders and tobacco use is marketing, as it is marketing and not depressive symptoms that predicts subsequent cigarette initiation. Since the early 1950s, the tobacco industry has actively invested in promoting its products, particularly targeting groups that have been economically and socially overlooked. In this pursuit they have closely aligned themselves with selected academic researchers, thereby influencing and shaping research on the association between mental illness and smoking. [59] As highlighted by various researchers, the tobacco industry has actively promoted the notion that individuals with schizophrenia smoke as a form of self-medication. [60] Although scholars have scrutinized the influence of corporate sponsorship on research findings concerning pharmaceutical agents, the bias in tobacco-sponsored investigations is often more subtle. As a result, tobacco industry sponsorship of research in the area of smoking and mental illness has helped support corporate–academic interactions and infrastructures, as well as product-based solutions to such problems as harm reduction and cessation interventions.

The multi-layered risk factors of tobacco use and co-occurring SUDs in populations with mental health disorders who use tobacco, also experience a disproportionate health burden and present a unique public health challenge. By exploring the combination of pharmacotherapy and behavioral support, challenging clinician attitudes and institutional norms, conducting outreach, and creating versatile interventions, this research document seeks to bridge gaps in developing effective tobacco cessation interventions to enhance optimal health for all. One perspective includes acknowledging the effectiveness of combined pharmacotherapy and behavioral support for individuals with serious mental illness in addressing tobacco use. In addition, prioritizing research efforts to understand the nuances of integrating these interventions into mental health care settings and exploring ways to improve their accessibility and utilization can yield positive results.

Our discussions also understand the changing clinician attitudes and institutional norms in shaping the approach to tobacco cessation for individuals with mental health disorders. We emphasize the importance of conducting research to identify barriers and facilitators to implementing evidence-based interventions within mental health care settings. In addition, developing strategies for changing attitudes and norms to create a supportive environment for tobacco cessation was highlighted as an area for advancement. These strategies include the need for undertaking proactive outreach to individuals with serious mental illness for tobacco cessation interventions, investigating innovative methods for identifying and engaging populations with mental health disorders, and recognizing the diversity of settings in which individuals with mental health disorders may receive care. Specifically, the group discussed designing interventions that are adaptable to various environments and considering the unique needs and preferences of individuals with mental health disorders in the development of these versatile interventions that can integrate co-occurring mental health and SUDs on tobacco use.

HIV and Smoking

Tobacco use is higher among people living with HIV, and it is a leading cause of death among people living with HIV compared to their non-smoking counterparts. [52] People living with HIV who smoke face increased risks of developing lung and other forms of cancer, pneumonia, chronic obstructive pulmonary disease, and cardiovascular disease. Furthermore, smoking exacerbates the progression from HIV infection to AIDS and

diminishes the response to antiretroviral therapy. [14] HIV, as a cross-cutting illness, intersects with comorbidities and interactions with health drivers, including serious mental illness. Despite these significant implications, limited research has been conducted to develop or evaluate tobacco cessation interventions tailored for people living with HIV.

The existing evidence suggests that people living with HIV demonstrate a poorer response to conventional pharmaceutical interventions for cessation, which may be attributable to faster nicotine metabolism affecting the efficacy of nicotine replacement therapy. Some studies using bupropion or tailored behavioral interventions have shown a measure of success, but evidence remains limited to make specific recommendations. Thus, there is a pressing need to develop and evaluate tailored tobacco cessation interventions for people living with HIV that take into consideration those with other co-occurring behaviors and comorbidities across different settings. In addition, research efforts should focus on identifying barriers and the development of strategies to effectively integrate tobacco cessation into HIV treatment settings.

SUMMARY

- While overall tobacco use has decreased in the United States and France, certain populations, particularly those with lower socio-economic status, mental health disorders, and specific racial and ethnic groups, continue to experience higher rates of tobacco use and related health issues.
- There is an urgent need for tailored tobacco prevention and cessation interventions for disproportionately affected groups, emphasizing new approaches and outreach that are salient to the intended population, rather than merely adapting existing programs.
- Significant gaps exist in understanding the roles of social support and institutional factors in tobacco use among various disproportionately affected subgroups.
- Integrating qualitative research methods to explore the lived experiences of tobacco users is crucial for developing effective interventions that address the complexities of their social and environmental contexts.
- Shifting research toward practical implementation of tobacco cessation interventions in underserved populations is vital, ensuring that they are not only effective but also feasible.
- Overcoming misconceptions about qualitative research methods and ensuring adequate funding for studies targeting populations that experience health disparities is essential for advancing effective tobacco cessation strategies.

CONCLUSIONS AND RECOMMENDATIONS

Tobacco is a highly addictive substance and the primary risk factor for cancer, as well as the leading cause of cancer-related mortality, significantly affecting public health. The tobacco product marketplace has seen considerable change with the arrival of new types of tobacco products, such as e-cigarettes, heated tobacco products), and more research is needed to gain a better understanding of their use patterns and overall effect on health. New consumption patterns are also emerging, including co-use of tobacco products and other substances (e.g., alcohol, cannabis, opioids), which can further increase the risk of certain cancers.

The United States and other countries are collaborating in the fight against tobacco use by providing dedicated research funding for to inform future efforts and define priorities. This effort has a particular focus on populations who are the most burdened by tobacco use, in line with the work started by Cochrane TAG.

The work conducted by NCI and INCa—in cooperation with experts participating in the scientific workshop—identified two research domains for enhancement: 1) effective tobacco prevention for disproportionately impacted populations; and 2) tobacco cessation interventions that reach and engage these same populations.

This strategic research plan also identifies three approaches for future development:

1. Interventions rooted in science (intervention research, implementation science)
   Accounting for the context of an intervention (for tobacco prevention or cessation): include the target population, integrate a whole-person methodology, and assess the intervention so that it can be readily implemented in other contexts.

2. Measurement and monitoring tools shared among countries

   Continue to monitor tobacco use prevalence and develop better methods to measure frequency and intensity of product use, especially for emerging tobacco products. Further, this could include assessing macro-environmental tobacco control interventions, collecting data on social and regional health differences, cancer epidemiology, the health impacts of tobacco and other co-substance use, and expanding survey data resources in the general population.

   These shared tools strengthen U.S. and international collaborations; however, better measures and sharing of surveillance across countries and common data elements are still needed. (e.g., France's Baromètre Cancer and the U.S. Population Assessment for Tobacco and Health [PATH] Study, the Tobacco Use Supplement to the Current Population Survey [TUS-CPS, the largest tobacco use dataset in United States], the Health Information National Trends Survey [HINTS, focused on health communication in cancer]). Greater consensus is also needed in establishing definitions for common measures (e.g., MTP use and "hard to reach" populations).

3. Insight into perceptions and attitudes among populations about tobacco

   The goals of this research are to propose suitable prevention and cessation strategies, measure the impact of social and economic and other determinants of use, and develop quantitative surveys in humanities and social sciences, epidemiology, and public health (such as the Barometer survey). To accomplish this, a better understanding of what individuals think about tobacco and new tobacco products within a broad continuum (e.g., knowledge, health impacts, harmfulness, regulations, standards) is needed.

This document compiles research recommendations for tobacco cessation interventions and is intended as a decision-making tool to guide research funding agencies and other interested parties, with a view to targeting their research strategy objectives. It outlines a holistic approach to advancing the science of tobacco cessation interventions, focusing on populations that have been disproportionately impacted by economic, social, health, or other risk factors. By embracing the lived experiences of individuals who smoke, leveraging collaboration, and incorporating innovative strategies, this agenda aims to drive impactful research to inform evidence-based interventions, ultimately reducing tobacco use differences and enhancing optimal health for all.

INSTITUT NATIONAL DU CANCER (INCa)

INCa's role is to disseminate knowledge about cancer, produce and share expertise, structure and guide French regional cancer control organizations, analyze data to better target initiatives, and foster scientific and medical innovation. For several years, INCa has been heavily involved in tobacco control research on a national and European level by funding research projects, disseminating research, and participating in joint initiatives.

NATIONAL CANCER INSTITUTE (NCI)

NCI is the United States federal government's principal agency for research, training, and information dissemination in relation to cancer. Within the extramural program of the Division of Cancer Control and Population Sciences, the Tobacco Control Research Branch sets relevant scientific priorities for this partnership with INCa, particularly in the use of tobacco products, including cigarettes and emerging tobacco products, tobacco-related subgroup differences, tobacco control interventions for underserved and at-risk populations, and tobacco cessation interventions at the individual, system, and population levels. In parallel, NCI's Center for Global Health strives to advance global cancer research and training by coordinating NCI engagement in global cancer control and has supported tobacco control research grants in more than 40 countries worldwide.

PARTNERSHIP

INCa and NCI each have their own missions, yet both agencies share several goals and research priorities, and tobacco control is a shared public health priority. Through this collaboration, INCa and NCI are defining scientific areas to inform the research community, that can contribute to our shared goals of ending morbidity and mortality form tobacco use.

PROJECT TEAM

The project team is made up of INCa and NCI, and is part of a scientific and institutional partnership, focusing on tobacco control issues.

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SCIENTIFIC EXPERT CONSORTIUM

This consortium brought together experts in the field of tobacco control research from the United States and Europe to inform the state of the science in the three identified domains It was co-chaired by Dr. Nancy Rigotti (Massachusetts General Hospital/Harvard University) and Prof. François Alla (University of Bordeaux).

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