




Behavioral Research in Cancer Prevention and Control: Emerging Challenges and Opportunities

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Abstract

It is estimated that behaviors such as poor diet, alcohol consumption, tobacco use, sedentary behavior, and excessive ultraviolet exposure account for nearly one-half of all cancer morbidity and mortality. Accordingly, the behavioral, social, and communication sciences have been important contributors to cancer prevention and control research, with methodological advances and implementation science helping to produce optimally effective interventions. To sustain these contributions, it is vital to adapt to the contemporary context. Efforts must consider ancillary effects of the 2019 coronavirus disease pandemic, profound changes in the information environment and public understanding of and trust in science, renewed attention to structural racism and social determinants of health, and the rapidly increasing population of cancer survivors. Within this context, it is essential to accelerate reductions in tobacco use across all population subgroups; consider new models of energy balance (diet, physical activity, sedentary behavior); increase awareness of alcohol as a risk factor for cancer; and identify better communication practices in the context of cancer-related decisions such as screening and genetic testing. Successful integration of behavioral research and cancer prevention depends on working globally and seamlessly across disciplines, taking a multilevel approach where possible. Methodological and analytic approaches should be emphasized in research training programs and should use new and underused data sources and technologies. As the leadership core of the National Cancer Institute's Behavioral Research Program, we reflect on these challenges and opportunities and consider implications for the next phase of behavioral research in cancer prevention and control.

As we celebrate the 50th anniversary of the National Cancer Act of 1971, cancer morbidity and mortality continue an extended downward trajectory (1). Enhanced screening technologies, new therapeutic targets, innovative treatments, and advances in genomic medicine offer the promise of continued reductions in the cancer burden (2-4). Importantly, cancer prevention and control depend greatly on human behavior. People need to engage in guideline-concordant screening and follow physician recommendations, including adherence to US dietary and physical activity guidelines (5,6) and medical regimens. Nearly one-half of all cancer cases are attributable to behaviors such as tobacco use, poor diet, alcohol use, sedentary behavior, and excessive ultraviolet (UV) exposure (7,8).

Accordingly, the behavioral, social, and communication sciences (abbreviated here to "behavioral sciences") have long been essential to cancer prevention and control (9). Tobacco control provides a particularly salient example. Approximately 42% of US adults were current smokers in 1965 (10,11), decreasing to 14% in 2019 (12). Behavioral research contributed to these reductions by, for example, conclusively demonstrating the health and economic benefits of smoke-free laws, higher tobacco taxes, and other policy interventions (13). Behavioral research also helped to document the effects of tobacco industry marketing, inform antitobacco communication efforts (14), design effective cessation interventions (15), and model effects of tobacco control policies on cancer incidence and mortality (16).

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Box 1. Contextual and contemporary influences to be considered.^a

- 1) COVID-19 pandemic
- 2) Health misinformation and scientific uncertainty
- 3) New information technology
- 4) Health equity and attention to understudied populations
- 5) Rapid growth of cancer survivor population

^aCOVID-19 = coronavirus disease 2019

Sustaining such contributions to cancer control will necessitate a rich understanding of the many ways in which the social climate, policy landscape, information milieu, and health-care environment are evolving, along with the use of new research frameworks and tools. The authors of this commentary constitute the leadership of the Behavioral Research Program at the National Cancer Institute (NCI). We reflect here on our perception of where behavioral research in cancer control is going—and perhaps needs to go—given the contemporary context. The goal is not to review the literature on behavioral research and cancer control, which has been accomplished elsewhere (9,17-20), nor to review the program's accomplishments and investments, but rather to look ahead at challenges we foresee and the context within which those challenges will be addressed. In so doing, we consider the entire cancer control continuum (21), given the role of behavior at all phases (primary, secondary, and tertiary prevention).

At the outset, we stress that research on human behavior must account for influences at multiple levels of analysis, not just the individual level (22). Behavior is a function of basic psychological processes, such as cognition, emotion, and motivation, but also of numerous multilevel sociocultural and policy-related factors. This principle is central when considering the profound impact of racism and other social determinants of health on health status and health care. Attempts to address some cancer risk factors at the individual level (eg, using health messaging to increase adherence to screening guidelines) may be ineffective if these efforts do not account for the effects of a complex interplay of factors, including race, ethnicity, culture, and socioeconomic status and the availability of adequate health-care access, insurance coverage, and follow-up care, as well as trust in the health system. For some behaviors, effective interventions need to account for the transgenerational and acute trauma of systemic racism and how it is exacerbated by discrimination, racial residential segregation, under- and unemployment, social unrest, and disinherited identities, particularly for Black, Indigenous, and People of Color (BIPOC) (23-25). In addition, most clinical trials do not include the kind of ample representation of underserved populations that would be necessary to optimize generalizability of clinical preventive services as well as behavioral interventions (26).

Multilevel research considers the role of racism in social and organizational structures, providing a richer view of the context within which cancer risk behaviors occur. Although the value of a multilevel perspective may seem intuitive, multilevel research is logistically complex. Many multilevel frameworks are available to assist, such as the social-ecological model (27-29). Complementing the value of a multilevel approach is the reality that the field benefits most when behavioral research is integrated with research from other disciplines (30,31), recognizing an openness to multiple perspectives (32-34).

Novel Challenges and Opportunities in Behavioral Research and Cancer Control

A strategic and well-conceived approach to behavioral research across the cancer control continuum—from prevention to end-of-life care—must reflect on several elements of the contemporary sociocultural context (see Box 1)

Coronavirus Disease 2019

Particularly salient at present is the downstream effect of the coronavirus disease 2019 (COVID-19) pandemic. On a population level, and particularly among some groups, the pandemic has undermined healthy cancer-relevant behavior patterns (eg, diet, physical activity, social support, and medical adherence to screening and cancer treatments) (35) and may have led to increases in stress and unhealthy behaviors (eg, sedentary behaviors, increased calorie and alcohol intake, and tobacco use) (36-38). Although the pandemic has accelerated interest in and use of telemedicine—a positive development needing further research to assess effectiveness—it has highlighted the effects of economic and health inequities present in access to health care and in cancer treatment, and it has underscored the increasing globalization of public health.

Health Misinformation and Scientific Uncertainty

The pandemic has also brought into sharp relief the potential impact of misinformation and disinformation in social discourse about public health (39,40). It is essential to better understand the public's understanding and trust of information regarding cancer topics such as human papillomavirus vaccination, new tobacco products, and sunscreen use. Communication research can address how best to decrease the spread and impact of misinformation and disinformation. Moreover, because social media is a common platform for dissemination of misinformation and disinformation, it behooves us to better understand how to use social media as an evidence-based communication platform and to do so in ways that maximize privacy and minimize ethical concerns.

Equally important is the need to contend with scientific uncertainty—a problem that has been heightened by not only the COVID-19 pandemic but also numerous other trends, including scientific advances in cancer control. These advances produce promising new interventions; however, their value must be rigorously evaluated through research that is inherently incremental and sometimes produces conflicting information. As a result, scientists often make conservative, contingent statements or render differing opinions, which are often interpreted by lay audiences as noncredible. This and other negative effects of scientific uncertainty can be accentuated by the

dissemination of conflicting information through mass media and social media channels, particularly given that people are more troubled by conflicting messages from opposing sources than by a lack of firm evidence (41,42). Research is needed to understand how patients and the general public interpret and respond to conflicting information and other forms of scientific uncertainty about cancer interventions and how to represent, communicate, and ultimately help people to manage and tolerate these uncertainties. Scientific uncertainty is one of many countervailing sociocultural and economic forces that limit the successful translation and adoption of evidence-based programs and policies. The field of implementation science (43) is well-positioned to help determine how scientific advances are best communicated and implemented in the context of these influences.

New Information Technology

Advances in information technology, computing, and data science have been beneficial to public health in many ways. Big data and new predictive analytic methods, including artificial intelligence and associated techniques like machine learning, as well as the development of wearable physiologic sensors and other personal health devices have increasingly been used to monitor health behaviors and outcomes and develop tailored interventions (44,45). There is potential in securely linking electronic medical records with data collected via novel sensor technologies, assuming privacy and ethical safeguards are in place. Involving users earlier in the development of health behavior applications and interventions (ie, user-centered design) increases impact and enables more seamless sharing of information (34,46).

Health Equity and Attention to Understudied Populations

Many new information technologies are highly dependent on widescale broadband or cellular internet access, which in some populations is an obstacle (47-49). Relatedly, the rapid move from landline to smartphone use—a development that facilitates communication and information access—requires researchers to use novel surveillance methods to collect accurate and representative data that have historically been collected via landline phone interviews. We have yet to fully adapt to this change and will need to do so to maximize representativeness in behavioral interventions.

When feasible, interventions need to be tailored based on the population in question, assuming adequate resources exist. Subpopulations vary on many different dimensions that position them to respond differentially to intervention approaches, as shown in meta-analyses of behavioral interventions that reveal high effect-size heterogeneity (50). Consider that nearly 20% of the US population resides in rural communities, where access to healthy foods, state-of-the-art health care, reliable internet, and other resources is often limited, with downstream effects on cancer and other health outcomes (51,52), thereby limiting the types of interventions that may be attempted in these communities. Optimal population-level strategies to address cancer-relevant behavioral risk factors need to be informed by research on underrepresented segments of the population, suggesting an essential need to evaluate and potentially replicate past findings by including widely generalizable and representative populations.

Rapid Growth of Cancer Survivor Population

Cancer survivors—both in active treatment and posttreatment phases of care—represent a particularly important population for behavioral researchers (53), and attention must be paid to screening and prevention of subsequent primary cancers among survivors. As cancer detection and treatment have improved, both the number and life expectancy of survivors have increased. Consequently, survivors face substantial risks of recurrence and secondary cancers (54) as well as morbidity and mortality from other diseases—notably cardiovascular disease and diabetes (55,56). Greater attention is needed regarding long-term effects of cancer treatment (eg, cognitive dysfunction, pain, peripheral neuropathy); financial implications (57,58) and added pressures on the individual and caregivers; manifestation of other diseases; assistance with decision making in life domains such as family planning and employment; adherence and decision making with respect to both acute antineoplastic and long-term maintenance therapies (59,60); comorbidities that accumulate over time; and effects of cancer and its treatment on perception, sensation, and other intra-individual processes (61-66). Moreover, as cancer survivors live longer, many experience accelerated aging, introducing an important new area of study that may inform our understanding of cancer as well as aging in the general population (67,68).

Behavioral Aspects of Cancer Control

With these contextual factors as a backdrop, several behavioral risk factors for cancer will need further attention over the next several years.

Prevention

Despite enormous progress, cigarette smoking *remains* the leading preventable cause of death in the United States, accounting for approximately 30% of cancer deaths (69). The tobacco control landscape has become considerably more complex over time. Research is needed to understand new tobacco products (eg, electronic nicotine delivery systems, heated tobacco products); changes in tobacco control policy at the federal, state, and local levels; and the impact of rapidly evolving social media and other communication technologies, among other complexities. Laws regulating cannabis are changing, along with the potential to influence patterns of tobacco use among youth and adults. Efforts to improve prevention and enhance cessation of tobacco use among all populations, especially those that are disproportionately burdened by tobacco use and its adverse health consequences, will benefit from renewed attention.

Energy imbalance (sedentary behavior, lack of physical activity, and poor diet resulting in excess body weight) constitutes another key preventable cause of cancer, and substantial efforts have considered the particular role played by obesity in the cancer burden (70,71). Yet there continue to be major gaps in the science. Contrary to classic epidemiological models that identify the health risk of single food items, emergent research focuses on overall healthy dietary patterns as well as timing of consumption (eg, time-restricted eating) (5,72). Recommendations for physical activity are moving away from being generic, instead being “dosed” based on individual profiles (73-75). This development offers a unique opportunity to extend precision medicine principles from medical care settings to interventions focused

on behavioral risk reduction (or what some have called “precision prevention”).

Encouraging more physical activity can have an unintended effect on cancer prevention: increased UV exposure. Indeed, outdoor physical activity is positively associated with melanoma risk (76). Much research on UV exposure has focused on intentional exposure, such as indoor tanning; however, we also need to understand exposure in the context of outdoor physical activity, such as in school and organized sports settings. This is particularly true in adolescent and young adult populations, where outdoor physical activity is common and occurs at an age when risk-increasing sunburns can accumulate (77,78). Research on successful messaging that maximizes the benefits of physical activity and minimizes the harms of UV exposure is greatly needed (79).

Contrary to high public awareness regarding the effects of tobacco use and obesity on cancer risk, the proportion of the population exhibiting awareness that alcohol is a risk factor for cancer is comparably low (approximately 30%-40%) (80). The World Health Organization labeled alcohol a carcinogen in 1988, but only recently has the link begun to receive widespread attention in the research literature and popular media. This emergence has coincided with studies suggesting that potential cardiovascular benefits of alcohol may have been overstated or taken out of context (81). Consequently, more research is needed to understand how best to communicate the cancer risks of alcohol use, particularly to cancer patients and high-risk groups (82-84). We also need to explore the potential of alcohol warning labels and other communication vehicles. Many of the best practices in tobacco control (eg, taxation, marketing restrictions) may be used to reduce alcohol use, with downstream beneficial effects on cancer mortality (85).

Scientific investigation of behavioral risk factors for cancer will continue to emerge, which will in turn accelerate efforts to reduce their impact on the cancer burden. For example, we need to better understand sleep quality—not only as a potential cancer risk factor, but also as a predictor and consequence of other behavioral risk factors (eg, tobacco use, alcohol consumption, physical inactivity). Some evidence suggests that sleep disruption can exacerbate and be exacerbated by tobacco use (86,87). There is also evidence that the potential impact of sub-optimal sleep patterns (88) is worth exploring further in the context of cancer risk and treatment outcomes.

Screening and Treatment

Behavioral research can also inform our understanding of several important features of cancer screening. Shared decision making (SDM)—a process in which patients and clinicians work collaboratively to make well-informed choices based on both the best available scientific evidence and patients’ personal values and preferences—is one key feature of screening (89,90). The Centers for Medicare and Medicaid Services has made SDM a mandatory process in low-dose computed tomography for lung cancer (91); however, SDM remains challenging to implement in clinical practice, and the optimal approaches remain to be determined. Information about the potential benefits, harms, and uncertainties of cancer screening and other interventions can also be confusing and ambiguous, particularly for individuals with low health literacy or numeracy and other sociodemographic characteristics (eg, race or ethnicity, language, poverty, place of residence) that limit access to medical care and information. For example, concepts such as overdiagnosis in cancer

screening are particularly challenging for clinicians to communicate and for patients to understand (92).

The same is true for germline genetic testing for cancer susceptibility, which often identifies “variants of unknown significance.” This problem has been magnified as genetic testing has evolved from single-gene assays (eg, BRCA1/2) to panel testing and next-generation sequencing (eg, whole genome or exome sequencing). Basic and applied behavioral research on risk perception, communication, and decision making can enable the development of interventions that facilitate effective communication and understanding of both the potential outcomes of cancer screening and the results of genetic and nongenetic screening tests and thereby promote SDM (93). Similar research is needed to ensure effective communication and understanding of the results of cancer genomic testing using next-generation sequencing tests, a rapidly disseminating technology that also often generates findings of uncertain clinical value (94-96).

Behavioral research can also facilitate patient decision making about treatment, well-being, and experiences with care. Both in the active treatment and posttreatment phases of care, cancer survivors have various psychological needs that are not only informational but emotional and relational. Fear of cancer recurrence is one major need that often goes unaddressed. Behavioral research can help to better characterize this need and other needs and to develop interventions to address them.

Interplay of Intra-Personal and External Influences

It is important to recognize that many behavioral processes often engage not only explicit, conscious processes but also implicit, nonconscious processes. Dietary choices and other behaviors, such as physical activity, are often a function of environmental cues processed below cognitive awareness (97,98). Policies can help change behavioral norms (99), as was the case for clean indoor air laws. In addition, features of the built environment, such as access to recreational facilities and outdoor space, can promote automaticity of physical activity with differing degrees of thought involved (100,101). For example, neighborhoods with playgrounds and sidewalks present relatively fewer obstacles to leisure-time fitness than gym memberships. This notion is central to the concept of “nudges” that encourage healthier behavior without necessarily requiring much reflection (102), such as defining human papillomavirus vaccination as standard procedure in pediatric checkups (ie, without the need for a separate appointment). Because many of these effects rely on implicit cognitive processes that do not vary greatly across populations, the behavioral effects may be more robust.

It is also important to recognize there are many intra-individual factors beyond behaviors themselves that play a role in cancer risk. Perception, attention, emotions, sensory processes, and interoception (the perception of physical sensations) underlie many health behaviors; for example, an individual’s emotional reaction to physical activity is a key predictor of future engagement (103-106). Cancer neuroscience research can identify brain mechanisms involved in cancer risk factors as well as cancer pathogenesis (107). Identification of underlying psychological, neural, emotional, and perceptual factors is essential to their delineation as targets of intervention and to the successful development and testing of effective interventions.

Of note, many behaviors occur in a dyadic context, as shown by the profound influence of close relationships (eg, parental, marital) on individual health decisions (108). The NCI Family Life, Activity, Sleep, Health, and Eating study has demonstrated that dyadic processes between parents and their adolescent children can have enduring effects on cancer-relevant behaviors of both generations (109). People are also more willing to entertain the notion that their intimate others are at risk than the idea that they are at risk themselves (110), suggesting that dyadic interventions could be more effective at changing health behaviors (111).

New Approaches, Resources, and Methodologies Will Facilitate Research

Tackling new and evolving topics in an ever-changing cultural and information environment is a daunting challenge. Nevertheless, it is one that can be facilitated by a wealth of resources and methodologies that were less available in the past and will need to be maximally harnessed in the future.

Big Data and Predictive Analytics

Behavioral researchers increasingly use big data to address a wide variety of research questions in cancer prevention and control. Big data and new predictive analytic techniques are already being deployed in clinical practice in various forms (eg, machine learning algorithms used to predict and manipulate consumer choice). Some novel data sources and modalities include using search engine trends data to track interest in information about cancer screening choices and using deidentified health insurance claims data to assess treatment adherence (112).

Social media provide a fruitful source of behavioral data, providing a window into how health misinformation spreads and how the stigma associated with risk factors such as obesity (113) may be disseminated and maintained. Data linkages and data integration—facilitated by strategic efforts to harmonize data—can address hypotheses that have been heretofore untestable and lead to better cancer analytics (114,115). In a new data-intensive world, behavioral researchers benefit from informatics and data science methods, such as machine learning, natural language processing, and data mining. Of course, enhanced training models are required to make appropriate use of big data and new analytic tools (116) and to determine how best to quantify, represent, communicate, and manage the uncertainties raised by all such efforts.

One of the most innovative uses of big data is intensive, longitudinal data collected from individuals over an extended period. Ecological Momentary Assessment has been a popular methodology for more than 20 years (117), yet the development of new sensor technologies has facilitated the collection of many behavioral constructs—providing a clearer window into antecedents of behavior as well as potential targets for intervention. For example, one can determine how behavioral variables such as stress and emotion are associated with behaviors such as physical activity over the course of a day (118-120). In recent years, there has been a growing emphasis on increasing the accuracy, precision, and predictive validity of these measures (121). New data sources may help redefine health behavior theories (122), many of which treat key variables (eg, self-efficacy) as static despite the fact that they change and interact over time with factors at multiple levels. Revising health behavior theories is an important pursuit given that focusing

systematically on mechanisms linking behavior change constructs (such as those found in health behavior theories) to health behavior holds relatively more promise for the design of effective interventions (123).

New Research Methodologies

These data sources are accompanied by a wealth of frameworks and methodological tools that remain underused. Although randomized controlled trials remain the gold standard, more nimble study designs and methods, especially in early phases of intervention development, can enable rapid, iterative, and timely development and testing of precisely targeted interventions. Use of innovative designs such as sequential multiple assignment randomized trials, just-in-time adaptive interventions, and micro-randomized trials are being used increasingly to this end (124). In addition, small-scale study designs that allow early proof-of-concept testing can allow intervention strategies to be tested in small numbers of individuals before testing in more costly and time-consuming randomized controlled trials. These designs ensure intervention “failures” are identified early, enabling further refinement. When random assignment is not feasible—for example, when assessing effects of policies or changes in the built environment—natural experiments and other quasi-experimental approaches (125) can provide useful proxies. Behavioral researchers can also take advantage of modeling tools such as agent-based modeling, which has been used to assess social predictors of obesity and tobacco use (126). Recent work has used modeling to determine the potential long-term impact of the COVID-19 pandemic on the cancer burden (due in part to dramatic reductions in cancer screening) (127).

When designing interventions and clinical trials, as well as later-stage implementation in clinical and community settings, behavioral researchers can also rely on several new models to facilitate the translation of their foundational research in areas such as addiction, stress, and physical activity. These models include the experimental medicine approach espoused by the National Institutes of Health’s Science of Behavior Change initiative (128), the Obesity-Related Behavioral Intervention Trials model (129), and the Stage Model of Treatment Development (130). Each of these models recognizes that there are several steps separating foundational research from practice that require careful thought and planning, an exercise facilitated by advances in implementation science (43).

Conclusions

Behavioral research has made many enduring contributions to research and practice in cancer prevention and control (9,131). Devoting close attention to the current sociocultural context will be critical in maintaining those contributions. Over the next several years, research on behavioral risk factors for cancer will need to take into account effects of the COVID-19 pandemic, the presence of misinformation and disinformation and a changing information environment, increasing methodological and technological innovation, and the importance of considering the unique needs of different populations as well as the increasing number of cancer survivors. Taking these factors into account, researchers can advance the field by focusing on how best to accelerate progress in tobacco control among all populations; approaches to energy imbalance that leverage new ways of defining and intervening on diet and physical activity; unintentional UV exposure; alcohol consumption; ideal methods of

communication to inform decisions under uncertainty in the context of cancer screening, genetic testing, and other health behaviors; and the promise of leveraging nonconscious and dyadic processes. Many such efforts will need to account for the long-standing and potent effects of systemic racism.

Fortunately, behavioral researchers have more data sources and methodological tools at their disposal than ever before. For maximal progress, research must take a multilevel, interdisciplinary approach, using findings from basic science disciplines such as the neurosciences, as well as designing interventions with an eye toward implementation. The value of team science has been demonstrated in many contexts (30), and it is increasingly clear that health behavior change and maintenance are best addressed by integrating perspectives from multiple disciplines—both within and outside behavioral research. Team-based approaches also benefit from the involvement of stakeholders such as cancer survivors and policymakers. Training programs in the behavioral sciences should emphasize these values and provide opportunities and training in disparate data sources and underused research designs (115).

Cancer incidence and mortality rates have been decreasing steadily for years (132), yet further gains are attainable. As we celebrate the 50th anniversary of the National Cancer Act, we must remain dedicated to sustaining reductions in the cancer burden for all segments of the population. Behavioral, social, and communication scientists will continue to play an essential role to that end. Adopting a careful, contextualized approach will advance the science and offer critical and lasting gains for public health.

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