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Behavioral Research in Cancer Prevention and Control:

A Look to the Future

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Abstract

Human behavior is central to the etiology and management of cancer outcomes and presents several avenues for targeted and sustained intervention. Psychosocial experiences such as stress and health behaviors including tobacco use, sun exposure, poor diet, and a sedentary lifestyle increase the risk of some cancers yet are often quite resistant to change. Cancer screening and other health services are misunderstood and over-utilized, and vaccination underutilized, in part because of the avalanche of information about cancer prevention. Coordination of cancer care is suboptimal, and only a small fraction of cancer patients enroll in clinical trials essential to the development of new cancer treatments. A growing population of cancer survivors has necessitated a fresh view of cancer as a chronic rather than acute disease. Fortunately, behavioral research can address a wide variety of key processes and outcomes across the cancer controbiol continuum from prevention to end-of-life care. Here we consider effects at the biobehavioral and psychological, social and organizational, and environmental levels. We challenge the research community to address key behavioral targets across all levels of influence, while taking into account the many new methodological tools that can facilitate this important work.

Introduction

Although rates of some cancers have decreased during the past 40 years, others have grown.[1, 2] Cancer remains a leading cause of mortality, with an estimated U.S. economic impact of $263.8 billion in 2010.[3] It is estimated that in 2013, about 580,350 Americans will die of cancer, accounting for approximately 25% of all deaths.[4]

The more general health landscape has also evolved dramatically in that time. In 2010, Congress passed the U.S. Patient Protection and Affordable Care Act, which spotlights prevention and patient-reported outcomes and established the Patient-Centered Outcomes Research Institute (PCORI).[5] The 2009 Family Smoking Prevention and Tobacco Control Act provides the U.S. Food and Drug Administration (FDA) with broad authority to regulate the manufacturing, marketing, and distribution of tobacco products. The U.S. Preventive Services Task Force has revised guidelines for mammography, cervical, lung, and prostate screening. The guidelines call for more shared decisions between physicians and patients

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given the importance of weighing costs and benefits of different screening modalities.[6, 7] Social media and crowd-sourcing platforms have altered the decision-making process and patient-provider dynamic[8, 9]; and the platform for health messages has evolved from print media to websites and mobile applications. Individuals can now obtain access to their genetic profiles (outside of the healthcare system), access personal health records, and share concerns and symptoms with thousands of online acquaintances.

At least three IOM reports[10-12] recognize the need to embrace multi-disciplinary, multilevel, and multiple-method approaches to quality health care and communication directly applicable to cancer control research. National Cancer Institute Director Dr. Harold Varmus observed in a 2006 *Science* editorial that

> concerted national efforts to ensure the vitality of all of the components of modern oncology—academic research, industrial development, and the delivery of new methods throughout the healthcare arena—are essential to an optimistic view of the prospects for transforming an understanding of oncogenic mechanisms into therapeutic benefits for our entire society.[13]

Given the centrality of human behavior to the etiology and management of cancer outcomes, Varmus' sentiments easily extend to behavioral mechanisms and many benefits beyond the therapeutic. In the end, *people* smoke, arrive at diagnoses, communicate risk, use information technology, use (and overuse) screening tests, and implement policies. A cancer diagnosis changes family dynamics, consequential decision-making, and other psychosocial processes.

Hiatt and Rimer's[14] seminal essay on the importance of population science research in cancer prevention and control makes clear that behavior is both a cause and consequence of cancer.[15] Most Healthy People 2020[16] goals center on improvements in health-related behaviors. Any successful cancer prevention and control strategy hinges on the effective application of what is known about the basics of human behavior. In this paper, we consider the promise of research on behavioral processes that cause, prevent, detect, or ameliorate the effects of cancer—processes that include not only tangible behaviors such as tobacco use but also a range of behavioral processes including stress responses, social interaction, and group dynamics. The focus is particularly on topics with the most potential impact (in terms of reduced morbidity, mortality, and healthcare costs), in lieu of focusing on potentially interesting topics with little downstream effect. Instead of critiquing previous work and untenable or unfeasible research paths, the emphasis is on new scientific opportunities for behavioral researchers.

Key Behavioral Targets

Tobacco use remains the nation's leading cause of preventable death, responsible for approximately one third of all cancer deaths in the U.S. Cigarette smoking causes the vast majority of lung cancers, and is causally linked to other cancers including cancers of the larynx, oral cavity and pharynx, esophagus, pancreas, bladder and kidney, cervix, and stomach. Despite decades of progress, about one in five U.S. adults were current cigarette smokers in 2011.[17] These overall prevalence figures mask large disparities in use based on educational attainment, race/ethnicity, geographic region, and other variables.[18] In addition, increasingly available alternative tobacco products such as hookahs and e-cigarettes will present a new set of challenges.

Rising obesity rates continue to capture the attention and concern of researchers, policymakers, health providers, and the media. Recent evidence suggests that 35.7% of the U.S. adult population is obese and an additional 33.3% are overweight.[19] Fewer than 10% of

U.S. adults engage in recommended physical activity.[20] Many parts of the country are considered "food deserts," given lack of access to nutritional foods.[21] Left unchecked, the epidemic of obesity will exact considerable costs on the healthcare system. Obesity has already been linked with numerous diseases including cancers of the breast, colon, and bladder.[22]

Other behaviors that increase cancer risk include human papillomavirus (HPV) exposure,[23] exposure to the sun,[24] and failure to ameliorate environmental exposures (e.g., radon in the home).[25] Moreover, increasing evidence suggests that interactions among health behaviors and other psychosocial experiences (such as stress, chronic depression, and lack of social support) may be related to cancer progression.[26, 27] Health behaviors themselves are intimately linked together by psychological processes such as executive control and impulsivity and by social processes such as peer relationships and socioeconomic status. It is important to understand how health behaviors interrelate, and how to address new health behaviors such as those that emerge from new consumer products.

Once a patient enters the healthcare system additional challenges ensue. Growing demands on physicians and the healthcare system highlight the importance of understanding how to maximize coordination in healthcare teams, reduce medical errors, maintain patient engagement and satisfaction, and keep costs manageable.[28] Patients are increasingly engaged in decisions about their care.[29,30] Many decisions are shared among family members or between patients and physicians, necessitating a better understanding of how these decisions are made and whether they lead to positive outcomes. These include HPV vaccination in adolescents, choice of cancer screening tests, and watchful waiting for slow-growing cancers. Clinical trial enrollment, an important shared decision, is abysmally low (estimates range from 3% to 5% of eligible patients),[31] slowing development of new therapeutic targets and undermining generalizability of clinical trial findings. Finally, as cancer treatments improve and the population of cancer survivors grows, the cognitive and emotional needs of survivors must be met as they re-enter the work force, re-define relationships, cope with other diseases, and make reproductive and other life decisions.

Elucidating the Levels of Influence

Behavioral research can address these and other challenges but must do so from the perspective of multiple levels of influence. Here we consider biobehavioral and psychological, social and organizational, and environmental influences in particular.

Biobehavioral and Psychological Influences

Depression, psychological distress, social isolation, stressful life events, and trauma have all been associated with higher risk of cancer progression and mortality (although less so with cancer initiation).[26, 32-34] Although causal evidence is lacking that would indicate that stress reduction helps to prevent and/or slow the progression of cancer, dampening the stress pathways (e.g., with beta-blockers) does appear to be associated with lower recurrence, progression and mortality of some cancers.[35, 36] When assessing the influence on cancer, new behavioral methodologies and paradigms are needed to capture the highly dynamic contributions of psychosocial experiences that vary over time, within individuals and between populations.[37] Calls from the research and clinical community have risen following the influx of genome-wide association studies for objective quantitative assessments of environmental exposures, including stress, lifestyle factors and behaviors.[37] Combining rich contextual information from the exposome (the comprehensive characterization of an individual's exogenous and endogenous exposure history from conception onwards)[38] with the genome promises to expand our ability to understand the relative contributions of psychosocial experiences and corresponding biological signatures.

Behavioral research can also help in understanding and improving cancer decision-making. People—including physicians—rely on decisional heuristics or "rules of thumb" when making judgments and decisions.[39] Used improperly, these heuristics can produce unfortunate consequences such as overestimation of risk (e.g., believing that one's breast cancer risk is higher than it is) and misuse of base rate information (e.g., ignoring cancer prevalence when interpreting a screening test result).[40] Behavioral researchers understand the factors that influence intertemporal choices (e.g., preferring a smaller short-term gain to a larger long-term gain), and the way in which people cope with uncertainty and ambiguity in predicting future outcomes.[41] This work might provide clues about how to communicate risk in difficult decision contexts, and how to help individuals prioritize health behaviors and navigate new health information.

Basic cognitive processes such as memory, language, and attention help individuals deliver and receive health messages about prevention, side effects, clinical trials, and more. Key attentional processes (e.g., cognitive load, figure/ground contrast, stimuli saturation) influence how people detect stimuli, with implications for clinical practice such as radiography. Language and comprehension are related to how patients make sense of health warnings, consent forms, physician communications, and personal health records. A nuanced understanding of taste, smell, hearing, touch, and vision – and how combinations of these senses interact – can elucidate health behaviors linked to cancer (e.g., smoking, consumption of bitter greens, preferences for fats) and documented side effects of chemotherapy.[42] Despite these possibilities, research connecting basic knowledge of perceptual, affective, and cognitive processes with health behavior and other cancer targets is surprisingly limited.

Health decisions are also influenced by motives such as self-enhancement, social comparison, predictability/control, favorable self-presentation, effective resource management, preparedness for bad news, goal attainment, and existential meaning.[43] These motivational processes easily influence the more basic attentional processes above. For example, the desire to counter potentially threatening information can direct attention toward or away from aspects of that information.[44] Fortunately, intervention efforts that protect the self from threat can reduce defensive responding to threatening health information.[45] More research is needed to help us understand how people balance multiple motives and under what circumstances such intervention efforts work (and why).

Many targets such as obesity are the product of repeated and consistent action such as over-eating and sedentary behavior, highlighting the need to understand not only how and when people *initiate* behavior but also how such behavior is *maintained* over time. A burgeoning literature on self-regulation[46] helps elucidate how people form and carry out short- and long-term goals, and how access to resources (cognitive, relational, emotional and otherwise) facilitates achievement of those goals. This research can be leveraged to address maintenance concerns, such as medical adherence. A timely example where such processes are important is HPV vaccination (for prevention of cervical cancer), which requires more than one dose over multiple visits to be maximally effective.

Social and Organizational Influences

Social-ecologic models provide a useful framework for public health interventions that focus on health behavior change within the population. These models acknowledge individual influences on behavior and mechanisms of behavior change, but also include socio-cultural and environmental influences.[47] Communities (worksites, churches, schools, community centers, military, and healthcare centers) have been highlighted as key settings for many health behavior interventions. More research is needed to identify mediating variables at the

social and organizational level that are most clearly related to the health outcomes and behaviors of concern.[48-50]

The starting point for most health care is a social interaction between patient and provider, which can be influenced by a number of factors including nonverbal signals and establishment of trust.[51] Implicit prejudice can emerge in healthcare interactions with downstream effects on satisfaction, adherence, and health outcomes[52]—thereby fueling health disparities—but little is known about how to prevent these effects. Research on relationship processes demonstrates that social support and intimate relationships buffer the effects of stress on health[53] and cancer survivors depend greatly on, and benefit from, social support.[54, 55] Less is known about how relationships influence everyday behaviors (e.g., how parenting influences adolescent diet decisions). Many health decisions are made by relationship dyads (e.g., patient-physician, parent-child, and spouse-spouse)[56] and yet the preponderance of research on medical decision-making takes an individual approach. Patient-provider interactions, which at one time were focused on one-way media, have become increasingly interactive, participative, and personalized with distinct implications for the design of health campaigns.[57]

Health decisions are also made in the organizational contexts where individuals seek care. Targeted research on medical team functioning can help reduce medical errors and associated costs and improve coordination of care.[58, 59] The current evidence does not yet provide an overarching definition for a well-functioning team; nor is there an evidence base of how to provide incentives for teamwork and what relationship there is between teamwork and cancer care outcomes. [60, 61] For example, within healthcare organizations, research suggests that healthcare workers do a better job when they have clear duties, acknowledged roles, and relational integration.[60]

Environmental Influences

These personal and social factors influence health outcomes within the larger (and richer) context of the information, policy, and product/physical environment.

Information environment—The disruptive influence[62] of a wholly new information environment must be marshaled to extend the reach, efficiency, and effectiveness of cancer control interventions.[63, 64] For example, patients often bring web-based information to clinic visits and providers may not be prepared to integrate this information into their care.[65] Cancer myths can spread virally through social networking sites, making it difficult for consumers to disentangle fact from fiction, or objective evidence from profit-motivated hyperbole.[66] At the same time, content analyses of reputable information sites hosted by government or academic sponsors reveal that the language in these sites is not accessible to all audiences, exposing disparities in health literacy.[67, 68] Continued work is needed to explore ways of supporting better processes of care by re-engineering communication channels and patient workflows within and outside medical environments.[69-73]

Policy environment—Laws, regulations, and political and institutional entities have profound effects on individual and organizational behaviors.[74] For example, in the 1990s, growing health concerns about trans-fatty acids led to policy changes in product labeling and increased consumer demand for reduced trans fats.[50] In an effort to address childhood obesity, policies have come under increasing scrutiny to address unhealthy food options and the amount of physical activity in schools. As policies have changed to reduce unhealthy snack options and sugar-sweetened beverage sales in schools and modify menu labeling to include caloric information, the consumption of healthier alternatives has increased.[74-79] Yet

we are only at the beginning of understanding what types of policies are most effective and why.

Tobacco taxes, smoke-free air, and other policies have long been a powerful force in tobacco control.[80, 81] The importance of tobacco control policy research has accelerated with the enactment of the 2009 Tobacco Act. The Act authorizes FDA to require disclosure of tobacco product ingredients; create standards for tobacco products; restrict tobacco sales, distribution, and marketing; and require stronger health warnings on packaging and in advertisements.[82] Within the framework of the Act, the National Institutes of Health has formed an interagency partnership with FDA to foster tobacco control regulatory research.[83] This research will help FDA understand tobacco and its ingredients and constituents, tobacco addiction, tobacco marketing and labeling, and adolescent tobacco use.

Physical environment—Complementing the communication and policy environment is the larger environment within which most health behaviors take place. These include products that influence health behavior (e.g., novel tobacco products and new foods) and the extent to which the physical environment helps or hinders adaptive behavior. The design of tobacco products is intended to facilitate addiction and long-term use. The wide variety of tobacco products including cigarettes, cigars, pipes, water pipe tobacco, and smokeless tobacco is intended to appeal to diverse consumers. Today, noncombustible tobacco products are often marketed with messages that encourage their use in indoor environments where smoking is prohibited. Dual use of smoked and smokeless products is already substantial,[84] and is likely to grow as consumers face more choices to facilitate and sustain addiction.

With respect to obesity, the design of neighborhoods will influence supermarket accessibility to purchase healthier foods or access to safe playgrounds for physical activity.[85] Environmental changes that improve access, combined with affordable pricing, can reduce the economic disparities of access to healthier foods and have a positive impact on health.[86] We need to better understand the relationship between the local food environment and health, and identify potential points for intervention.[85] In general, there is increased need for research on the macro-environment, including media; technology; food production, distribution, and marketing; urban development and transportation systems; and health systems. Without further research on these outside influences, interventions targeting the individual, home, or local neighborhood will continue to demonstrate minimal to modest effects in producing long-term, sustainable public health impact.[87] In addition, further efforts should be made to strengthen our understanding of key environmental changes that may address the needs of hard-to-reach population groups (e.g., those with lower educational attainment, lower incomes and language barriers).[75,88,89]

Methodologic Innovation

The impact of behavioral research at all of these levels—biobehavioral and psychological; social and organizational; and environmental—requires a keen understanding of methodologic barriers as well as effective use of new methodologic approaches. As illustrated in examples throughout this paper, cancer risk behavior data are increasingly multi-disciplinary and multilevel; as well as dense and longitudinal in nature, which require new analytic research approaches.[90, 91]

Several of the behavioral constructs discussed relevant to cancer control research are difficult to observe (e.g., self-efficacy, relational dynamics), necessitating precise, efficient, and flexible self-report measures. Newly developed methods need to be up to the task. As an example, Item Response Theory (IRT) introduces greater flexibility of administration given the use of computer-adaptive testing (CAT).[92] A benefit of IRT is that existing instruments

measuring the same construct can be co-calibrated with these banks. The result is that any existing instrument can be expressed on the same scale or metric.[93]

It is also becoming increasingly easier to combine measures from more than one study conducted in disparate populations using techniques such as integrative data analysis. Successful data harmonization requires both consensus measure development and co-calibrated measures. It requires research infrastructure, such as the NCI Grid-Enabled Measures portal (GEM),[94] to support sharing of measures and their attributes.

Despite attempts to harmonize health behavior theories or their component constructs, the field has more theories and constructs than ever before (many with limited empirical support).[95, 96] Consequently, the field remains unable to answer essential questions, such as which theories better predict or explain certain behaviors, or what amount of variance is accounted for by specific theoretical constructs.

New measurement and technologic advances may provide better data and improved precision to answer these questions. Experience sampling, or Ecological Momentary Assessment (EMA), and sensor technologies allow us to capture behaviors and their putative effects in real-time and in the proper context. This provides intensive longitudinal data to explain and predict behaviors that may be associated with cancer risk. Using random or event-based prompts, researchers gather participant experiences (such as smoking or eating behavior) throughout the day.[97]

With smartphones, researchers can also obtain location and movement, and audio and video capture.[98] Sensor technologies build on smartphone features by providing automated direct observation. Accelerometer sensors can identify general categories of movements (e.g., sitting, running, walking) and specific targeted behaviors. Body sensor networks provide real-time physiological monitoring capabilities.[99] Additional sensors provide a window into relevant community, environmental, and other multilevel constructs.[100] The datasets that result from these tools require newer analytic approaches such as hierarchical linear models,[101] latent curve models,[102] and time-varying effect models[103] to capture the variability and richness of the data provided. These data also provide the opportunity to use system dynamic modeling, both at the macro[104] and micro[105] level, to model the nonlinear interrelationships of variables over time. New technologies will transform not only measurement and theory testing, but also intervention design. Although technology-delivered interventions may result in less human interaction, they are infinitely scalable with minimal additional cost, and fully maintain treatment fidelity. The wealth of data obtainable from these technologies allows interventions to be adaptable and responsive to behavioral context and prior intervention responses. The advent of mobile, wireless, and near continuous data streams will allow adaptation to interventions not just initially, but throughout the intervention.[106, 107] These advances will increasingly require collaboration among the more traditional social and behavioral science fields with the fields of engineering, computer science, biostatistics, research methodology, mathematical modeling, and biological sciences.

At the same time, use of multilevel designs necessitates a nuanced understanding of how interventions interact (and possibly undermine each other), how their impact may vary over time; and the extent to which interventions are effectively implemented.[108] For example, the traditional epidemiologic model of agent, host, vector and environment is useful for understanding the diverse influences on tobacco use at the individual and population level. As described by Giovino, the agent (diverse tobacco products and secondhand smoke), host (individual user), and vector (tobacco manufacturers), interact in an environment that includes familial, social, cultural, historical, legal, regulatory, economic, media, and other

influences.[109] The integration of these influences is central to the Cancer Intervention and Surveillance Modeling Network (CISNET), a consortium of NCI-sponsored investigators that uses statistical modeling to improve understanding of cancer control interventions in prevention, screening, and treatment and their effects on population trends in incidence and mortality. Such integrated paradigms are necessary to best understand what combination of approaches will be most effective.

Conclusion

Behavioral research has made many important contributions to reduce the cancer burden.[15] In the last 20 years, we have learned how to frame health messages,[110] use new measurement techniques to capture *in vivo* experiences related to cancer risk factors[110], involve communities in health interventions, and much more. Evidence-based approaches that have been shown to alter behavior in some domains can inform other research efforts. For example, increasing taxes on sugar sweetened beverages will likely decrease consumption of these products, just as increasing tobacco taxes on tobacco products has been shown to decrease tobacco use.[80]

Nevertheless, there are several problems that require sustained attention, all of which involve or are influenced by human behavior. The current paper, rather than reviewing past work, identifies several opportunities for new work from disparate disciplines. Research on biobehavioral and psychological influences; social and organizational influences; and environmental influences is necessary to address the behaviors and behavioral processes that increase cancer risk. Behavioral research in decision-making could improve attempts to decrease tobacco use, sun exposure, virus exposure, and controllable environmental exposures; increase physical activity and healthy diets; increase appropriate use of screening and treatment adherence; inform attempts to improve clinical trial enrollment; identify the circumstances under which shared decision making is most beneficial; reduce medical errors; and improve the performance of medical teams. It can yield a better understanding of how health behaviors are associated with psychosocial experiences; and how to design effective and scalable interventions in both public health and in the healthcare setting. Thoughtful research at all levels of influence by researchers who understand mechanisms underlying human performance will be paramount to addressing key outcomes across the cancer control continuum.

Behavioral scientists must become comfortable with new platforms, new data sources, new methodologies, and new conceptual and analytic approaches. In addition, a multi-disciplinary team approach might be more cost effective and may lead to more interventions capable of dissemination. At the same time, behavioral research will only make inroads in addressing key proximal cancer targets by resisting the temptation to focus exclusively on individual psychological processes, given that those processes emerge in a dynamic social, physical, and informational environment. To the extent that behavioral researchers take on these challenges, they will help in meaningful ways to address concerns raised in multiple IOM reports[10-12] about the quality of cancer care, and will advance medicine toward the ultimate goal of decreased cancer morbidity and mortality.

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