

Cancer Prevention from the Viewpoint of UVA Comprehensive Cancer Center

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ABSTRACT

Prevention is a cornerstone of the guiding mission of the University of Virginia Comprehensive Cancer Center, which is “to reduce the burden of cancer for the patients of today, through skilled, integrated, and compassionate care and to eliminate the threat of cancer for the patients of tomorrow, through research and education in an environment that promotes diversity, equity, and inclusion.” We find it useful to conceptualize different opportunities for cancer prevention using NCI’s Health Behaviors Research Branch’s multilevel translational framework. The latter considers three intersecting continuums: cancer control—from prevention through survivorship; translation—from basic sciences to

dissemination and implementation; and level of influence or impact—from genetics to policy. An advantage of this heuristic is that “prevention” is inherently defined as an inter-programmatic concept cutting across basic, clinical, and population science research rather than solely as a programmatic domain of Population Sciences. Through the UVA community outreach and engagement, we apply this multilevel framework to mitigate the social determinants of cancer risk and outcomes that drive cancer inequities in our catchment area. Below, we provide examples of our prevention research and translation along the model continuums and focus on equity.

Introduction

Prevention is the cornerstone of the mission of the University of Virginia Comprehensive Cancer Center (UVACCC), which is “to reduce the burden of cancer for the patients of today, through skilled, integrated, and compassionate care and to eliminate the threat of cancer for the patients of tomorrow, through research and education in an environment that promotes diversity, equity, and inclusion.” Prevention is one of the original mandates of the National Cancer Program signed into law in 1971 by Congress, stating “*that new scientific leads, if comprehensively and energetically exploited, may significantly advance the time when more adequate preventive and therapeutic capabilities are available to cope with cancer.*” (1) In this paper, we use the generic term “prevention” to refer to the spectrum of primary, secondary, and tertiary forms of prevention.

Our approach to cancer prevention can be conceptualized using NCI’s Health Behaviors Research Branch’s multilevel translational framework (Fig. 1; ref. 2), which updates biobehavioral models by the inclusion of genetics, policy,

and dissemination research. Applying this model to the broad field of prevention, we consider three intersecting continuums: cancer control—from prevention through survivorship; translational—from basic sciences to dissemination and implementation; and level of influence or impact—from genetics to policy.

An advantage of this heuristic is that “prevention” is clearly defined as an inter-programmatic concept cutting across basic, clinical, and population science research rather than solely as a programmatic domain of Population Sciences. Furthermore, through our community outreach and engagement, we apply this multilevel framework to help identify and prioritize prevention goals and their optimization to reflect the needs of our catchment area and opportunities for impact to reduce the burden of cancer. Below we describe our catchment area, prevention goals and provide key examples of our prevention research drawing uniquely from each dimension.

Catchment Area Priorities

The influence of our catchment area is evident in the primary, secondary, and tertiary prevention of cancer. The UVACCC catchment area is defined as the geographic region in which approximately 80% of our patients and research participants live. This geographic region constitutes an 87-county region (74 in Virginia and 13 in West Virginia) of 3.2 million people across Virginia and into the eastern portion of West Virginia. The catchment area includes the Appalachian region of far southwest (e.g., Big Stone Gap) and eastern West Virginia; the agricultural regions surrounding Danville in the south; the numerous small to mid-size cities of central Virginia (e.g., Christiansburg, Charlottesville); and the northern reaches

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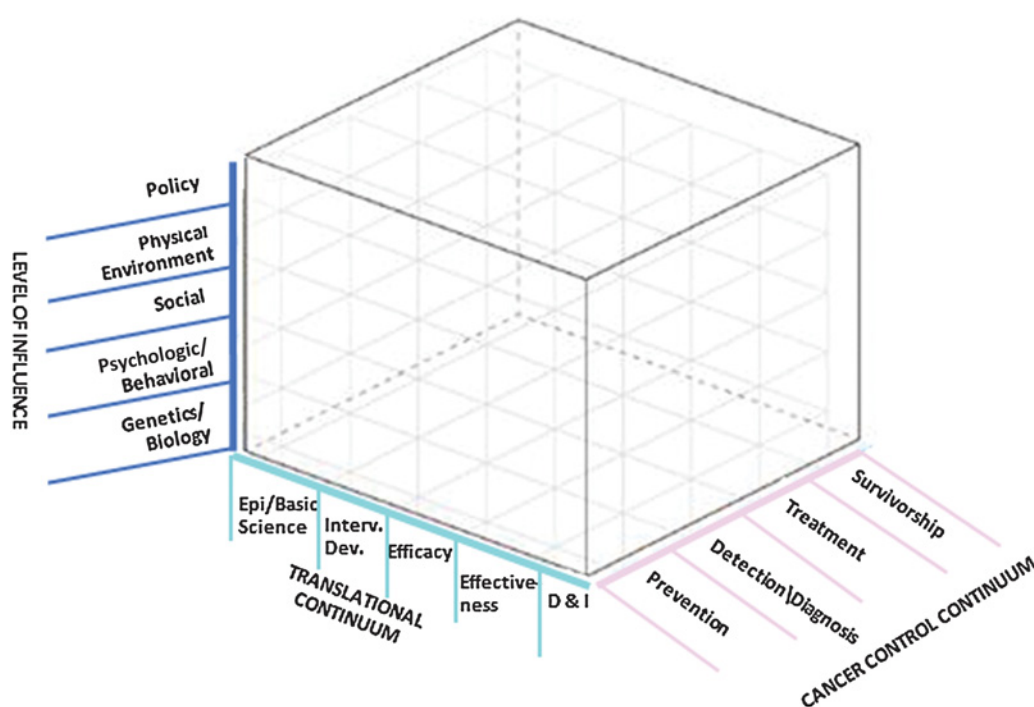


Figure 1. Translational Framework from the NCI’s Health Behaviors Research Branch (2).

of Virginia, including the city of Culpeper. The UVACCC itself is located in Charlottesville, VA, a small urban area with a 2020 population of 47,000 situated in the foothills of the Blue Ridge Mountains. The surrounding Albemarle County adds another 106,000, for a total of 153,000 people in close proximity. However, many patients live distant from the Cancer Center and drive up to 300 miles or five hours, with an average of an almost 2-hour drive each way for an appointment. Significant variation exists within the catchment area in rurality, health care access, socioeconomic status, cancer incidence, morbidity, and mortality. The latter factors are important in understanding our cancer disparities and shaping our prevention initiatives.

Demographics and socioeconomics

Approximately one third (31.6%) of UVACCC catchment area residents live in rural settings, creating vulnerabilities in access to care and lower cancer screening rates. Demographic distributions of race/ethnicity, rurality, and poverty status vary widely by geographic region and contribute to important regional cancer disparities. Overall, 11% of catchment area residents are Black; 4% are Hispanic; 2% are Asian; and less than 1% are Native American. However, the Black population ranges from 3% in far southwest Virginia (Appalachia) to 22% in southern Virginia. In southwest Virginia, only 16% percent of the population has a bachelor’s degree or higher, while 36% of the population in central Virginia have obtained this level of education.

Cancer burden

Compared with the US as a whole, the UVACCC catchment area has a disproportionate burden of cancer mortality in several cancer types despite lower overall incidence, including higher age-adjusted mortality of lung and colorectal cancers (Table 1). In addition, our catchment area has significant

Table 1. Cancer incidence and mortality.

Cancer site	Mortality	
	UVACCC catchment area	U.S.
All	175.2	161.0
Colorectal	16.2	14.2
Lung	49.2	41.9

Cancer site	Incidence	
	UVACCC catchment area	U.S.
All	422.5	448.0
Colorectal	40.4	38.7
Lung	66.8	59.2

^aAge-adjusted Incidence Rate calculated using the VA Cancer Registry data 2011–2015 for the catchment area counties in Virginia and the NCI State Cancer Profile data 2012–2016 for counties in West Virginia (Rates calculated using SEER*Stat. Population counts for denominators are based on Census populations as modified by NCI. The 1969–2016 US Population Data File is used for SEER and NPCR incidence rates).

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concentrations of cancer or “hotspots” with generally poor prognosis, such as higher incidence and mortality of melanoma in western Virginia and higher rates of advanced-stage breast cancer in the southern region. Other forms of cancer stand out from their excess in specific regions based on population and economic contextual factors. For example, in the Appalachia portion of our catchment area, cervical cancer incidence and mortality are highest compared with non-Appalachian and more affluent regions. In the southern region of our catchment area, with higher Black populations, prostate cancer mortality is higher, as is breast cancer mortality, than what is observed in other regions.

Unique challenges and strategies

Together, the unique patterns and differences in cancer types, population conditions, and contextual factors point to barriers in access to care and services, and social and behavioral risk factors resulting in a likelihood of later stage diagnosis and a poorer prognosis. Each of these underlying barriers or vulnerabilities have strong prevention opportunities including programs and research aimed at decreasing behaviorally based risks such as smoking and obesity, and genetic-based risks; improving uptake of screening services and follow-through; and supporting patients with advanced cancers in communities who might otherwise lack services. We use geospatial analyses of population and community-level data (i.e., cancer registry data, survey data, and health-care claims data) and catchment area survey data as important tools to identify cancer disparities at the community level or region, and then seek to understand how this disparity can be reduced or even eliminated. For example, many rural counties in our catchment area have a smoking prevalence at or above 30%, far exceeding smoking prevalence across Virginia (16%) and the US (17%). Ecological correlates of this high tobacco-linked cancer burden are an undersupply of preventive services and public health supports that discourage the adoption of smoking or help with cessation. Approximately 38% of the adult population in poor and underserved counties meet the Centers for Disease Control and Prevention’s (CDC) classification of obese (3), compared with 20% in Virginia as a whole and 31% in the US overall. Food deserts, food insecurity, and commercial promotion of unhealthy diets are of concern. Overall, more than half of the catchment area is classified by HRSA as medically underserved, which translates to lower uptake of recommended screening services and follow-through, and barriers in accessing services to lower cancer risk.

To overcome barriers of distance and lack of supply of local preventive services and support for risk factor modification, the UVACCC has developed prevention research infrastructures to more efficiently translate cancer prevention to people and communities in need. One of these is our Center for Behavioral Health Technology’s *Cancer Hub* which focuses on developing and evaluating cognitive behavioral therapy (CBT) interven-

tions delivered over the internet and on mobile platforms. These pioneering studies are designed to adapt evidence-based CBT for health risk and access through highly interactive, tailored, and engaging web- and mobile-based programs. To locally base community-participatory research in Southwest and Southside Virginia, we have our Community-Based Health Equity Research Center located in rural Christiansburg, VA. This infrastructure is focused on enhancing support for lifestyle cancer risk factors in rural populations using models of community-based participatory research. A third infrastructure is our support for an alliance of Federally Qualified Healthcare Centers (FQHC) serving our catchment area to conduct clinic-based participatory research emphasizing preventive services.

Prevention Research Aims and Advances

Comprehensive community programs for cancer prevention and control effectively reduce cancer risk and disparities in survival. Adapting a multilevel translational framework for cancer prevention as depicted in **Fig. 1** and applying it to our catchment area needs, we have initiated several key research and outreach aims at UVACCC, exemplified below by their levels or combinations of translational dimensions addressed (i.e., location within the continuums of cancer control, translation, and level of influence).

Prevention/ dissemination and implementation/behavior

This level of prevention research is focused on the cultural adaptation, dissemination and implementation of evidence-based interventions designed to reduce cancer risk, with an emphasis on rural and underserved regions where there are barriers to adopting evidence-based practices. Key examples of current work at UVACCC include research collaborations with FQHCs to reduce cervical cancer risk in Appalachia (P01CA229143) and implementation research with patient navigation for colorectal cancer screening (Jeffress Foundation grant, and ACS).

Prevention/efficacy/behavior

Research within this intersection of prevention is aimed at developing novel interventions to reduce cancer risk factors such as obesity and to promote smoking cessation in rural populations. Our Community-Based Health Equity Research Center is testing and adapting a series of behavioral interventions called SIPsmartER (Zoellner; ref. 4) aimed at reducing excessive consumption of sugar-sweetened beverages, a major source of excess calories in obesity. To expand dissemination in Appalachia, this team is adapting SIPsmartER using an innovative e-health platform called iSIPsmarter guided by the RE-AIM framework (R01 MD015033). Another key of prevention research is to increase the efficacy and reach of interventions for smoking cessation and nicotine addiction in

underserved rural populations, a major barrier and cause of excess cancer in our catchment area. Advances in access to cessation support gained from tobacco quitline interventions can be translated to reach a broader base of smokers who are “not ready to quit” but who are contemplating quitting (Klesges, Little and Talcott R01 CA193245). While approximately 70% of smokers may contemplate quitting in a 12-month period, only 10% to 20% meet the criteria of most smoking cessation programs, which include a firm intention to quit within the next 30 days. Likewise, to overcome the barrier of nearly sole reliance on primary care practices to initiate ‘ask, advise, and connect’ with patients who smoke, UVACCC researchers (Little, R01 CA267963) are adapting the provision of this preventive service by local independent pharmacies servicing rural regions with high tobacco use (5).

Prevention/epidemiology/genetics, biology

The goal of this nature of prevention research is to identify and characterize novel risk factors through molecular and epidemiologic research that advances our understanding of how disparities in cancer risk and etiology arise at the cellular or mechanistic level. An example of UVACCC research in this area is the work of Casey, Duvall, and Li (6) in testing the impact of environmental risk factors (ethanol, aspirin, calcium, etc.) on gene expression and differential patterns of expression between right and left colon that are noted in racial disparities of colon cancer. Exposure of 3D organoids to several known environmental risk factors *in vitro* revealed differences in downstream gene expression between organoids derived from the left versus right colon, supporting growing evidence that cancer risk factors differ across the colon. In another example of prevention aimed at cancer etiology, Yan uses mouse model-based systems to mechanistically study the impact of exercise, energy balance, and insulin sensitivity relevant to cancer risk and prevention (7).

Treatment/effectiveness/policy

The research focus within treatment, efficacy, and policy is tertiary prevention, aimed at reducing the effects of cancer once diagnosed through optimal access to cancer treatment and its management. Within health services research (HSR) frameworks, we access large patient databases such as Surveillance, Epidemiology, and End Results (SEER), Medicare and Medicaid, and electronic medical records (EMR) data, as well as primary data collection needed to test hypotheses about the effectiveness of therapies and treatment approaches, including access to care in rural settings. Examples of our HSR research include real-world studies evaluating outcomes of guidelines recommending omission of radiotherapy in older women treated with adjuvant endocrine therapy at risk for nonadherence to long-term endocrine therapy regimens (8) and the study of facility factors (policies, practices, and resources) in the uptake of mammograms in underserved rural Appalachia (Anderson, RSGI-18-224-01), and real-world patterns in the effective use of CDK4/6 inhibitor therapies (Anderson, RWIA-21-123-01). We examined time and activity-based costs of

radiation therapy for cervical and prostate cancers within rural regions of our catchment area and found significant discrepancies between brachytherapy treatment costs and reimbursement rates. This finding offers an explanation for the disappointing trends of poor compliance with the potentially curative modality of brachytherapy and is now stimulating intervention designs (9).

Survivorship/efficacy/psychologic

A final (but not exhaustive) key example of prevention research is also tertiary, but focused on the needs and processes of survivors after active treatment, outside the walls of the cancer center, within the community. A major focus, inspired by the needs of our catchment area, is our concept of a “Cancer Center without Walls.” Under the latter, we are testing the use of momentary assessments, web-based platforms and smartphones in cancer survivors to lower barriers to timely and optimal therapies that support self-care, adherence, symptom management, and improve wellbeing. This includes the use of mobile and wireless technology to optimize pain management among cancer survivors and their caregivers, and monitoring adherence among women with breast cancer using smartphones, wireless medication event monitoring systems, wireless beacons, and wearable sensors that collect continuous adherence assessments (R01 CA239246). A UVACCC research team developed an interactive program for mobile technology platforms to monitor and treat episodes of depressive affect in cancer survivors using a scalable suite of mobile apps. This intervention effectively reduced general distress and symptoms of depression and anxiety over a 7-week study period compared with usual care (10).

Dissemination and Impact

Disseminating evidence-based findings and best practices to community organizations and individuals in our catchment area is an essential component of our strategy for cancer prevention. The cornerstone of dissemination is through our extensive community partnerships and a vibrant network of community advisory boards (CAB). Our primary CAB consists of 22 individuals representing all areas of our catchment area, including health centers, community groups, and individuals who are cancer survivors and caregivers. This CAB reviews research proposals and results, advises the cancer center on dissemination activities and reviews prevention objectives in our cancer center-wide strategic plan. A good example of our dissemination strategy is through our Community Profiles. These are snapshots of the cancer and risk factor burden throughout the catchment area based on the cancer center’s survey. Each community receives its own profile, which is used to set collaborative priorities for prevention activities.

Conclusion

Substantial progress in reducing and eliminating cancer disparities and optimal care of cancer can be achieved

across an expanded framework of prevention that includes intersecting continuums of cancer control, translation, and level of influence. It is critical that prevention research is broadly conceptualized to include basic, clinical, and population sciences, and guided by community engagement and detailing (a process of tracking and reporting community patterns and risk factors). We continue our work to reach and meet the needs of our

catchment area and beyond to reduce the burden of cancer.

Authors' Disclosures

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