

An Overview of the National Cancer Institute's Initiatives to Accelerate Rural Cancer Control Research



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Introduction

A recent publication by the Centers for Disease Control and Prevention (CDC; ref. 1) reported that nonmetropolitan rural counties had lower 5-year annual age-adjusted cancer incidence rates (2009–2013), but higher average annual age-adjusted death rates (2011–2015) for all cancer sites combined compared with nonmetropolitan urban and metropolitan counties. In addition, nonmetropolitan rural counties had higher incidence and death rates for cancers associated with smoking (e.g., lung and laryngeal cancers), and higher rates of incidence of cancers that can be prevented by screening (i.e., colorectal and cervical cancers; ref. 1). These numbers are comparable with the recent Annual Report to the Nation on the Status of Cancer (2), which stated that incidence and mortality rates overall are decreasing in the United States, but did not specify the rates in rural communities. Other studies have also shown that there are significant rural–urban differences in cancer incidence and mortality rates in the United States for certain cancer types, exemplifying the disparities in cancer prevention and control between rural and urban populations (3). Not only do people living in rural areas experience challenges to accessing health care services (4, 5), but also have higher rates of risky health behaviors such as tobacco use, alcohol consumption, physical inactivity, poor diet, and lower adherence to cancer screening and human papillomavirus vaccination (5–8), placing them at an elevated risk of preventable and screenable cancers (1, 9, 10). To better understand and improve cancer control in rural communities across the continuum (prevention, screening, diagnosis, treatment, survivorship, end-of-life), the NCI conducted an assessment of the current state of research through a progressive series of portfolio analyses, meetings, and funding opportunity announcements.

As one example of the NCI's recent efforts, the Division of Cancer Control and Population Sciences (DCCPS) undertook an in-depth analysis of its extramural research portfolio over the past 5 years and found that approximately 3% of the division's portfolio focused on rural populations. This is in contrast to the fact that 14% to 19% of the U.S. population resides in rural communities (3). These findings, as well as the growing cancer disparities noted previously, provided impetus

for the NCI to increase its investment in rural cancer control research and initiate strong partnerships with other national health agencies in this domain.

To further understand the challenges of conducting rural health research, a one-day meeting, "Understanding Definitions of Rural/Rurality: Implications for Rural Cancer Control," was held on October 27, 2017, at the NCI. This meeting brought together representatives from various federal agencies and the extramural community to discuss the varied definitions of rural residence and rurality, and consider how NCI could strengthen support for research on rural cancer control. At the meeting, speakers from the U.S. Department of Agriculture (USDA), Health Resources Service Administration (HRSA), National Center for Health Statistics, CDC, and the U.S. Census Bureau presented overviews of "rural" definitions and their contexts of use. Researchers working in the field also presented their respective region's cancer burden and the challenges that come with defining and conducting research in special rural areas such as Appalachia, the Delta, Alaska, and American Indian Reservations. With the myriad of rural-oriented definitions discussed, it was recommended that NCI and extramural researchers consider rurality as a continuum rather than a dichotomous distinction (i.e., urban or rural, metropolitan or nonmetropolitan), and that depending on the goal, multiple dimensions should be defined and used (11–13), including population density, distance to an urban area, and overall number of people living in an area.

In extending its commitment to understanding measurement and data collection issues in rural communities, NCI, in partnership with the NIH Office of Behavioral and Social Sciences Research and the National Institute on Minority Health and Health Disparities, supported a meeting hosted by the National Academies of Science, Engineering, and Medicine focused on "Improving Health Research on Small Populations." Across the one-and-a-half-day public workshop held in January 2018, panelists and attendees discussed the challenges with conducting health research in small and/or underrepresented populations (14). Participants considered innovative ways to address accessibility, logistical, and cost issues through discussions focused on novel methodologies for data collection, study design, and statistical analysis.

Following these two workshops, the NCI focused on creating rural cancer control funding opportunities to help build research capacity across NCI-Designated Cancer Centers and the extramural research community. In spring 2018, an administrative supplement opportunity directed at NCI-Designated Cancer Centers solicited applications focused on developing cancer control research capacity in rural communities with special attention to remote/isolated rural counties. The funding opportunity emphasized the need for applicants to design programs in collaboration with local clinics and community organizations serving low-income and underserved rural or

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Native American populations, and utilize evidence-based cancer control programming with a focus on sustainability. One or more stages of the cancer care continuum could have been a focus of the supplement application, depending on the needs of each rural community (e.g., increased cancer screening, improved survivorship outcomes). The NCI awarded 21 supplements in the fall of 2018. One of the outcomes of this funding opportunity was the creation of a consortium of NCI-Designated Cancer Centers that will share resources, best practices, and lessons learned in building rural cancer control research capacity across the United States.

Simultaneous to the NCI-Designated Cancer Centers' supplement announcement, an R01 funding opportunity focused on "Improving the Reach and Quality of Cancer Care in Rural Populations" (<https://grants.nih.gov/grants/guide/rfa-files/RFA-CA-18-026.html>) was announced to the extramural research community. The 5-year awards will allow for two types of research focused on low-income and/or underserved rural cancer populations: (1) observational studies that also include pilot testing of an intervention, or (2) intervention research studies that address known predictors of cancer disparities in rural low-income and underserved populations. Applications are encouraged to address cancer care delivery challenges in rural populations, including access to care barriers, social determinants of health, limitations to information technology, mistrust of the medical system, lack of coordinated collaborative care between oncology specialists and primary care, and discordant cancer care, among other issues. Similar to the supplement opportunity, applicants are expected to collaborate with community stakeholders and rural health care delivery partners as well as other grantees.

To continue the momentum established by the previously described initiatives and further address the challenges and opportunities faced by researchers in rural cancer control, the NCI hosted a national meeting on May 30–31, 2018, on the NIH campus that brought together academic researchers, medical and public health practitioners, federal scientists and staff, and community organizations. The goals of the meeting were to (1) identify gaps in research and practice in rural cancer control, (2) build partnerships across the country and various health-related entities to address challenges and disseminate solutions, and (3) highlight and identify methods to address competing and common agendas of health care providers, health systems, researchers, cancer patients, and community members (<https://cancercontrol.cancer.gov/research-emphasis/meetings/arcc-meeting.html>). Conference speakers represented NCI and other national agencies' (e.g., HRSA, USDA, National Rural Health Association) as well as rural communities from across the country (e.g., Appalachia, Delta, Navajo, Alaska, Hawaii, Colonias), providing in-depth examples of priority intervention areas, successful research outcomes, and impactful community-based collaborations. Herein, we highlight key discussion points and recommendations from the conference sessions that elucidate the opportunities and challenges to accelerating rural cancer control.

Meeting Recommendations

The conference discussions varied in topic area; however, each focused on the challenges, opportunities, and recommendations for successfully accelerating rural cancer control. Summaries of

the main discussions around defining rural populations, surveillance and epidemiologic research, methodologic challenges, the use of multilevel interventions, and the role of implementation science in rural cancer control are summarized below.

Defining Rural

Different government agencies define rural–urban classification codes based on either county, Census tract, or aggregation of zip codes. Previously, DCCPS did not request investigators to provide a definition of rural or carefully identify the geographic boundaries of the population or community in which research teams were working. As stated in the two recent funding opportunities and moving forward, DCCPS has adopted the USDA Economic Research Services' 2013 Rural-Urban Continuum Codes (<https://www.ers.usda.gov/data-products/rural-urban-continuum-codes/documentation/>). This classification differentiates metropolitan counties by the population of the area and nonmetropolitan counties by the degree of urbanization and adjacency to metropolitan areas, with codes 4 to 9 all considered nonmetro counties. Through the adoption of a single definition of rural, cancer control efforts at NCI can focus on areas with the greatest need. The recommendation was to not have a dichotomous understanding of rural/urban, but a more continuous measure of rural that specifies the areas being studied within the codes 4 to 9. DCCPS chose a county-level classification also used by the U.S. Census over the use of a zip code classification, which is commonly collected on surveys. County-level classification has significant limitations, especially given the large variation in county size within and across states. Zip code boundaries, however, can change as post offices close in smaller rural areas (15). In the future, the definition will need to be revisited as methods and data sources evolve, and adapted to the changing nature of rural communities, their geographic context, and evolving cancer control priorities (11–13).

Surveillance and Epidemiologic Research

Despite recognition of the socioeconomic, access to care, and behavioral risk factors that contribute to increased cancer incidence and mortality rates among rural populations, challenges persist in addressing these risk factors and improving cancer control (4, 10, 11, 16). Populations living in these communities are often heterogeneous, with individuals representing many different racial/ethnic groups, cultures, and historic experiences, and each carrying different cancer burdens. Language differences often exist among these diverse populations, with rates of low health literacy compounding communication barriers. Although these challenges persist in rural regions across the country, researchers have found opportunities to work hand-in-hand with communities to successfully improve cancer control efforts (17, 18).

One recommendation culminating from the meeting is for researchers to focus on the multilayered granularity of regional data, within the context that people live. In addition, it is important to understand the issues within the larger system of rural health care delivery and reimbursement systems. Especially important to understand in the rural setting are the differences among rural health clinics, critical access hospitals, Federally Qualified Health Centers, and private practices. Each of these health care systems operate under different state and federal laws and regulations, with varying sources and levels of reimbursement for services provided. These highly complex sources of variation

complicate the task of understanding geographic variation in healthcare access and outcomes.

Utilizing existing systems and infrastructures that can facilitate identification of at-risk communities and areas of greatest need is warranted. Cancer registries at the state and national levels can provide accurate, cancer-specific rates, enabling researchers to design their studies to focus on cancer control programs in vulnerable areas. Tumor registry data can often be linked to other data sources such as health insurance claims and patient experience surveys (19, 20), providing even greater insight into the population of interest. Local population health assessments such as those conducted by NCI-Designated Cancer Centers in their respective catchment area communities can also be insightful in identifying and intervening on local cancer disparities (ref. 21; <https://cancercontrol.cancer.gov/brp/hcirb/catchment-areas.html>). For example, recent assessments have identified quality of care and survivorship care issues in rural communities as lacking in adequate rural research.

Culturally tailored interventions have been successful in increasing screening rates for colorectal, breast, cervical, and lung cancers in various rural regions (22–25). Community outreach and engagement are also crucial to the success of cancer control efforts (21). When members of rural communities are invested in local cancer control efforts, participation in screening and lifestyle change programs (e.g., tobacco cessation and exercise programs), cancer clinical trials, and research in general increases. This also leads to sustainable practices that can continue after the research has ended, to help improve health care to the broader community.

Methodologic Challenges

An important component in conducting effective research across the cancer continuum in rural communities is to apply the appropriate study design and related methodologies. Relevant and novel methodologies have been utilized in successful health studies conducted on small populations, and have the potential to be adapted to rural health settings (26). There are many approaches that extend beyond traditional methods that are statistically well understood, allowing researchers to make accurate statements about a population, such as venue-based sampling (14). From the identification and recruitment of patients, to intervention implementation and data collection and analysis, traditional strategies have been expanded to allow diverse methods to be used when appropriate.

Context is an important factor to consider when looking at health and cancer. Individual context is often incorporated into analysis to control for complex interactions among social, political, cultural, and economic conditions that are not specific to the individual, but may affect individual outcomes. To make informed decisions, two aspects of context, the scale at which a context operates and relevant boundaries delineating where a contextual effect is expected to operate, should be considered. Mis-specifying contextual scale is a classic example of Simpson's Paradox in which competing effects may cancel each other or lead to inaccurate representations of conditions shaping a particular health effect (27). It is important to note that even when scale is accurate, it may not be useful and could potentially mask or magnify the health issue being examined. Boundaries are also critically important and not always clearly defined. Often whether someone is considered "in or out" matters with regards to context (28). To advance the use of

context in rural health research, it is important to understand how context changes with scale, and to quantify uncertainty associated with the boundaries one chooses to use.

One recommendation to overcome methodologic challenges while working in rural populations is to consider incorporating qualitative work that can complement quantitative efforts. This is an important consideration with the use of emerging technologies and increase in interdisciplinary research (e.g., medical anthropology, sociology, demography, geography). When designing sampling schemes or data collection, tradeoffs are made with inference and generalizability. The previously mentioned National Academies of Science, Engineering, and Medicine report (14) has suggestions for working with small populations for observational and intervention studies. With the increasing set of options to consider when making analytical decisions, it is important that contextual considerations, ethics, and issues of anonymity are considered when conducting research on small groups such as rural populations.

Multilevel Interventions

Implementing interventions at multiple levels in rural areas, from the individual patient to the community level, has led to greater success in cancer prevention, screening, detection, and treatment adherence and uptake. Gaining buy-in to be part of the research (trial or intervention) from the level of patients and health care providers is often a difficult task, and is most likely combined with external challenges such as economic conditions of the community, poor standardization of electronic health records, and access issues for patients. Careful steps should be taken to ensure the successful delivery of multilevel interventions. Engagement from health care providers is crucial to successfully implementing cancer control intervention efforts. Although limited by time and resources, engaging staff and providing health care professionals with the necessary training to correctly implement and sustain an intervention is essential. Incorporating tailored interventions that suit the provider's needs, such as telemedicine infrastructure and support or mobile health options to assist with screening, cancer symptom management, and survivorship care, creates strong relationships that intertwine the needs of the researcher and health care provider (29). An example of a recent infrastructure effort to improve cancer-related outcomes in rural Appalachia is the L.A.U.N.C.H. (Linking & Amplifying User-Centered Networks through Connected Health) project (<https://www.fcc.gov/health/cancer>). The NCI partnered with the Federal Communications Commission to launch the program in 2017, with the aim of increasing broadband access and adoption in rural areas and assessing how connectivity can be leveraged to improve symptom management for rural cancer patients.

A recent study has shown that when rural patients receive the same treatments as their urban counterparts, and therefore issues with access to care are eliminated, disparities in outcomes are also eliminated (30). It is important that interventions implemented at the hospital or clinic level are uniform to those implemented in other areas, but tailored to reflect the rural environment. With regard to individual-level interventions, rural cancer control efforts should be culturally and personally tailored with fidelity to fit the person's needs, rural lifestyle, and the rural context (31). Patients engaged in the research from the early planning and implementation stages often feel their needs are heard and met, leading to greater participation.

Role of Implementation Science

Recommendations in this area include understanding how sustainable evidence-based practices and interventions work in rural communities with changing context and how these practices can be adopted and evolve over time. In rural communities, interventions can be scaled up across systems and networks, and should also be deimplemented when practices and interventions are proven ineffective or dated. It is equally critical that interventions are both created in rural communities, and adapted and implemented appropriately from other communities according to scale (31). Context is critical in the sense of implementation, in that an evidence-based intervention is only useful when it can be properly adopted, delivered, and received within a particular population (31).

Whether it be through community hospital networks or practice-based research networks, solidifying relationships with reliable partners is crucial to success. To scale up and extend efforts into hard-to-reach communities, outreach programs specifically tailored to the rural communities have been successful in expanding and implementing screening and prevention programs (31, 32). It is important that the interventions and care being disseminated are of high quality and incorporate measurable outcomes and comprehensive evaluation strategies. When thinking about scale-up efforts, researchers should consider the fact that there are multiple levels of impact. At the individual level, researchers should consider reach, efficacy, and effectiveness when scaling up, whereas adoption, implementation, and maintenance are key when thinking of scaling up at a larger setting level (33).

Realizing that implementing cancer prevention or screening programs adds time and use of resources to the providers' and health care systems' daily workload is important. Providing the economic resources needed to support facilities and planning for sustainability of a project is key. Establishing monitoring and evaluation systems, along with the incorporation of goals that span from immediate to long-term, has been shown to help with successful multilevel implementation efforts (34). External community partners from domains outside of cancer control and health care, such as social services, housing, faith-based organizations, and community development, are needed for interventions to scale up in rural areas. Researchers should focus on the adaptation and implementation of cancer prevention, detection, and treatment interventions to a broader community level. The partnerships and collaborations established within the community enable the interventions to be successful and sustainable.

Future Directions

The workshop "Accelerating Rural Cancer Control Research Meeting" served to identify both gaps and opportunities in rural cancer control research and was one component of a larger strategic agenda for NCI to hear from the research and practice communities on how to best advance the field of rural cancer control. NCI understands how vital partnerships and collaborations with other federal, state, and local agencies are to make an

impact on cancer control efforts in rural populations. A special recognition goes to HRSA's Federal Office of Rural Health Policy, which has facilitated numerous meetings between NCI and key stakeholders across the United States. Similarly, workshop discussions alluded to the need for researchers in the field to partner with other disciplines and incorporate a collaborative approach when studying rural populations. The field is heterogeneous and multisector in nature, and investigators are unable to understand the complexities of the population without knowledge of geographic, socioeconomic, historical, behavioral, and cultural factors.

In addition to the use of interdisciplinary research methods, the need for diverse cancer control partners from multiple sectors to collectively work together was emphasized. Community organizations, academic institutions, cancer centers, state and federal programs, rural health and policy agencies, and nonprofit organizations each have different purposes and goals concerning cancer, but all share the common foundation of improving cancer control and addressing disparities in underserved rural communities. Taking this into consideration, it is important that research and study designs align with specific questions and hypotheses that address the needs of academic and rural health practitioner constituencies and community representatives.

With an extensive portion of the meeting focused on the dissemination and implementation of evidence-based health practices and policies in rural areas, researchers restated the need for customizing and personalizing these practices, but also the need to scale up. A fundamental part of science is generalization, but it is important to avoid ill-informed over-generalizations when considering rural cancer control efforts. The goal of scaling up and generalizing is to find the underlying common mechanisms that different populations share, and the lessons learned that can be applied to other rural populations, while keeping local context in mind.

Moving forward, NCI will continue to engage national, state, and local research and practice communities for input and guidance on how best to move the field of rural cancer control forward. Increasing the development and adoption of evidence-based cancer prevention and control interventions and improving the delivery of high-quality cancer care are key components of the larger rural cancer control research agenda. The initiatives developed will provide a foundation for cancer and public health communities to progress forward with the most effectively targeted investments to accelerate rural cancer control.

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No potential conflicts of interest were disclosed.

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