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Opportunities for Cancer Prevention During Midlife:

Highlights from a Meeting of Experts

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Abstract

This paper provides highlights from a CDC-hosted meeting on opportunities for cancer prevention during midlife (roughly ages 45–64 years). Positive changes during this phase of life have the potential to prevent cancer incidence later in life, making this phase an opportune time for targeted prevention efforts to facilitate healthy aging and increased longevity. Risk and protective factors discussed during the meeting included exposure to radiation from medical imaging procedures, circadian disruption, chemical exposures, dietary factors, alcohol consumption, obesity, physical activity, diabetes, and the human microbiome. Although many of these factors are well recognized as being related to cancer incidence, others are not as widely recognized or have emerged as growing areas of research.

Meeting participants discussed promising strategies for cancer prevention targeting this age group. Just as there are multiple determinants of cancer risk, there are likely multiple solutions. Changes to social and physical environments may facilitate healthy behaviors and minimize harmful exposures. Information shared during the meeting about health disparities in the U.S. highlighted the need to go beyond traditional approaches to cancer prevention to truly reach vulnerable populations. Partnerships are also a key component to prevention efforts; community-based and nonprofit organizations, the healthcare system, research institutions, state health departments, and federal agencies were all noted as important partners in prevention efforts. Coordinated, multidisciplinary efforts across multiple chronic diseases may provide opportunities for synergistic effects. Further, leveraging key partnerships and existing communication channels can maximize success and facilitate timely translation of research findings into public health practice.

Introduction

Cancer continues to be a leading cause of morbidity and death in the U.S. ^{1,2} Further, the number of adults with cancer is expected to grow as the U.S. population ages. ³ The Healthy People 2020 goal for cancer is to reduce the number of new cancer cases, as well as the illness, disability, and death caused by cancer. ⁴ A greater emphasis on the primary prevention of cancer is needed. ^{5,6}

Staff within the Division of Cancer Prevention and Control at CDC organized the Cancer Prevention Across the Lifespan (CPAL) workgroup in an effort to foster innovative public health approaches to cancer prevention. The workgroup is using a life-course approach to explore the evidence linking risk and protective factors to subsequent cancer risk and to identify promising strategies to reduce cancer risk and promote health at every age. The CPAL workgroup started by focusing on preadolescence and adolescence⁷ and has now expanded its efforts to examine opportunities for prevention during midlife. For practical purposes, the workgroup defined midlife as roughly ages 45–64 years. However, the workgroup recognizes that these age cutoffs are somewhat arbitrary and that this phase of life may be experienced at younger or older ages.

The workgroup conducted an in-depth literature scan to examine the evidence linking factors during this phase of adult life with subsequent cancer risk. In addition, the workgroup convened a 2-day meeting in October 2012 to discuss the state of the evidence and explore potential strategies to intervene during midlife to prevent cancer occurrence later in life. The structure of the meeting enabled participants to share their perspectives through brief presentations and engage in facilitated discussion. Participants (listed in the acknowledgements) contributed knowledge from a variety of fields, including aging, behavioral science, cancer etiology, cancer prevention and control, chronic disease prevention, circadian rhythm disruption, community health, environmental health, epidemiology, gastroenterology, healthcare research and quality, health communication, health disparities, health promotion, nursing, nutrition, primary care, and radiology.

Meeting discussions focused on topics related to the prevention of future cancer cases. Although cancer screening, early detection, treatment, and survivorship are important public health issues among adults, ^{8,9} these topics were beyond the scope of the meeting. Early life exposures, though important in the context of lifetime cancer risk, ¹⁰ were also considered outside the scope of the meeting. The group intentionally excluded discussions about tobacco control and occupational exposures to carcinogens because these topics are already addressed by other units of CDC (Office on Smoking and Health; National Institute for Occupational Safety and Health). This paper provides highlights from the discussions that may be particularly useful to prevention researchers and public health practitioners, with a focus on opportunities for future public health action to reduce cancer risk and increase the "healthspan" of adults.

Meeting Highlights

Marcia Ory set the stage for the 2-day meeting with a presentation on the unique life changes and transitions faced during midlife. ¹¹ This phase of life covers a large portion of the life span and constitutes the second-fastest-growing segment of the U.S population. ¹² Adults in this phase of life often juggle multiple roles (e.g., caregiver to parents and/or children, working professional) and must balance work and family responsibilities amid the physical and psychological changes that come with aging. ¹² Adults may also begin experiencing wake-up calls either personally or through their peer network in the form of early signs of chronic disease, which may increase interest in improving health behaviors to promote healthy aging. ¹³ Positive changes during this phase of life can potentially prevent

the incidence or reduce the severity of chronic diseases and disabilities, ¹⁴ making it an opportune time for targeted prevention efforts.

Radiation Exposure from Medical Imaging

Rebecca Smith-Bindman provided data on excess radiation exposure in the medical care setting. The use of diagnostic imaging, particularly computed tomography (CT), has increased tremendously over the past 20 years. Despite the improvements in health care offered by this technology, radiation doses from CT scans, typically 100 to 500 times those from conventional radiography, can pose a health risk, including increased risk for certain cancers. Here are currently no comprehensive standards or guidelines for appropriate CT dosage, which can vary greatly across types of CT studies as well as across and within institutions. Additionally, a considerable number of these imaging examinations may not be necessary, as demand can be driven by patient request, malpractice concerns, and high profitability. The data Smith-Bindman presented highlighted the need to change medical imaging practices, given the potential for reducing cancer burden among the increasing number of patients in midlife who undergo CT scans. 17,18

Circadian Rhythm Disruption

David Blask described another emerging area of research for potential cancer-prevention opportunities during his presentation on circadian disruption and cancer risk. Blask described the circadian rhythms of the body, including patterns of sleep, body temperature, and certain hormones (e.g., melatonin). The presence or absence of light helps synchronize the body's circadian rhythms so that they occur on a 24-hour cycle. ¹⁹ Melatonin peaks at night during exposure to total darkness, while exposure to light, particularly blue wavelengths of light, shuts off melatonin production. ¹⁹ This is relevant to cancer-prevention efforts because evidence suggests that melatonin inhibits the proliferation of human cancer cells. ^{19,20} In the U.S., exposure to light at night is ubiquitous, with artificial sources of light ranging from indoor lighting to electronic devices to street lights. Exposure to light at night disrupts the body's natural circadian rhythms and reduces melatonin production, potentially increasing the rate of tumor growth and, at least partially, explaining the observed association between nighttime shift work and cancer risk. 19,21–23 Further, this information suggests that reducing exposure to light at night (e.g., minimizing the use of lights and electronic media at night and sleeping in total darkness) may reduce subsequent cancer risk and tumor growth.²⁴ This information is particularly salient during midlife because nearly 70% of adults aged 45–64 years report insufficient sleep in the past 30 days.²⁵ and more than 12% of workers in this age group are shift workers.²⁶

Alcohol Consumption

Susan Gapstur described the evidence linking alcohol consumption to cancer risk during her presentation. More than half of U.S. adults aged 45–64 years are regular drinkers,²⁷ and approximately 13% report binge drinking.²⁸ These statistics are based on self-reported information and likely underestimate true levels of drinking.²⁹ Alcohol consumption is considered one of the top 10 leading causes of disease in the world,³⁰ and consumption increases risk for multiple cancers, including cancers of the oral cavity, pharynx, larynx, esophagus, liver, colorectum, and female breast.^{31,32} Unlike most other cancer risk factors,

light to moderate alcohol consumption (1–2 drinks per day) is associated with a decreased risk for cardiovascular disease.³³ Several leading health organizations recommend consuming no more than two drinks a day for men and one drink a day for women and not to start drinking if you do not currently drink alcohol.^{34–36} However, the risk for certain cancers has been shown to increase linearly with alcohol consumption with no safe threshold,^{32,37,38} suggesting that even moderate levels of alcohol consumption pose some risk.

Dietary Factors

Diet also plays an important role in cancer risk and prevention. Isabelle Romieu provided an overview of a report issued by the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR), which reviewed evidence on the beneficial and harmful effects of food, nutrition, and physical activity on 16 different cancer sites. ³⁶ Based on the evidence, the WCRF/AICR report provides dietary recommendations for cancer prevention that are similar to the U.S. Department of Agriculture Dietary Guidelines for Americans. ³⁵ However, most U.S. adults fall short of these recommendations. ³⁹ A companion report released by WCRF/AICR on policy and action for cancer prevention emphasizes the many complex factors that influence dietary behaviors, including economic, cultural, and environmental factors. ⁴⁰

Dietary factors are particularly relevant during midlife as they relate to risk for diabetes. Nearly 12% of U.S. adults aged 45–64 years have received a diabetes diagnosis, and rates of diabetes have steadily increased since 1990. All Romieu reported results from the large European Prospective Investigation into Cancer and Nutrition study, including recent findings on the association between breast cancer and glycemic load, which may shed light on the links among the insulin pathway, diabetes, and cancer. All Gapstur reported additional data on the association between diabetes and cancer, which indicate that diabetes is associated with increased risk of liver, pancreas, endometrial, colon, rectum, and possibly bladder cancer.

Overweight and Obesity

More than one of every three adults aged 40–59 years is obese, with a BMI of 30 or higher. He for women, the prevalence of obesity is even higher (42%) among those aged 60 years. He for women and 66% of women aged 40–59 years are above what is considered a healthy weight given their height. He Gapstur reviewed several large studies that indicate an increased risk for certain cancers, including colorectal, postmenopausal breast, endometrial, pancreas, kidney, and esophageal adenocarcinoma, with increasing BMI. Some workshop participants questioned whether emphasizing healthy weight is appropriate for this age group, given the challenges of weight loss and weight-loss maintenance. However, participants noted the interactions among diet, physical activity, sedentary behavior and obesity, and some suggested that making relatively small changes in physical activity could potentially have a great impact.

The Gut Microbiome

Ilseung Cho described the gut microbiome and its implications for cancer prevention. The human microbiome refers to the community of microbes that resides on or within the human body. Most bacteria associated with the human microbiome have yet to be studied, as sequencing was previously limited to culturable organisms. However, new sequencing technologies are now available to expand this area of research. The latest evidence suggests that the human microbiome may have future implications for colorectal cancer prevention and control. Changes in the microbiome with age may lead to a host inflammatory response and a process often referred to as "inflamm-aging." There is currently no established direct causality between the gut microbiome and colorectal cancer, but researchers have observed a relationship between microbial content of the gut and the development of colorectal cancer. A deeper knowledge of the gut microbiome and its relationship to colorectal cancer and a better understanding of how to manipulate the gut microbiome may inform more targeted efforts in cancer prevention in the future.

The Complexity of Cancer Risk-Related Factors

Given the breadth of factors that influence cancer risk, the group could not adequately address all factors considered relevant in midlife during the meeting. John Vena explained this through an environmental health paradigm, describing the complex web of potentially harmful exposures. Cancer risk is influenced by countless exposures, some of which interact with each other, creating synergistic effects. Additionally, exposure effects are modified by an individual's genetic susceptibility. Vena cited the relationship between polychlorinated biphenyls (PCBs) and breast cancer risk as an example. Epidemiologic studies suggest that exposure to PCBs alone may not increase a woman's risk of breast cancer. However, PCB exposure may play a role in breast cancer development among genetically susceptible subgroups. Although cancer risk is complex, there are actions that the public health community could be taking now to reduce harmful exposures.

Translating Research Into Public Health Practice

To that end, workshop participants discussed opportunities to put research findings into public health practice. Prevention initiatives have frequently involved efforts to educate the public and health providers through the issuance of guidelines and the development of simple messages. Although such efforts are important, education alone may not be sufficient to change behaviors. As reflected in CDC Director Thomas Frieden's health impact pyramid⁵⁰ and the National Prevention Strategy,⁵¹ an integrated approach that includes environmental changes may be needed. Sometimes, it is possible to engineer out the problem (e.g., environmental and policy controls to reduce the public's exposure to carcinogens).⁴⁹ At other times, environmental changes are made with the intention of making healthy behaviors the easier choice.⁵⁰ David Meyers pointed out that although personal responsibility is important, the role of public health is primarily to address community-level problems and modify the context in which behaviors occur.⁵⁰ Dileep Bal echoed similar sentiments when he pointed out that community norms are often determined by policies and social structure.⁵² The federal government can promote prevention

messages, but decisions that support healthy and safe community environments are often made at the local level.

Strategic Partnerships

Partnerships are also an important component of prevention initiatives and can be critical for influencing decision makers, leveraging resources, and identifying innovative solutions.^{53–56} For example, the National Prevention Strategy was developed by a partnership of 17 federal departments, agencies, and offices. 51 Kathy Sykes described several creative approaches to partnerships that have been undertaken by the U.S. Environmental Protection Agency. For example, the Green Heart Initiative⁵⁷ sought to add an environmental component to the Million HeartsTM initiative.⁵⁸ Million Hearts emphasizes aspirin use for people at risk, blood pressure control, cholesterol management, and smoking cessation to reduce risk for heart disease and stroke. The Green Heart Initiative encourages those at risk to also look at the air quality index and reduce their exposure to air pollution as another simple step for prevention. Similar opportunities might exist to piggyback cancer-prevention messages onto other public education efforts. Linda Nebeling described the Five-a-Day/Fruits and Veggies —More Matters as an example of a successful public–private partnership. 59,60 The private sector can bring a different perspective, such as seeing the public as customers and clients. Other participants shared from experience how business interests and financial concerns can differ from public health goals, creating conflicts that are not easily overcome.

The Role of Healthcare in Primary Prevention

David Meyers described the healthcare system as another important partner in prevention.⁶¹ Patients often rely on healthcare professionals for advice, and the medical home can provide or refer patients to evidence-based counseling, empowering patients to initiate and sustain behavior change.^{62–64} The healthcare system can also take the lead in certain areas of prevention, such as reducing unnecessary exposure to medical radiation.¹⁶ Creating a healthcare infrastructure that provides a means to record, measure, track, and follow up with patients may facilitate the role of healthcare in primary prevention.

Cancer Prevention in the Workplace

The workplace was discussed as a promising setting for cancer-prevention interventions targeting adults. ^{65,66} Specifically, worksite interventions can target three areas of focus: (1) individual behavior change; (2) changes to the work environment (physical, psychosocial, and organizational) to promote health and positive health behaviors; and (3) the interface among work, family, and broader community systems. ⁶⁶ Targeting all three areas creates opportunities for collaboration, integration, and synergy and can make interventions both more effective and more sustainable. ⁶⁶ Nebeling cited a skin cancer–prevention intervention targeting U.S. Postal Service (USPS) letter carriers (Project SUNWISE) as an example of this conceptual framework in action. The intervention included the brief delivery of educational sun-safety messages plus environment-based components: increased access to protective hats and sunscreen and visual cues to prompt the use of sun-safe strategies. ⁶⁷ Researchers not only found the intervention to be effective for increasing sun-safe behaviors, but they found institutionalizing the intervention components to be highly feasible, creating the potential for lasting change. ⁶⁸

Strategies for increasing intervention uptake and dissemination in the workplace include marketing the benefits to the employees, employer, and larger community. High-lighting the more immediate benefits (e.g., reduced number of sick days used and increased productivity) may be more effective than highlighting solely the long-term benefits. In addition, creating resources and infrastructures that enable employers to identify and adopt evidence-based programs can facilitate dissemination.⁶⁹

Addressing Health Disparities

Michele Evans challenged workshop participants to consider whether health disparities require an altered perspective on the best approach to designing effective cancer-prevention strategies. To Evans defined health disparities as differences in health related to characteristics such as SES, gender, race, ethnicity, and education. Disparities in life expectancy across racial and ethnic groups and SES are widespread and persistent. For example, there is a 21-year gap in life expectancy for urban black men compared to Asian women and a 25% higher age-adjusted death rate for non-Hispanic blacks compared to whites. Turther, the rate of cancer death is higher for blacks than whites of both genders. Evans's research is based on a model of disparities that includes elements of SES and considers race as a biologic and psycho-socio-cultural construct. She hypothesizes that aging and health disparities result in similar health outcomes but with different trajectories or time frames. To test this framework, Evans and colleagues have developed the Healthy Aging in Neighborhoods of Diversity across the Life Span study, a longitudinal study of normal aging in a biracial cohort (handls.nih.gov/).

Lisa Muirhead continued the discussion by focusing on two special populations that have typically been neglected in cancer-prevention efforts: the homeless and the mentally ill. The More than 600,000 people in the U.S. experience homelessness on any given night, and chronic homelessness disproportionately affects those born during 1954–1966. One in four U.S. adults experiences mental illness, facing unique challenges in daily life and disparities in income, employment, education, homelessness, full community participation, and life expectancy. Although the causes of death for those who are homeless or who have a mental illness mirror those of the general population, their life expectancy is lower. This is due to a disproportionate burden of smoking, alcohol use, poor nutrition, hepatitis B and C, low health literacy, and poor access to medical care. Intervention efforts targeting these vulnerable populations may require different approaches that take into account cultural differences and the challenges associated with low health literacy, limited access to healthcare, and potential mistrust of formal systems.

The Role of Comprehensive Cancer Control Programs

Heather Dacus spoke about the role of CDC's National Comprehensive Cancer Control Program (NCCCP) in cancer-prevention efforts. ⁸¹ Comprehensive Cancer Control is a collaborative process through which a community and its partners pool resources to reduce the burden of cancer. ⁸² As noted by Bal, the NCCCP provides an extensive network, which could be used to strategically disseminate information and resources discussed during the meeting to NCCCP grantees and other stakeholders (e. g., community organizations and policymakers).

Strategic Messaging

Providing access to actionable and easy-to-understand information is a key step toward empowering people to make healthy choices. ⁵¹ Where appropriate, information about cancer prevention could be translated into plain language, ready for use by NCCCP and other partners. Given the plethora of health messages targeting adults, strategic communication channels are essential. For example, Terry Keenan suggested including cancer-prevention information in AARP's monthly bulletin, a source of information for millions of AARP members aged 50 years (www.aarp.org/bulletin/). Additionally, experts could work with CDC to provide webinars on cancer-prevention topics of interest to grantees and partners.

Use of Existing Surveillance Systems

Given that CDC also collects data on the health and health-related behaviors of U.S. adults through a variety of surveillance systems, ^{83,84} several participants suggested that some of the data already collected could be used to explore new research questions about cancer risk—related exposures and behaviors (e.g., red meat or alcohol consumption). Further, new questions could be added to capture additional information on health behaviors and exposures (e.g., exposure to light at night or medical imaging procedures).

Conclusion

Throughout the workshop, participants shared compelling information that reinforced the concept that cancer is preventable and that midlife is an important time at which to take action. 85 Some of the factors discussed have been recognized as being related to cancer incidence for decades (e.g., dietary factors and physical activity). Other exposures have been extensively studied, but their contribution to cancer risk is not as widely recognized (e.g., environmental carcinogens, alcohol, and medical radiation). The science also continues to evolve in many areas, including the role of circadian integrity and the microbiome. The transdisciplinary nature of the discussions challenged many preconceived ideas and revealed the value of learning from different fields.

Workshop participants emphasized the need to translate the complex science of cancer causation into purposeful action for prevention. CDC was viewed as particularly strong in science translation. For many cancer-related factors, the CDC-supported Community Preventive Services Task Force provides evidence-based recommendations on the effectiveness of interventions in community settings. Ref In addition, for certain areas of cancer prevention, CDC may serve as a connector and facilitator with other federal agencies. CDC was also seen as the source of surveillance data on cancer incidence and risk factors. Several workshop participants emphasized the need to get actionable information to the right people. Messages need to be focused and specific for the target audience. Depending on the topic, there may be many different audiences, including the general public, healthcare providers, and policy- and decision-makers.

Several of the exposures and risk factors discussed could be modified, at least in part, by an individual's behaviors. Health communication research has provided insights into the best ways to inform and influence adults at different ages. As several participants mentioned, when not done right, public health messages can be stigmatizing or ineffective. In the case

of dietary recommendations, some health messages have changed over time, ^{87,88} and some RCTs^{89,90} of supplements have had unexpected adverse findings. This can lead to public misperception about the importance of a healthy diet, and a lack of appreciation that the science evolves over time. The low health literacy of many adults and the needs of special populations present additional challenges to effective health messaging.

Workshop participants highlighted the importance of systems and environmental changes to support healthy behaviors and reduce harmful exposures. Current chronic disease prevention efforts to promote good nutrition, increased physical activity, and a healthy weight may reduce cancer risk. Lessons could be learned from the many community-based prevention programs currently underway. Prevention efforts across different chronic diseases could be coordinated to enhance the opportunity for synergistic effects. Some of the current programs could be leveraged and their community-based groups mobilized to address the unique circumstances of adults at midlife. Additionally, the workplace may be particularly relevant for some cancer-prevention efforts at midlife whereas other cancer risk factors (e.g., medical radiation) may require a completely different approach and some workers may not work at traditional worksites. Just as there are multiple determinants of cancer risk, there are likely multiple solutions. Regardless of the approach taken, partnerships will be critical.

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Appendix

The members of the Cancer Prevention Across the Lifespan (CPAL) workgroup were instrumental in the preparations for the workshop. Workgroup members included Vicki Benard, Jennifer E. Boehm, Natasha Buchanan, Donatus Ekwueme, Jeffrey D. Glenn, Melissa Grossman, Jane Henley, Dawn Holman, T'Ronda Joseph, Chunyu Li, Jun Li, Antonio Neri, Brandy Peaker, Lucy Peipins, Juan L. Rodriguez, Katherine B. Roland, Heather Ryan, Sherri L. Stewart, Laura I. Tison, Katrina F. Trivers, Meg Watson, Hannah Weir, Mary C. White, and Susan White.

Workshop participants included Dileep Bal, David Blask, Ilseung Cho, Heather Dacus, Michele Evans, Susan Gapstur, Terry Keenan, David Meyers, Lisa Muirhead, Linda Nebeling, Marcia Ory, Isabelle Romieu, Rebecca Smith-Bindman, Kathy Sykes, and John Vena.

In addition to CPAL workgroup members, the following CDC staff participated in the workshop: Lynda Anderson (Healthy Aging Program); David Brown (Division of Nutrition, Physical Activity, and Obesity); Johnni H. Daniel (Environmental Hazards and Health Effects Program); Randy Elder (Division of Community Preventive Services); Ingrid Hall (Division of Cancer Prevention and Control); Nikki Hawkins (Division of Cancer

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