Charting the Future of Cancer Health Disparities Research: A Position Statement from the American Association for Cancer Research, the American Cancer Society, the American Society of Clinical Oncology, and the National Cancer Institute

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Introduction

The academic field of cancer health disparities was stimulated by the U.S. civil rights movement. Concerns about civil rights led to concerns about equality in health care. The first publications to make the observation that black Americans have higher rates of death as a result of certain cancers compared with white Americans were published by the early 1970s (1, 2). The discipline concerned with these differences was first called “minority health research” and later “special populations health” or “special populations research.” The National Cancer Institute (NCI) defines cancer health disparities as adverse differences in cancer incidence, cancer prevalence, cancer mortality, cancer survivorship, and burden of cancer or related health conditions that exist among specific population groups in the United States (3). However, with greater and renewed acknowledgment of health disparities as rooted within the context of historical and contextual inequities in the United States, many health disparities are considered health inequities (4).

The National Cancer Act of 1971 created the Surveillance, Epidemiology, and End Results (SEER) program within the NCI. This program began collecting incidence, mortality, and survival data by race in the early 1970s from a number of population-based registries around the United States. The SEER program improved documentation of differences in outcomes and analyzed them through its black-white studies (5). These studies especially demonstrated differences in treatment patterns, with a higher proportion of blacks receiving inappropriate cancer care compared with whites.

The discipline grew from a focus on black-white differences to encompass differences in outcomes for a number of racial and ethnic groups, as well as for cohorts defined by age, sex, socioeconomic status (SES), and other social determinants of health. There is now even greater appreciation for disparities among communities, whether rural versus urban or even by state or region. The definition of health outcomes also broadened beyond death rates.

The field of health disparities was once simply a description of population differences and a call for cultural competence among health care providers. Today, the field is transdisciplinary, integrating basic science, clinical science, policy, epidemiology, and the social sciences. It involves people trained in diverse nonmedical fields, such as education, economics, sociology, religion, geography, and anthropology. The field is also dynamic. It changes as better and more granular statistics, greater understanding of causes of health disparities, and new challenges to mitigate these underlying causes have emerged. As an example, in the 1970s, the breast cancer death rate for black and white American women was the same. Today, the death rate is substantially higher for blacks compared with whites (6). Policy changes have also created opportunities and challenges. The Affordable Care Act has allowed for Medicaid expansion in each state. Expansion has been adopted by 32 states and the District of Columbia. This will create a new challenge, because poor residents of some states have expanded access to care and residents of other states do not. It is essential that any future policy changes should be carefully designed to increase, rather than decrease, equitable access to care throughout the cancer continuum. Population categorizations also are being redefined. The Asian category includes Korean Americans and Pakistani Americans. The Pacific Islander category, often merged with the Asian category, includes native Hawaiians and Samoans. These populations are incredibly heterogeneous and have dramatically different cancer statistics.

In 2015, representatives from four leading cancer organizations, the American Association for Cancer Research, the American Cancer Society, the American Society of Clinical Oncology (ASCO), and the NCI, began to meet to discuss the state of health disparities in the United States. These discussions involved the state of cancer health disparities research and what could be done to move it forward. The discussions were purposely not meant as a comprehensive review of
cancer health disparities research. Rather, the meeting and the resulting document aimed to identify issues in health disparities research and make specific recommendations to improve the way disparities research is conducted and disseminated.

This statement presents a unified strategy among four of the leading cancer organizations in the United States to promote cooperation among investigators in all areas of the cancer health disparities research community, to ensure that cancer research benefits all populations and patients regardless of race, ethnicity, age, gender identity, sexual orientation, SES, or the communities in which they live.

**Defining Measures and Tools for the Next Generation of Cancer Health Disparities Research**

**Background**

Disparities in outcomes across the cancer continuum have been identified in numerous medically underserved populations, including racial and ethnic minorities and patients of lower SES. In addition to individual social status, social contextual and community factors, such as neighborhood safety, social cohesion, availability of healthy foods, and residential segregation, play an important role in health of both individuals and populations. All of these factors can intersect to generate larger disparities (7, 8).

**Current issues/state of knowledge**

To understand and fully address cancer health disparities, complete, consistent, and accurate collection of patient, community, and structural factors that put people at risk for disparate outcomes is essential. Unfortunately, cancer health disparities research has often been fraught with missing, inaccurate, or overly simplified patient-level data, and most research has failed to consider the community-level factors described above (9–11).

For the most part, the manner in which data are collected and integrated in disparities research is suboptimal. The literature is characterized by variable methodology for collection of the factors that put patients and communities at risk for disparate care and outcomes. For example, although race and ethnicity are distinct constructs, they are often conflated such that a person is identified as Hispanic without identification of his or her race. Many studies that investigate cancer care or outcomes according to socioeconomic position have only area-level data on socioeconomic position, whereas others use only composite measures. While valuable in many cases in identifying disparities, such measures fall short in providing the richness of data needed to understand an individual’s socioeconomic position. Health literacy and numeracy are rarely assessed in practice and are not available in administrative and research databases. Finally, methods for uniform data collection of information on sexual orientation and gender identity are in their infancy, despite calls for such data collection from the Institute of Medicine, among others (12).

**Recommendations**

- A standard set of race and ethnicity as well as sociodemographic measures should be agreed upon by the cancer health disparity research community. To the greatest extent possible, these core measures should be included in clinical registries and in research protocols funded by the National Institutes of Health, private foundations, and pharmaceutical companies regardless of the hypothesis being tested. As much as possible, the most granular measures possible should be selected, and, in the case of race and ethnicity, questions should address ancestry, immigration status, and enclave effects. To assess neighborhood and structural effects on health, measures of the built (man-made) environment should be included, or patient address should be collected and geocoded, so that physical and other contextual effects, in addition to individual-level effects, can be considered (13).
- Measures of race, ethnicity, sexual orientation, and gender identity should be self-reported, not based on observation, and should be collected by all researchers and all clinical settings on all of their study subjects and patients. To understand the environment and the context in which patients live, the expertise of epidemiologists and other social scientists should be used, and community members should be engaged in disparities research endeavors.
- Providers, patients, and the public should be educated regarding the rationale for and importance of collecting sociodemographic data, some of which may be perceived as potentially sensitive questions (e.g., sexual orientation and gender identity). Standard guidelines to facilitate collection and to mitigate patient or participant concerns should be offered.
- The cancer health disparity community should establish reporting standards for measurement variables, similar to CONSORT and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, for journal editors and peer reviewers to facilitate and standardize assessment of the quality of the data collection method when evaluating health disparity research findings for publication. For example, justification for selection of socioeconomic measures should be provided; constructs of race and ethnicity should be provided in the description of the conceptual framework and sampling frame; and other measures that define medically underserved populations, such as low-literacy populations, should be clearly specified. When publications fall short of these guidelines, authors should explicitly acknowledge the limitations of their research when key factors, such as wealth, are not accounted for. Statements such as “findings controlled for socioeconomic status” would no longer be sufficient in most publications. Researchers should be asked to provide their study protocols, just as clinical trialists do now.

**Biologic and Environmental Determinants of Cancer Incidence**

**Background**

Disparities in cancer incidence are pronounced and longstanding. Drivers of these disparities are multifactorial and multilevel, and they include sociodemographic factors, access to health care, risk factor profiles and lifestyle/health habits, cultural perceptions, biologic differences, and genetic predisposition. Disparities in cancers for which single etiologic factors account for a substantial proportion of disease (e.g., human papillomavirus and cervical cancer, or Helicobacter pylori and stomach cancer) can be reasonably understood and explained, but disparities for many of the common etiologically heterogeneous cancers, such as breast, prostate, and colorectal cancers, remain much less well understood.

**Current issues/state of knowledge**

Multilevel approaches are needed to advance knowledge relevant to addressing disparities in cancer incidence rates. One
approach is to design and implement observational studies focused on a population in which disparities exist to advance knowledge about etiology and to inform novel prevention strategies. A successful example of such an effort is the African American Breast Cancer Epidemiology and Risk (AMBER) Consortium, a multicenter consortium that has combined data and biospecimens from 7,500 African American patients with breast cancer and 17,000 healthy controls, representing the largest study of breast cancer in African American women in the United States (14). It has yielded a number of insights on multilevel risk factors specific to the major molecular subtypes of breast cancer among African American women (15–17).

There is also a need for studies focused on identifying the genetic contributors to cancer health disparities. Recent work has focused on the prioritization of candidate variants relevant to prostate cancer risk within the context of genetic ancestry (based on ancestry informative markers) across those with European, African, Japanese, or Latino ancestry (18). Furthermore, the African Ancestry Prostate Cancer Genome-Wide Association Studies (GWAS) Consortium has reported on susceptibility loci for aggressive prostate cancer specific to men of African ancestry (19).

Although some cancer risk factors are well established, the biologic mechanisms through which their impact on cancer risk varies across different populations remain incompletely understood. For example, variations in diet are hypothesized to be the primary driver of the dramatic variations in colorectal cancer incidence rates observed across populations. Recent research has evaluated the impact that different diets have on microbiota composition and function, which in turn affects the production of metabolites that either promote mucosal health or are proinflammatory/neoplastic in the gut. A study that compared Americans with African ancestry (who have a relatively high incidence of colorectal cancer) with rural South Africans (who have a comparatively very low colorectal cancer incidence) demonstrated that a typical U.S. diet with high meat and fat intake increases mucosal proliferation rates (a marker of cancer risk) when fed to both populations, whereas typical high meat and fat intake decreases mucosal proliferation rates when fed to both groups. This demonstrates that diet can have a profound and fairly immediate impact on the gut microbiome that can either promote or suppress tumors (20).

Recommendations

- Develop international studies aimed at better understanding the roles of environmental, lifestyle, and cultural factors on differences in cancer incidences across countries and regions.

Biologic, Environmental, and System-Level Determinants of Postdiagnosis Survival

Background

Cancer outcome disparities are well documented for racial and ethnic minorities, and presentation at more advanced stages of cancer explains much of this difference. However, even when controlling for the stage of cancer at diagnosis, the survival disparities persist. What is most concerning is that rather than improving over time, for cancers such as colon cancer, the stage-specific disparities are actually worsening (21). The reason for this growing disparity is not completely clear but involves socioeconomic issues such as education status and the level of insurance and access to medical care. Even in studies that normalize socioeconomic issues (with the limitations cited in the Defining Measures section), disparities that disproportionately affect U.S. minority populations can still be demonstrated for several cancers and may highlight the not-so-well-understood interplay between genetic predisposition and environmental exposure, such as lifestyle and diet, that modifies cancer risk (22, 23). Ultimately, growing postdiagnosis survival disparities are caused by the interplay of system, social, biologic, and environmental factors.

Documenting and addressing each of these and their interactions are key to eliminating these disparities.

Current issues/state of knowledge

System. The role of system-level and social determinants in explaining cancer health disparities is best demonstrated by recognizing that disparities vary widely across the United States; some states show almost no disparities, whereas others show striking ones (24). We also know that disparities in treatment of cancer differ and that when treatment differences are accounted for, either through the use of standardized therapies on a clinical trial or through multivariable modeling, cancer-specific survival disparities often disappear. We also have clear examples of successful system-level reform (21, 25, 26). We know, therefore, this is a solvable problem.

The key step toward improving care and reducing cancer health disparities requires accurate measurement of meaningful variables, fed back in real time to key stakeholders in the system, followed by meaningful action and continued monitoring to ensure that the action was successful. Determining meaningful measurement across the cancer spectrum may vary by sociocultural factors and require patient and stakeholder input. These system-based practices formed the core of a recent Institute of Medicine report, "Systems Practices for the Care of Socially At-Risk Populations" (27). Systems can be thought of at a macro level, such as state, county, or city governments, all the way down to the individual practice or physician level. Implementation science can inform the best approaches to ensure delivery of high-quality cancer care.

Gene/host/environment. Cancers can start as a result of chronic inflammation, and inflammation can modify the behavior of cancer. Biomarkers, such as elevated microsatellite alterations at...
selected tetranucleotide repeats (EMAST) that can be detected from inflammation-laden cancers, are associated with worse patient outcome and increased metastasis and appear to be more common among African Americans compared with whites (28). Both EMAST and MSI have implications for (1) chemotherapeutic response and (2) immunotherapeutic response. In terms of race, these aspects have not been studied. Furthermore, there is much evidence that the microbiome can influence (1) inflammation, (2) response to chemotherapy, and (3) cancer or precancerous lesion formation; also, the microbiome itself can be determined by diet and other factors. These aspects have not been examined with race in mind. Additionally, driver genes may be different within the same type of cancer from patients with different genetic backgrounds, which have implications for correct, definitive therapeutic approaches (29).

Most studies that use human specimens to study aspects of cancer and race or ethnicity come from limited individual collections with sparse clinical–epidemiologic information, with rare exception. The exceptions tend to be NCI-funded projects, such as the North Carolina Colon Cancer Study, in which peer review and thoughtful input about how the collection was made with controls, surveys, and linked information to make the collection more meaningful, comprehensive in information, potentially useful for other future studies, and possessed of longevity. However, these types of collections or biorepositories, which include tumor and nontumor specimens, have not been created from diverse samples representative of the U.S. Census population.

Recommendations

System.

- Develop, in concert with representatives of at-risk populations, and validate cancer care quality metrics across the cancer spectrum most relevant to oncology practices that operate in low-resource environments.
- Design risk-adjustment methodologies for oncology practices in low-resource environments that hold them accountable for high-quality care but do not penalize them for taking care of high-risk patients.
- Assess the clinical and financial effectiveness of alternative oncology payment models that provide up-front infrastructure investment for practices in low-resource environments.
- Hold systems accountable for real-time monitoring and feedback of cancer health disparities. These systems should include city and county health departments and state Medicaid programs. An excellent example of this is Rapid Quality Reporting System (RQRS) developed by the Commission on Cancer (CoC). The RQRS is a reporting and quality-improvement tool that provides real clinical time assessment of hospital-level adherence to quality of cancer care measures. This is a mandatory reporting program for all CoC sites as of January 1, 2017 (30).

Gene/host/environment.

- Develop or enhance existing national biorepositories that contain specimens of solid cancers from underserved populations (e.g., racial/ethnic minorities, low SES, medically uninsured, gender minorities) that are at least representative of the population demographics of those groups, and oversample individuals from these groups in biorepositories aimed to address disparities. The National Institutes of Health can use P20, U01, and U56 mechanisms for their development, with specimen and data-sharing plans available to those who might meet criteria to use them and program announcements designed to address the limitations of current biorepositories for cancer health disparities research. These collections should be annotated with appropriate sociodemographic information, as outlined in the Defining Measures section.
- Fund additional studies to determine the role of inflammation and the microbiome on the biology of cancer and its effects on cancer among underserved groups and to determine how inflammation and the microbiome affect cancer stage, stage-specific survival, and recurrence rates.
- Fund additional studies of human population genetics to inform interpretations of disparate effects of antineoplastic drugs across patient populations.

Advancing Community Engagement Strategies throughout the Cancer Care Continuum

Background

Current models of health care delivery are highly focused on the use of technology and innovation to improve patient outcomes across disease processes, as demonstrated by the focus on precision medicine in cancer treatment (32–36). Although oncology attempts to embrace this approach, the impact of innovative treatments has been hampered by poor translation of innovation into health care systems and patients from diverse community settings (37, 38). As precision medicine in cancer is accelerated as part of the Beau Biden Cancer Moonshot and other initiatives, the importance of community engagement to ensure that all patients benefit from these advances cannot be overlooked. Cancer health disparities must be taken into consideration in the design, execution, and evaluation of all such programs.

Current issues/state of knowledge

Community-engaged research (CER) has been documented as an effective, beneficial method for engaging communities and formulating research that has relevance and impact for both researchers and affected communities (39–42). Involving relevant community stakeholders in research at the planning stages allows for a deeper understanding of community needs, allows researchers to have an iterative method for evaluating research questions in an active realistic milieu, and simultaneously creates a valuable vehicle for active dissemination of the research findings into the communities they are intended to serve. CER offers the potential to improve processes and outcomes in several areas, including care delivery, continuity of care, managing comorbidities, and supportive care (42).

Unfortunately, there is a dearth of support for oncology health professionals who choose to work in CER, given its necessity for infrastructure and relationship building, the complex personal interactions with communities and community organizations, and the need to establish long-term benefits to the community after the research project is completed. Importantly, CER requires...
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not only a broad range of expertise across multiple disciplines, but also investigators skilled in a team science approach (43). The benefit of this type of team science has been touted across disciplines; however, its implementation has been limited (44).

A lack of workforce diversity has been identified as a barrier to improving access to care for underserved minority groups as well as to advancing research on health disparities (45, 46). Organizations, including ASCO and the American Society of Hematology, have sought to increase workforce diversity in oncology through awards and mentoring programs that expose underrepresented minorities to careers in oncology at the medical student, resident, and fellowship levels. In addition, the NCI Center to Reduce Cancer Health Disparities and the American Association for Cancer Research administer several programs aimed at training the next generation of competitive researchers in cancer and cancer health disparities research. Increased efforts of these types are needed to develop an oncology workforce that reflects the diversity of the patients it serves.

Finally, CER does not often align with most traditional grant timelines and will require investment on behalf of the research institutions in both personnel and resources. Without such an investment, it will remain difficult to create a true synergy between CER and the rapid discoveries that occur in cancer research.

Recommendations
- Specific criteria should be developed by experts in CER to aid cancer centers in establishing meaningful community research partners.
- Requirements for NCI comprehensive cancer center designation should include meeting meaningful CER criteria including sustainability plans for maintaining community relationships beyond typical grant funding cycles.
- To ensure a diverse workforce with varied life experiences, research and mentoring efforts aimed at improving workforce diversity in oncology should be expanded.
- Academic deans and chairs should establish separate promotion criteria, such as an extended promotion “clock,” to account for the added infrastructure and relationship-building time required for this type of research.

Redesigning Clinical Trials to Acknowledge and Address Cancer Health Disparities

Background
Clinical trials are the most important and reliable means available to provide scientific evidence for effective care and management of patients with cancer and individuals at risk for cancer (47). Complex trials that incorporate advanced technologies necessitate new approaches from clinical care teams and diverse oncology practices. Because the putative goal of clinical trials is to provide evidence that is both valid and generalizable, future trials must include research questions that consider the multifactorial and multilevel components that characterize populations with the greatest cancer burden. This section proposes strategies to advance disparities research within the current cancer clinical trials system and/or within a new network of disparities-focused programs.

Current issues/state of knowledge
Stringent criteria for participation in cancer clinical trials and common procedures for providing trial information have been barriers to enrollment for racial/ethnic minorities; rural residents; older patients (≥65 years); and patients with lower SES, limited English proficiency, low health literacy, and comorbidities. The high and increasing prevalence of chronic diseases and of risk factors for chronic diseases, such as obesity and early-onset diabetes, must inform eligibility criteria to represent these populations fully in cancer protocols. As an example, African Americans bear a disproportionate burden of the comorbidities that typically exclude participants from studies, and it is difficult to determine which comorbidities could be reasonably eliminated as exclusion criteria or could be sufficiently monitored or managed within the study framework (48). In addition to those front-end enrollment barriers, experience from cancer prevention and treatment trials also has shown that underrepresented populations often are enrolled later in the recruitment process, and subsequent power calculations frequently do not support sub-population analyses.

Recommendations
- More members of minority health care teams/community investigators need to be involved in study design, with specific emphasis on inclusion and exclusion criteria.
- Successful tools of CER need to be used and evaluated to inform underrepresented populations about clinical trials and improve recruitment of these populations to clinical trials.
- Sponsors of clinical trials and agencies, such as the Centers for Medicare & Medicaid Services, must collaborate to eliminate cost and coverage barriers to clinical trial participation. It is particularly important for the Medicaid program in all 50 states to cover the routine care costs of clinical trials.
A better understanding of how best to help low-resourced institutions recruit participants to trials, when there is an ever-increasing requirement to collect complex biospecimens, is needed.

2. Trial design should be fostered to extend the recruitment periods to meet designated targets of underrepresented populations.

3. Disparities questions should be integrated into efficacy questions to assess a hypothesis-driven correlative science question, or to test an innovative recruitment strategy. One example of trials that offer more real-world conditions and greater efficiency is the reciprocal control design, in which participants in each arm of the reciprocal control trial receive an intervention for a particular disease but also serve as controls for a different intervention and disease in the other arm.

4. Funding mechanisms for clinical trials programs that focus exclusively on cancer health disparities are needed.

Conclusion

The field of cancer health disparities has evolved into a complex science and an established multidisciplinary field of cancer research. Unfortunately, the rigor required to conduct this research has not been uniformly applied, and the infrastructure needed to take it to the next level, where lasting solutions can be found, is limited. The purpose of this article, which has been jointly written by experts from these four esteemed organizations, is to guide the development of advances in this area. Our hope is that this statement will be used by both public and private organizations to inform specific investments made to improve cancer health disparities research, thereby ultimately eliminating identified disparities in cancer incidence, quality of care, and outcomes.

Several recommendations for action items emerged.

1. The tools needed to define sociodemographic and economic characteristics of individuals and groups have become very sophisticated, and it is incumbent upon researchers and those who fund and publish their work to ensure that the highest-quality tools to measure the most granular data are used.

2. If our intention is to study minority and underserved populations in a "cell to society" manner, then we need to create multiple consortia explicitly established to gather all of the relevant biospecimen, clinical, individual, and contextual data needed to conduct adequately powered hypothesis-driven health disparities research. The development of a health disparities research network, similar to the Cancer and Aging Research Group, could aid in designing such studies and recruiting individuals to participate (53).

3. Best-practice strategies must be designed and used to ensure that underserved patients, their providers, and institutions are adequately targeted and informed about opportunities to participate in research studies and clinical trials.

4. To develop a comprehensive approach to health disparities, we need researchers who are adequately trained in CER. In addition, criteria for appropriate academic promotions that account for the time to conduct CER should be established for these researchers. Funding for CER should be made with the expectation that the enhanced infrastructure and outreach made possible by grants should be sustained beyond funding cycles.

5. Because patients with cancer exist in a web of health care systems, these systems have an obligation to understand how these patients are being treated in real time and to intervene when system errors occur.

We have clearly entered a new phase in cancer health disparities research—one that has the potential to benefit significantly from collaborations across disciplines and sectors. Given the looming crisis in cancer incidence and mortality disparities that affects minorities and the medically underserved, it is our collective hope that in this period of cancer research when significant breakthroughs are being discovered, there will be opportunities to apply this new knowledge to all populations, and thus eliminate cancer health disparities for current and future generations.

Disclosure of Potential Conflicts of Interest

B.N. Polite has acted in a consulting or advisory role for AstraZeneca and Pfizer and as a paid member of the Speakers’ Bureau for Bayer/Onyx, has received research funding from Merck, and has received other fees from the Gerson Lehman Group. C.R. Flowers has acted in a consulting or advisory role for OpumRx, Seattle Genetics, Bayer, and Gilead Sciences, has received research funding via his institution from Aetna Health, Infinity Pharmaceuticals, Otsuka, Janssen Oncology, Gilead Sciences, Celgene, TG Therapeutics, Genentech/Roche, Pharmacyclics, AbbVie, and Immune Design; and has received travel and accommodations expenses from Gilead Sciences, Celgene, and Genentech/Roche. C.S. Lathan has received honoraria from PER; has acted in a consulting or advisory role for the Gerson Lehman Group, Lilly, and Bristol-Myers Squibb; and has received research funding from CVS Health. J.L. Lichtenfeld reports stock or other ownership in General Electric, IBM, and Johnson & Johnson; has received honoraria from Aetna; and has received travel and accommodations expenses from Aetna. E.D. Paskett reports, for both herself and an immediate family member, stock or other ownership in Pfizer and Meridian Bioscience and has received research funding via her institution from Merck Sharp & Dohme. No potential conflicts of interest were disclosed by the other authors.

Authors’ Contributions


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References

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