Chapter 1
Advancing the Science of Cancer in Latinos

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Introduction

Cancer is the second leading cause of death among non-Hispanic white (NHW) men and women in the United States—but is the leading cause of death among Latinos [1]. The US Latino population was 60.6 million in 2019, as one of the largest, youngest, and fastest growing minority groups in the United States, its population will nearly double by 2060, making up 27.5% of the projected US population [2, 3]. Thus, advancing the science of cancer in Latinos has become an imperative for the nation, as Latinos will contribute a significant portion to its future cancer burden.

The good news is that age-adjusted cancer mortality rate in the US population has steadily declined, dropping 31% from 1991 to 2018 [4]. Later in the decade, Latino cancer mortality rate also declined and is now lower than most other groups in the United States. For example, the overall cancer mortality rate (per 100,000 population) during 2014–2018 for Hispanics was 110.8–30.8% lower than NHWs [5].

Despite this encouraging news, cancer health disparities stubbornly persist among the US Latino population. While Hispanics as a group have lower incidence rates than NHWs for most cancers including breast, colorectal, lung, and prostate, they experience higher incidences of gallbladder cancer and infection-related cancers of the stomach, liver, and uterine cervix [1]. For some cancers such as liver and stomach cancers and pediatric acute lymphoblastic leukemia, Hispanics are diagnosed with more aggressive or advanced disease and experience higher mortality

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rates than other groups [6]. Furthermore, compared to NHWs, Hispanics are more likely to be diagnosed with cancer at a later stage when it is more difficult to treat, and they are also more likely to experience longer delays from diagnosis to treatment leading to poorer treatment outcomes.

Why these disparities exist is the result of a complex interplay of many factors. One determinant is socioeconomic status (SES). Compared to NHWs, Hispanics are more likely to live in poverty, which also means they are less likely to have health insurance and access to health care, including cancer screening and preventive care. They are also more likely to have fewer cancer treatment options, more treatment delays, and lower treatment adherence rates [7]. Other important factors are in the cultural domain. Hispanic ethnic identity, values, and beliefs can influence healthy behavior, engagement with health providers, and how one copes with cancer diagnosis and treatment. Generational status, level of acculturation, and country of origin are also associated with varied cancer outcome. Paradoxically, low acculturation is associated with lower cancer burden despite being associated with lower income and less access to health care. As individuals become more acculturated to the United States, however, their cancer incidence rates rise and may even surpass that of NHWs [1]. Finally, differences in cancer burden and treatment outcomes may be a function of inherited genetic variation. Hispanics are not a homogeneous group, but rather comprise subgroups that differ by geographic regions of origin and varying degrees of genetic admixture from predominantly Indigenous American, African, and European ancestries.

Building Collaboration for Action

Because of the multifactorial nature of cancer disparity, finding solutions requires a collaborative and transdisciplinary approach. The second national conference—Advancing the Science of Cancer in Latinos—was designed to provide opportunities for collaboration to build implementation science to better address cancer health disparities and reduce the burden of cancer in Latino communities. Held in San Antonio on February 26–28, 2020, the conference was co-hosted by the Mays Cancer Center and the Institute for Health Promotion Research at UT Health San Antonio and was sponsored by the National Institute on Minority Health and Health Disparities. Bringing people together from across the cancer continuum, it included those with expertise in genetics, social determinants of health, early detection and screening, diagnosis, treatment, and survivorship. Furthermore, it brought the voice of the community, researchers, educators, and intervention specialists. Attending were people from academia, government, professional organizations, businesses, and non-governmental organizations. So, the breadth of expertise and experience was wide. There were opportunities for formal and informal discussions during the meeting, and the material presented reflected this diversity of backgrounds and interests. Joining people with these backgrounds was meant to serve as a stimulus

for developing new joint research and interventions—particularly in implementation and dissemination science.

The following sections set some context and briefly describe the papers contributed by many of the conference presenters. Note that the terms Hispanic, Latino/a, and Latin(x) are used interchangeably and reflect the preferences of the authors or US federal designation.

Vulnerable Populations and Health Threats in the Latino Community

Vulnerable populations experience significant health disparities, suffering greater disease risk, morbidity, and mortality than the general population. The vulnerable among them includes racial/ethnic minorities, the poor, those with chronic health conditions or disabilities, the elderly and the young, those who are socially vulnerable such as members of the LGBTQ+ community, and those who are geographically isolated.

Acute Lymphoblastic Leukemia (ALL) in Latino Children Latino children are a vulnerable population who experience a higher incidence of acute lymphoblastic leukemia (ALL) and poorer treatment outcomes than non-Latino children. This cancer disparity, like many others, is cross-cutting along the cancer treatment continuum from heightened risk to less favorable treatment outcome and untoward treatment effects that last into survivorship. Brown et al. describe research that suggests Latino children with ALL may be more vulnerable to the adverse neurotoxic effects of CNS-directed therapy with methotrexate. From their own study of pediatric patients, they found a nearly 2.5-fold increased risk of neurotoxicity in Latino pediatric patients compared to non-Latino patients. In addition to these short-term adverse effects of therapy, they propose that Latino survivors may also be more vulnerable to long-term neurocognitive impairment that affects quality of life in survivorship. Why these disparities exist is unknown and may be related to inherited genetic variation and sociocultural differences such as acculturation and socioeconomic status.

Population Health Challenges and the Affordable Care Act The Patient Protection and Affordable Care Act (ACA) became the US law in 2010. Its purpose was to make health insurance more affordable and accessible by offering insurance plans through marketplaces, expanding Medicaid, and providing incentives to improve cost and quality of care. In Part II, Ortega describes how the ACA affects healthcare access and utilization among Latinos. His research confirms that, in general, Latino adults and youth overall have benefitted from the ACA; however, they still fared worse when compared to non-Latino whites. A subgroup comparison of Latino heritage groups (Puerto Rican, Mexican, Cuban, Central American, and other Latino) showed that most reductions in disparities were experienced between

Puerto Ricans and non-Latino whites; Mexicans and Central Americans experienced more pervasive inequities—especially non-citizens and those in states that have not expanded Medicaid as part of the ACA.

Financial Hardship and Food Insecurity For cancer patients and survivors, the high cost of cancer treatment and care can cause financial hardship such as inability to pay medical bills, debt, and bankruptcy. Such hardship may put cancer survivors at risk for food insecurity—the inability to access enough food for a healthy lifestyle because of insufficient money or other resources. McDougall et al. present results from a cross-sectional survey comparing financial hardship and food insecurity among population-based Hispanic and non-Hispanic cancer survivors in New Mexico. They found that Hispanic cancer survivors were more likely than non-Hispanic cancer survivors to be unable to cover the cost of medical bills and were more likely to reduce spending on food and clothing as a result of cancer treatment. The prevalence of food insecurity among Hispanic cancer survivors in the year after cancer diagnosis was about 47%—considerably higher than the 36% for the overall project and 11% for US adults. While there were no significant differences by ethnicity, new and persistent food insecurity for the project was strongly associated with forgoing, delaying, or having to make changes to cancer care. The results of the study point to the need for food-insecurity screening and interventions that specifically address financial hardship and food insecurity among cancer survivors.

Disparities Research Along the Cancer Control Continuum

Cancer Prevention and Screening

Strength-Based Approach to Cancer Prevention US Latinos overall have a lower cancer burden than other groups; however, as Latinos become acculturated to US culture, their risk for cancer rises [1]. Torrez-Ruiz et al. point out that less acculturated Latinos still retain the cultural and behavioral patterns of their home country, which influences the quality of diet and the level of physical activity—two lifestyle factors that contribute to cancer risk. They consume more nutrient dense foods such as fruits, vegetables, and whole grains and are more physically active than their more acculturated US counterparts. As Latinos become more exposed to US culture, they often become less active and adopt a less healthy diet. To lessen these effects of acculturation, the authors advocate using a strength-based approach that focuses on the positive aspects of Latino culture to inform intervention research. Specifically, they propose developing culturally appropriate interventions that leverage values such as collectivism, *personalismo*, and *familismo*—Latino cultural elements that can promote healthy protective behaviors and lower cancer risk.

Cervical Cancer Elimination Some viral and bacterial infections are linked to cancer; the four most common cancer-related infectious agents are human papilloma virus (HPV), hepatitis B virus (HBV), hepatitis C virus (HCV), and *Helicobacter pylori*. Fortunately, many of these infections can now be treated or prevented, making them potentially modifiable risk factors [8]. In her paper, Giuliano describes the goal and strategy for preventing HPV-related cancers (cervical, vulvar, vaginal, anal, oropharyngeal, and penile), the majority of which are preventable with the use of three readily available tools—HPV vaccine (e.g., Gardasil and Gardasil 9), cervical cancer screening, and treatment for pre-cancerous lesions. Despite the fact that these tools exist, the cervical cancer incidence in the US Hispanic population is higher than in other groups; Hispanic women are about 40% more likely than non-Hispanic white women to be diagnosed with cervical cancer [9]. Furthermore, among non-Hispanic white women, the incidence of cervical cancer declines after age 40, but among Hispanic women, the incidence of cervical cancer continues to increase with age. These disparities in incidence likely result from women either skipping screening or not receiving treatment. Compared to other groups in the United States, vaccine uptake is as high or higher in the adolescent Hispanic population, but to eliminate cervical cancer, we must promote all three prevention tools—vaccination, screening, and follow-up treatment for abnormal dysplasia.

Cancer Treatment

Treatment Delays among Latino Breast Cancer Patients Breast cancer incidence among Hispanic women is lower than that of non-Hispanic white women, yet Hispanic women are more likely to be diagnosed with more aggressive disease and to experience delays in treatment, contributing to worse outcomes. Malinowski and Chavez Mac Gregor describe some of the unique challenges in cancer care delivery that Hispanic breast cancer patients face including the detrimental effects of treatment delays. To determine whether biological factors alone can explain disparities in outcome, the authors evaluated breast cancer patients treated with similar neoadjuvant preoperative chemotherapy and found that race or ethnicity was not associated with the rates of pathological complete response. In another study, they analyzed patients taking part in phase II/III clinical trials and found that when Hispanic breast cancer patients received uniform treatment and follow-up in a highly controlled setting, their survival outcomes were similar to that of non-Hispanic women. The authors hypothesized that differences in outcomes between Hispanics and non-Hispanics may be less a function of biology and more the result of differences in social determinants of health such as lower economic stability, language differences, lower health literacy, lack of health insurance, and poorer access to regular medical services.

Compared to non-Hispanic white women, Hispanic women experience disparities along the entire cancer continuum, contributing to adverse breast cancer outcomes. These disparities run the gamut from lower mammography screening prevalence and diagnostic delays to longer times from diagnosis to surgery and delays in chemotherapy, radiation therapy, and endocrine therapy. To address this issue, the authors are beginning a new qualitative study to identify why breast cancer patients experience delays in the start of chemotherapy. Using validated instruments, they will examine factors at the operational, medical, and personal/social level including social support, health literacy, and trust in health providers.

Genetic Ancestry and Precision Medicine Approaches

Genetic Ancestry and Breast Cancer Subtypes Breast cancer is the most common cancer among Hispanic women. However, as a group, Hispanic women have a lower incidence of this cancer than non-Hispanic white or black women. There are intrinsic biological subtypes of breast cancer, each associated with different prognoses. In clinical practice, these subtypes are inferred by immunohistochemical markers for the estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2). Compared to the other subtypes, ER−/PR− tumors [10] have fewer treatment options and poorer prognosis. Tamayo et al. describe results of studies examining correlations between genetic ancestry and breast cancer subtypes among US Hispanic or Latin American patients. According to the authors, studies show that Hispanic women have a 20–40% higher risk than non-Hispanic white women of developing ER−/PR− HER2+ and ER−/PR− HER2− breast cancer. There is also an emerging body of research that suggests there is an association between genetic ancestry of Hispanic women and breast cancer subtype. For example, evidence points to an association between the degree of Indigenous American ancestry and HER2+ tumors and an association between degree of African ancestry and ER− tumors. The authors conclude that more studies are needed to improve understanding of tumor subtype etiology of breast cancer in admixed minority populations.

Precision Medicine Approaches for Patients at Risk of Lung Cancer African ancestry is associated with worse clinical outcomes for chronic obstructive pulmonary disease (COPD) and lung cancer, and the degree of African ancestry varies among some Latinx subgroups. Thus, there is a need to develop risk stratification strategies and targeted lung cancer therapies that consider genetic admixture among Latinx populations. Lung cancers in all racial and ethnic groups are often diagnosed too late for a surgical cure, so there is also a need for early biomarkers of disease.

Ramos et al. propose that the current precision medicine approaches for treating lung cancer should be refined by improving risk stratification for patients with COPD, who are at heightened risk for lung cancer. In their paper, Ramos and his

colleagues review their research on ORF1p—a protein encoded by the retroelement, Long Interspersed Element-1 (LINE-1). Overexpression of ORF1p is associated with genetic instability and poor prognosis in patients with non-small-cell lung cancer (NSCLC). Because it accumulates in lung cancer cells and is found in circulating exosomes, the authors hypothesized that circulating ORF1p may be used as a sensitive biomarker of genetic instability in patients with COPD and lung cancer. Further, the authors found that the cellular protein, nucleolin (NCL), regulates ORF1p expression and that using NCL antagonists can stop NSCLC growth in a mouse model of lung cancer.

Outcomes and Survivorship

Obesity and Breast Cancer Survivorship The number of Hispanic breast cancer survivors in the United States is increasing as the Hispanic population grows and breast cancer survival improves. Further, this growing population is more likely than non-Hispanic whites to experience increased obesity and related comorbidities into survivorship. To address these issues, Bandera, Hong, and Qin compared Hispanic and Black breast cancer survivors in a pilot study and found that the cohort of Hispanic breast cancer survivors had lower patient-reported health-related quality of life (QoL) scores, particularly those who were obese. Among breast cancer survivors, the association between obesity and patient-reported outcomes is poorly understood and not well studied among Hispanic women, emphasizing the need for more research on cancer survivorship in this vulnerable population.

Latino Men Cancer Survivors Compared to Hispanic women and other racial/ethnic groups, Hispanic men overall experience higher incidence of most cancers and higher cancer-related mortality. The number of Hispanic men cancer survivors (HMCS) continues to grow and their unique supportive care needs have not been adequately addressed. Based on evidence from recent preliminary research, Martinez Tyson and Ruiz describe unmet supportive care needs of Hispanic men cancer survivors. HMCS participants reported the need to overcome language barriers so that they not only can understand treatment information but also can ask clarifying questions; they prefer bilingual conversation and do not trust that interpreters accurately convey their concerns. These men want culturally competent care that includes, for example, the constructs of *confianza* and *personalismo* so that they can build better rapport with providers and speak more openly about their concerns. Many participants felt the need for more information about their treatment and its effects, a better understanding of post-treatment follow-up including screenings, and a more holistic approach that focuses on overall health and wellbeing. Along with the demands of cancer therapy or employment changes, many were troubled by changing gender role expectations within the family brought about by the financial and emotional burden placed on female family members. Furthermore, the authors found many HMCS want to connect with other survivors and discuss their shared

experiences. How do HMCS cope with their cancer diagnosis? Many survivors believe that overall attitude is important in overcoming the disease process; they advocate maintaining a positive outlook through optimism, humor, and faith in God. For some, incorporating home remedies into the overall treatment plan and making lifestyle changes gave them a sense of agency and self-efficacy. They also reported their social support systems helped them feel less isolated and more able to contend with the logistics of attending appointments and going to treatments.

E-health Interventions in Cancer Control and Survivorship Now that cell phone use is becoming commonplace among US Hispanics, smartphone applications can be used to deliver scalable, evidence-based supportive care interventions, reaching out to those who may have logistical barriers to in-person cancer care. Hispanic breast cancer survivors (BCS) experience worse health-related quality of life (HRQOL) and symptom burden than non-Hispanic BCS. To reduce these disparities in psychosocial outcomes, Baik et al. used community-engaged research approaches to develop and evaluate two culturally informed, bilingual smartphone applications—*My Guide* (intervention) and *My Health* (control)—tailored to address the unique needs of Hispanic women. Even though the results were similar between the intervention and control groups, the researchers were able to demonstrate the feasibility and efficacy of these applications in improving cancer symptom burden and HRQOL. Participants of both groups said they would have liked to have also used these applications during breast cancer treatment, so the researchers expanded the scope of *My Guide* to address the needs of Hispanic women in active breast cancer treatment. *My Guide* and the newer *My Guide for Breast Cancer Treatment* are among the first bilingual, supportive-care smartphone applications, which have the potential to improve patient-reported outcomes among Hispanic women during both active cancer treatment and into survivorship.

Cross-cutting Research and the Future of Cancer Care

Optimizing Engagement of the Latino Community in Cancer Research Baezconde-Garbanati et al. describe signature initiatives designed to engage Latino communities in cancer research by reducing barriers toward inclusion. Two of their population-based studies in Los Angeles—*Es Tiempo* and *Tamale Lesson*—were designed using a community-based participatory research approach to optimize participation and retention of Latinos in cervical cancer and HPV trials. These model interventions included *promotores de salud* and community members who took part in all stages of research, from conceptualization, recruitment, translation, cultural adaptation, and information dissemination. The intent was to make the members of the participating communities feel they were an essential part of the research. A promising third exploratory study used virtual reality to better understand vaccine hesitancy and explore end-of-life improvements for immigrant Latinos. To influence attitudes and behaviors that place Latinos at risk for cancer,

the researchers used bidirectional communication; educational information was broadcast out to the community while knowledge was received by academic researchers who learned about community issues and barriers to participation. Their strategies for increasing Latino participation in cancer research focused on three key areas: (1) information delivery or knowledge transfer; (2) consultation with Latino community stakeholders and partners, including community advisory boards, patient advocates, and citizen scientists; and (3) collaboration with community opinion leaders.

Advancing Inclusive Research Melissa Gonzales from Genentech describes how one biotechnology company is addressing clinical research disparities to achieve personalized healthcare for everyone, including the most vulnerable Hispanic communities. Their initiative—*Advancing Inclusive Research*—aims to expand inclusion of diverse patient populations into their clinical research. To accomplish this, they intend to imbed inclusive research principles so that clinical trial enrollment reflects real-world populations; expand site networks to include more diverse catchment areas; and identify and remove barriers to participation in clinical trials such as providing transportation and child care. Further, they will increase genomic data and scientific insights from underrepresented populations and will leverage relationships with external partners to develop strategies for increasing participation of underrepresented groups in clinical trials.

Exposome-wide Association Study Approach Because Latino cancer disparities are so persistent and their underlying causes so varied, Juarez et al. propose that we need a new way of conducting disparities research that accounts for environmental, endogenous, and social factors. They suggest using a research strategy based on the exposome—all of the external and internal exposures experienced by individuals across their lifespans from conception to death and how these exposures affect health. Applying an ExWAS approach can help identify how environmental exposures alter key biological pathways at the cellular, molecular, and system level, and help explain the increased risk for population-level cancer disparities among Latinos. Measured exposures can be linked to biochemical and molecular changes through the use of prognostic and diagnostic biomarkers based on "omics" technologies such as genomics, epigenomics, transcriptomics, metabolomics, proteomics, and lipidomics.

Implementation Science There is often an unacceptable lag time of years and even decades before new research evidence becomes part of broadly adopted medical practice, and many new, effective, health interventions are not reaching Latino populations to the same degree as the general public. Gila Neta from the National Cancer Institute (NCI) points out that to ensure new cancer discoveries reduce the cancer burden for Latinos, researchers must focus not only on what evidence-based interventions can improve outcomes but also on how those interventions can be adopted, implemented, and sustained. To bridge the gap between research and practice, NCI supports research in implementation science—the study of strategies to

adopt and integrate evidence-based health interventions into clinical and community settings, improving individual outcomes and benefitting population health [11]. This science also includes studying strategies to de-implement practices that are ineffective, unproven, low value, or harmful. In her paper, the author describes the discipline and goals of implementation science and the role of the National Institutes of Health (NIH) in providing trans-NIH funding opportunities in this field. Neta further emphasizes that implementation science must consider the multilevel context and engage stakeholders in two-way communication so that strategies not only address critical barriers but are also workable and appropriate for the relevant settings and populations, and are likely to be integrated, sustained, and scaled.

The Changing Demography of Cancer Even though Latinos have a lower cancer burden than other groups in the United States, their disproportionate growth will likely shift the demography of cancer in the future [12]. Sáenz examined this trend by analyzing recent cancer statistics from the CDC and population projections from the US Census Bureau. The analysis was based on two time periods—past (1999–2016) and future (2016–2060).

Sáenz found that compared to non-Latino whites and blacks during 1999–2016, US Latinos had the lowest age-adjusted cancer incidence and death rates, and they made up only a fraction of the nation's cancer cases (8.2%) and deaths (6.6%) in 2016. However, because of their growing population, Latinos contributed to nearly one-fifth (18.8%) of the increase in US cancer cases and two-fifths (39.5%) of the increase in cancer deaths between 1999 and 2016. Because the population growth of Latinos is expected to outpace that of non-Latinos, the percentage of Latino cancer cases and deaths will likely double from 2016 to 2060. Latinos will account for one-third of the US projected increase in cancer cases and one-fourth of the projected increase in cancer deaths during this time frame. By 2060, Latinos will still be a younger group, so they will make up a larger share (25%) of cancer cases and deaths among those less than 45 years.

The author points out that the growing presence of Latinos in the future has implications for public policy. For example, current inequities in access to affordable health care and lack of health insurance will increase the risk of Latinos having cancer and dying from the disease. In addition, public policy that discourages migration from Mexico to the United States could erode the Latino morbidity and mortality advantages they currently possess.

Conclusion

The Advancing the Science of Cancer in Latinos conference brought together a diverse group of health professionals to encourage collaboration and a free exchange of ideas from different perspectives; the papers in the following chapters show the breadth of their research across the cancer care continuum. Exploring this book, you

will learn about vulnerable Latino populations, Latino lifestyles, and health threats in the Latino community; cancer prevention, cancer outcomes, and survivorship among Latinos; genetic ancestry and precision medicine; advances in cancer therapy, clinical trials, and engaging Latinos in cancer research; and implementation science and innovative technologies. The papers and posters presented here are part of an ongoing dialogue, providing new insights and solutions to the problem of cancer disparities among Latinos.

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