Access this article online

Quick Response Code:

Website: www.carcinogenesis.com

DOI: 10.4103/jcar.JCar_13_17

Evidence-based approaches to reduce cancer health disparities: Discover, develop, deliver, and disseminate

Priyanka P. Desai, Jana B. Lampe, Sulaimon A. Bakre, Riyaz M. Basha, Harlan P. Jones, Jamboor K. Vishwanatha

Abstract:

The Texas Center for Health Disparities (TCHD) at the University of North Texas Health Science Center is a National Institute on Minority Health and Health Disparities-funded, specialized center of excellence for health disparities. TCHD organized its 12th annual conference focusing on "Evidence-Based Approaches to Reduce Cancer Health Disparities: Discover, Develop, Deliver, and Disseminate." At this conference, experts in health care, biomedical sciences, and public health gathered to discuss the current status and strategies for reducing cancer health disparities. The meeting was conducted in three sessions on breast cancer, prostate cancer, and colorectal cancer disparities, in addition to roundtable discussions and a poster session. Each session highlighted differences in the effects of cancer, based on factors such as race/ethnicity, gender, socioeconomic status, and geographical location. In each session, expert speakers presented their findings, and this was followed by a discussion panel made up of experts in that field and cancer survivors, who responded to questions from the audience. This article summarizes the approaches to fundamental, translational, clinical, and public health issues in cancer health disparities discussed at the conference.

Keywords:

Breast cancer, colorectal cancer, health disparities, prostate cancer

Introduction

The 12th Annual Texas Conference on Health Disparities was organized by the Texas Center for Health Disparities convened on June 8–9, 2017, at the University of North Texas Health Science Center (UNTHSC) in Fort Worth, Texas. The conference addressed health disparity issues related to breast, prostate, and colorectal cancers (CRCs). The participants sought to identify strategies and initiatives for discovering, developing, and delivering evidence-based approaches focusing on these cancers. Each session opened with presentations by leading clinical, biomedical, and community experts in each of the focused cancer areas and concluded with a discussion panel which included the speakers, cancer survivors, professors, as well as students. Audience members comprised of biomedical, medical, and public health students, postdoctoral fellows, health science faculty, and community participants asked questions and shared their ideas and opinions. The sections mentioned below provide a summary of the critical issues facing prostate, breast, and CRC presented by each speaker, panelist, and audience participant.

Keynote Address

The conference opened with a keynote address by Rebecca Garcia, Chief Prevention and Communication Officer, at the Cancer Prevention and Research Institute of Texas (CPRIT). In her presentation, entitled "From Awareness to Action: Addressing

Texas Center for Health Disparities, University of North Texas Health Science Center, Fort Worth 76107, Texas, USA

Address for correspondence:
Dr. Jamboor K. Vishwanatha, University of North Texas Health Science Center, 3500 Camp Bowie Blvd., Fort Worth 76107, Texas, USA.
E-mail: jamboor.vishwanatha@unthsc.edu

Received: 24 December, 2017
Accepted: 28 December, 2017
Published: 28 February, 2018

How to cite this article: Desai PP, Lampe JB, Bakre SA, Basha RM, Jones HP, Vishwanatha JK. Evidence-based approaches to reduce cancer health disparities: Discover, develop, deliver, and disseminate. J Carcinog 2018;17:1

Cancer Disparities," Dr. Garcia highlighted the disparities in cancer risk and mortality among diverse populations. The chances of developing diseases, such as cancer, have been broadly linked to socioeconomic factors such as income, education, or poverty level. However, additional elements embedded within these historical structural indicators of cancer risks are equally significant to understanding cancer health disparities. Defining various factors helps researchers understand why people who live in rural areas are more likely to smoke and die of lung cancer. They can also determine how a person's physical environment affects his/her access to quality health care. Furthermore, it has also been shown that a person's insurance status can play a critical role in disease and mortality outcomes. Those who live in border areas, such as those in the Rio Grande Valley, have an increased chance of disease than those in nonborder regions.[1] Furthermore, individual behavioral choices such as nutrition, physical activity, and other lifestyle decisions have emerged as influential factors related to cancer risks. For example, groups that typically do not seek screening and early care are more likely to die prematurely from their disease. African-American (AA) men and women, for example, have higher cancer mortality rates than Caucasian men and women. Hispanic men have the highest risk of developing liver cancer. Dr. Garcia suggested that inclusion in just one of these groups increases the chance that a person will not have adequate education and screening for cancer and other diseases. In addition, age and genetics play a role in disproportionate increases in the numbers of minority populations who tend to develop aggressive tumors.[2] According to the Texas Cancer Registry, between 2009 and 2013, blacks, as compared to other races or ethnic groups, had mortality rates that were higher than average. Thus, while the most common factors are poverty and exposure to carcinogens, risk factors encompassing socioeconomic, physical environment, behavioral, biological, and access to health care produce a sophisticated framework for identifying solutions needed to eliminate cancer disparities.

Dr. Garcia closed by highlighting the efforts of how the Centers for Disease Control, the National Cancer Institute (NCI), and the CPRIT are working toward addressing cancer health disparities. CPRIT supports many programs that strive to reach underserved populations that have a higher than average percentage of cancer incidence. The organization also provides financial backing for many programs with grant funding.[3,4]

Session 1: Breast Cancer Disparities

BCa is the most common malignancy in women in the United States, but significant disparities exist for AA women compared to Caucasian women. In addition to the nonbiological indicators known to impact BCa disparities, emerging evidence also suggests that biological characteristics of the primary tumor also play an essential role in defining inequalities. This session focused on bringing forth known and emerging findings across clinical, translational, biomedical, and community-based research aimed at addressing breast cancer (BCa) disparities. The session on BCa disparities was chaired by Dr. Ritu Aneja, Professor at Georgia State University, Atlanta, Georgia, and included presentations by a basic science researcher, a prevention researcher, and a clinician.

Dr. Arun Shreekumar, Professor and Academic Director of Metabolomics Core at the Baylor College of Medicine, Houston, presented "Metabolic basis of racial disparity in breast cancer;" Dr. Shreekumar's research focuses on developing biomarkers using a high throughput metabolomics platform to identify an efficient metabolomic marker to study cancer progression. Dr. Shreekumar presented data on differences in metabolomic alterations in triple-negative BCa (TNBC) patients comparing the AA cohort and the European-Americans (EA). Among his recent discoveries was the use of high throughput mass spectrometry and cancer (onco-) metabolomics to identify the small molecules that function in processes that drive cancer such as angiogenesis, immune response, and reactive oxygen species production.[5]

One of the oncometabolites is D-2-hydroxyglutarate (2-HG), which has been found to be higher in breast tumors than in benign tumors. From his research, Dr. Shreekumar was able to show that 2-HG was detected in higher amounts in AA TNBC patients than in EA. This can be attributed to a mutation in isocitrate dehydrogenase (IDH), a key enzyme in the citric acid cycle. The mutation is a result of increased DNA methylation and inhibition of demethylases (TET [ten-eleven translocation] methylcytosine dioxygenase 1 and 2 [TET1 and 2]).[6] His work with 2-HG also demonstrated that its hypermethylated form observed in estrogen receptor (ER)-positive and benign BCa cell lines proved 2-HG as an epigenetic modifier in BCa. From this initial finding, Dr. Shreekumar was able to identify different methylation signatures in response to high 2-HG. From these data, ER-negative AA patients were segregated from the other patients and were analyzed for the signatures. 2-HG was found to be increased in these patients with increased S-adenosyl homocysteine and S-adenosyl methionine which signaled toward the increased hypermethylation in the cell.[7] Data also suggested that there was significant upregulation of IDH1/2 in patients with no mutation. Thus, overexpression of gene IDH2 was found to be regulated by promoter-specific methylation, which

induces a distinct methylation signature and the increase in 2-HG was because of overexpression of IDH.

In addressing the clinical relevance of this change, Dr. Shreekumar presented data from the gene expression signature associated with the patients showing high 2-HG, which is associated with a high, specific methylation phenotype, is also associated with a gene expression signature in patients who have poor disease-free survival. Gene expressions were subjected to a publicly available dataset, and it confirmed that 2-HG was associated with poor prognosis. Pathway analysis performed using bioinformatics analysis also showed that these gene expressions were associated with an epithelial-mesenchymal transition-like (EMT) phenotype where 2-HG leads to an increase in demethylation which increases EMT.[8] Further, bioinformatic analysis was employed to identify upstream oncogene and transcription factors (TFs), which regulate the phenotype. TFs, such as Myc, which govern glutamine metabolism were shown to increase when 2-HG levels rise.[9]

From these findings and his ongoing research, Dr. Shreekumar is making significant progress in defining molecular signatures with the promise of distinguishing BCa progression across races. Dr. Shreekumar summarized his talk by concluding that 2-HG is an oncometabolite, which accumulates in AA TNBC patients and these patients have an unfavorable prognosis. Accumulation of 2-HG is a result of Myc activation in AA TNBC patients. The clinical relevance of this study is that 2-HG can be used as an indicator for glutaminase inhibitor therapy and to develop a noninvasive test to select patients for TNBC treatment.[10]

Dr. Elisa V. Bandera, from the Cancer Prevention and Control Program at the Rutgers Cancer Institute of New Jersey, spoke about the racial and ethnic disparities in obesity and BCa. BCa represents about 30% of cancer in females and is also responsible for about 40% of cancer mortality. Developed countries have the highest rates of incidence (parts of the US, Europe, and Australia), whereas the highest mortality rates are predominantly found in the underdeveloped countries. The striking discrepancies can be attributed to better access to care in the developed countries. In the US from 2009 to 2014, whites had the highest incidence of BCa compared to other races, but the highest mortality rates were found among AA women. The trend in the incidence rate in whites has been relatively stable but has increased in AA women, reaching a convergence with whites in 2012.[11] There is a wide divergence in the trend of long-term BCa mortality rates between AA and whites with a 42% higher mortality in blacks compared to whites. The 5 year survival rate is lower in AA compared to whites for nearly all cancer types. For BCa, the 5-year survival rate is lower in AA (80.3%) and highest in Asians and Pacific Islanders (91.6%) compared to other races. AA tend to be diagnosed at a more advanced stage, and survival is lower at any given stage.

Early menarche, late menopause, nonfull-term pregnancies, giving birth at an older age, not breastfeeding, hormone therapy, and obesity all contribute to the disparities among races. AA have the highest prevalence of obesity with 56.6% obese and 82% overweight, followed by Hispanics, non-Hispanic whites, and finally, non-Hispanic Asians after age adjustment. The body composition, metabolic profile, and related biomarkers are different when comparing AA to whites. AA women have higher lean mass, lower fat mass, lower visceral adipose tissue, and elevated levels of subcutaneous adipose tissue when compared to whites. They also have more insulin resistance, higher levels of leptin and inflammatory markers such as C-reactive protein, interleukin-6, and lower levels of adiponectin compared to whites after adjusting for body mass index (BMI). Furthermore, increased body fat leads to increased bioavailable steroids, increased bioactive insulin-like growth factor-1, oxidative stress, and immune function. These factors lead to more aggressive tumors, increased tumor growth, metastasis, and decreased response to therapy.

AA women are more likely to develop ER– and TNBC which have a poorer prognosis than ER+ BCa and are more likely to be diagnosed at an earlier age with a more aggressive disease. However, few studies have looked at the impact of general and central obesity on BCa in AA women. A meta-analysis found that obese women are more likely to develop postmenopausal BCa but less likely to develop premenopausal BCa. Regarding race, the risk of developing BCa in obese women does not differ significantly, but for women with postmenopausal BCa, the risk is higher in whites compared to other races. BCa is classified into four types: luminal A and B which belong to the ER+ group and human epidermal growth factor receptor 2 (HER2+) and TNBC which belong to the ER– group.

Dr. Bandera also discussed the Women's Circle of Health Study, a case–control study that started in New York City and expanded to 10 counties in New Jersey including women aged 20–75 years. The results of the study showed that premenopausal obese women had higher odds of having TNBC with an odds ratio (OR) of 1.13, but there was an inverse association in postmenopausal women with an OR of 0.6 compared to those with a healthy BMI. Obese women with BMI 30–34.99 had the highest risk of premenopausal TNBC. Whereas, women with a waist–hip ratio >0.88 had the highest risk of TNBC

in postmenopausal women. For ER+ tumors, obesity was associated with increased risk of postmenopausal BCa and the risk is higher for obese women who were thin when they were young adults. In addition, having a high BMI reduced the risk for ER+ tumors in premenopausal women while a high waist–hip ratio increased the risk of ER+ tumors in premenopausal women. For postmenopausal women, there was an inverse association between recently high BMI and TNBC, but there was an increased risk of TNBC with a higher waist–hip ratio.

Furthermore, she spoke about the possible factors responsible for reduced BCa survival in AA women. She highlighted the fact that more aggressive tumors are identified at a more advanced stage and grade in black women. They are also diagnosed more often with triple-negative tumors, which are associated with a poorer prognosis. Many disparities in health are marked by poverty, inadequate access to care, and suboptimal treatment, which are known indicators of mortality. Dr. Bandera's research also points to the high prevalence of central and general obesity and related comorbidities as additional reasons for BCa mortality in AA women.

Dr. Bandera concluded by talking about unresolved racial and ethnic disparities in BCa incidence and mortality. She emphasized the need for a multidisciplinary approach to better understand the causes of the inequalities in medical care in the United States. More studies need to be done on hormone receptor status that will include a substantial number of minorities to fully evaluate its relationship to obesity when considering the imbalance of its impact on AA as compared to white women.

The clinical perspective of BCa was presented by Dr. Robyn Young, Clinical Director of the Center for Cancer and Blood Disorders in Fort Worth, Texas. Dr. Young explained that BCa could not be considered one disease. Instead, it should be divided into subtypes. Due to the vast number of cancer permutations, developing effective treatments is a daunting task. Therefore, Dr. Young urged the biomedical community to make personalized therapeutics a priority in both primary research and translational medicine. In her talk, Dr. Young discussed BCa subtypes, diagnostic methods, and treatment options. She illustrated these concepts with three case studies that emphasized racial disparities, socioeconomic disparities, BCa subtypes, and systemic treatment differences. She also stressed the need for free screening, more clinical trials, and promotion of education for groups that have a higher risk of BCa.

Dr. Young explained that ductal carcinomas could remain in the ducts and not metastasize. However, the longer the cancer stays in the ducts, the more likely it is to metastasize into the fatty tissue, which is much closer to the vasculature and lymph nodes. Lymph nodes are used for prognosis. As the number of nodes involved with cancer increases, the risk of metastasis to the other organs of the body also increases. The rate of proliferation or rate of cancer tumor growth, number of lymph nodes involved, tumor size, and degree of metastasis are factored together in the staging of BCa.[12]

ERs, progesterone receptors (PRs), and HER2 were once used to predict invasive or metastatic cancer; they are now considered cancer subtypes. ERs are the proteins that estrogen binds to on a cell surface. When the estrogen ligand and the receptor bind, a cascade of chemical messengers signal the DNA to make more of a specific protein and to cause cell division. The HER2 receptors do not have ligands. Instead of being activated by a ligand, HER2 cells dimerize with another HER2 or HER3 receptor to stimulate cell growth. The prognosis for HER2 cancers is very unfavorable. As Dr. Bandera previously mentioned, intrinsic subtypes include luminal A tumors (ER and PR positive), luminal B (PR negative), basal like, and HER2.[13]

Prognosis and response to endocrine therapy can be predicted based on analysis of ER, PR, and HER2.[14] The luminal A subtype is always HER2 negative and has a low rate of proliferation, good prognosis, excellent survival rates, and low recurrence rates, but does not respond well to chemotherapy. The luminal B subtype is PR negative and HER2 positive or negative. It has high proliferation rates and typically leads to an unfavorable prognosis. Untreated, HER2-positive cancers are more likely to have an early recurrence, poor survival rates, and an increased chance of brain metastasis. Basal-like TNBC is characterized by its lack of ER, PR, or HER2 receptors. It is highly aggressive and known for its poor prognosis.[15]

Differences in testing amplify disparities in cancer outcomes. The Oncotype DX Test looks at 21 different genes in a tumor. The invasiveness gene is used to calculate a recurrence score from 0 to 50. Chances of recurrence are divided into low-, intermediate-, and high-risk groups. This tool helps physicians predict which treatment or combination of treatments would give a patient the best outcome. Women in the low-risk categories tend to do well with hormone therapy. High-risk patients respond best to chemotherapy. Primary treatment options are a modified radical mastectomy with axillary dissection, a simple mastectomy including sentinel lymph node mapping, or a lumpectomy with axillary dissection or sentinel lymph node mapping (SLN mapping) combined with radiation therapy.[16]

Dr. Young discussed three different clinical cases to illustrate the complexity of TNBC and reminded the

audience that BCa is not a single disease. Moreover, she emphasized the importance of getting yearly mammograms and regular clinical breast examinations. Dr. Young cautioned that TNBC is so aggressive that a mammogram every 2nd year is inadequate. She also believes that analyzing ER/PR/HER2 and genomic profiling of tumors are two of the best tools an oncologist has when determining a prognosis and in choosing an adjuvant treatment. For example, AA women have a higher risk of the more aggressive form, TNBC. In addition, the outcomes after treatment are far less favorable than for patients of other races.

Session 2: Prostate Cancer

The session on prostate cancer (PCa) was chaired by Dr. Riyaz Basha, Associate Professor, UNTHSC, who introduced the first PCa speaker, Dr. Shiv Shrivastava. In his basic science presentation, Dr. Shrivastava, Professor, and Co-Director at Center for Prostate Disease Research (CPDR), Washington D. C., presented his work on race- and ethnicity-associated differences of PCa. He also discussed his research on genomic alterations and assessment of broadly applicable biomarker panels across races. In his talk, Dr. Shrivastava emphasized that PCa is the most frequent nonskin cancer of males with the highest rate of incidence in African descents. He presented his research findings on erythroblast transformation specific-related gene (ERG), a frequently overexpressed oncogene in PCa.[17] ERG is found to be active in 50%–70% of PCa patients. Therefore, it could be used as a precise marker. He further discussed the biological function of ERG in PCa. ERG increases tumor cell invasion and abrogation of prostate cell differentiation collaborating with PTEN, PARP, WNT and NKX3.1 and targeting c-Myc, HPGD, and NOTCH. The frequency of ERG+ in the index tumors is much higher in Caucasian Americans (CA; 63.3 % (frequency of ERG positive index tumors), 91 samples) as compared to AA (28.6 % (frequency of ERG positive index tumors), 91 samples).[18]

Moreover, the prevalence of ERG-negative high-grade tumors is higher in AA than in CA patients with Gleason values between 8 and 10. The study on the PCa patients enrolled in the CPDR longitudinal military cohort showed that there is a lower prevalence of ERG alterations in the index tumors of AA when compared to those of CA (AA, n = 336, 23.2% and CA, n = 594, 49.3%, $P < 0.0001$). Moreover, in collaboration with NCI, DOD's Joint Pathology Center, University of Ghana,and Standford Cancer Institute, Dr. Shrivastava and his lab studied ERG-positive tumors. The study was carried out using immunohistochemistry in 262 West African men from Ghana suffering from PCa. Their study showed that there is 18% frequency of ERG+ tumors among the West African patients. Furthermore, the meta-analysis of African, Asian, and European PCa patients revealed that the prevalence of TMPRSS2-ERG gene fusions is higher in European men (49%) as compared to Africans (25%) and Asians (27%).[19,20] The whole genome analysis involving 435 CA and AA patient samples revealed known and new alterations in PCa genome, showing higher interchromosomal changes in AA and mutation in genes such as SPOP, MED12, and p53. ERG rearrangement with PTEN tumor suppressor deletion was seen in CA. A deletion study by The Cancer Genome Atlas (TCGA) SNP array data of the LSAMP gene, which is a cell adhesion protein gene at the 3q13.31 locus in 44 AA and 260 CA tumors, was shown to be associated with the rapid progression of disease in AA.[21]

Dr. Shrivastava's group also evaluated the association of BRCA1 and 2 mutations with disease progression in AA and CA patients where an increased frequency of BRCA1/2 pathogenic germ-line mutations was detected in patients with metastasis as compared to those with localized tumors. Thus, Dr. Shrivastava stated that the screening of BRCA1 and 2 germ-line mutations in high-risk AA and CA patients might enhance new treatment strategies. Moreover, he discussed the nanostring, long noncoding (lnc) RNA PCa gene panel where PCGEM-1 lnc RNA was shown to be associated with AA PCa patients. Thus, it has a potential to be a useful biomarker as it also can activate androgen receptor function and c-Myc.[22,23] He also showed data from CPDR Nanostring, RNA seq and TCGA RNA-seq, showing a panel of genes like PCA3, AMACR, ERG, PSGR, DLX1, NKX2-3, HOXC4, HOXC6, COL10A1, PSA and SPDEF that could be used as biomarker to study PCa genome differences between AA and CA. Furthermore, a combination of ERG mRNA and PCA3 showed improved diagnostic value over serum PSA among CA patients.[24] Dr. Shrivastava also explained his collaborative studies with Genomic Health Oncotype DX. Together, they are exploring gene expression studies on non-DRE urine exosomes isolated from CA (n = 55) and AA (n = 36) PCa patients. The evaluation of urine exosome gene expression in AA PCa patients showed the presence of PCA3, PSGR, and PCGEM1 gene. Validation of a gene panel from the PCa CPDR database in a group of racially diverse patients also showed COL1A1, BGN, and SFRP4 to be associated with worse outcomes in PCa.[25] He also elaborated on differential frequencies of ERG and PTEN, common drivers of PCa, suggesting that there are distinct biological mechanisms in CA and AA. He is also looking forward to the development of more therapeutic approaches and using ERG as a biomarker in PCa detection in the future. Moreover, he stated that studying the cancer genome, proteome, and metabolome will have broader implications for developing novel biomarkers and therapeutic targets.

The clinical perspective on PCa was presented by Dr. Judd Moul, M. D., Professor of Surgery and Director of the Duke Prostate Center at Duke University Medical School, Durham, NC. In his presentation entitled "PCa Diagnosis and Treatment 2017: Special Focus on Race and Ethnicity," Dr. Moul explained the effects of the prostate-specific antigen (PSA) test on men's health. Although the PSA test is not tumor specific, it is the only indicator we currently have that indicates the probability of PCa. When the test was first introduced in the early 2000s, well-known Americans such as Senator Robert Dole, General Norman Schwarzkopf, General Colin Powell, and others participated in a media campaign to urge men to get PCa screening.[26] Even though the number of men being screened was still suboptimal, the PSA test took a big hit from the United States Preventive Services Task Force (USPSTF). In 2008, the task force stated that screening for men over 70 years of age was unnecessary. In 2011, the same task force downgraded the screening, giving it a "D-rating," reporting that the test does more harm than good. They no longer recommend a PSA screening for any men, not even those with high-risk factors. The long-term impact of this decision has not yet been studied. However, in a report in 2012, it was reported that fewer men were being diagnosed with early-stage disease. As a result, the number of men who were being diagnosed with more aggressive cancers that are resistant to treatment was increasing.

Even in the United States, racial disparities in PCa outcomes abound. Black men have 1.5 times the risk of PCa and 2.5 times higher rate of mortality.[27] The explanations for this asymmetry are multifactorial. Genetic propensities, cultural attitudes, and behaviors combined with lower access to care all have an impact on the poor outcomes found in AA populations. Racial disparity in PCa rates existed before the D-rating. It has yet to be seen what the effect of the D-rating will be. Interestingly, when President Obama turned 50 years old, he underwent a PSA test during his physical examinations, ignoring the recommendation of the USPSTF. This decision was controversial because many under Obamacare will not be able to receive the same test.[28]

On April 11, 2017, the USPSTF announced in the online Journal of the American Medical Association, new guidelines on PSA testing. Even though they still do not recommend the test for men over age of 70 years, they have changed the rating to a C-rating. They now suggest that men between the ages of 55 and 69 years discuss the pros and cons of the test with their primary physician before deciding whether the test fits with their "values and preferences."

Dr. Moul proposed a question, "Do black American males die more often (and more quickly) because, as a group, they have less access to care or because they seek medical treatment later when their disease has progressed to an advanced stage?" Uninsured men typically have lower screening rates even for A-rated tests. Black and Hispanics comprise a high proportion of uninsured populations. Indeed, access to health care is a problem for AA men. Overall, men do not go to the doctor as often as women, but uninsured men are much more likely to go without care or may not fill prescriptions due to cost barriers.[29] In 1996, NCI reported that, despite the more aggressive nature of PCa in black men, they are less likely to have a radical prostatectomy. This shows a treatment disparity in the category of men who need the most aggressive treatment. A study published online in the journal, Urology, in 2016, showed that AA men with the highest risk of PCa mortality are 38% less likely to receive the best treatment for their condition.[30]

At the start of his position at Duke University Medical Center, Dr. Moul was part of a team that initiated the Duke Prostate Center database. They analyzed 10,530 patients from 1988 to 2006 who had been diagnosed with PCa. This "pro-screening era" was divided into 3-year groups: 1988–1994, 1995–1999, and 2000–2006. Each group was sectioned into AA and non-AA divisions. The findings showed that from 1988 to 1994, only 20.5% of AA men were treated with radical prostatectomy compared to 33.8% of non-AA men and 25% of AA men died from the disease, while only 13.6% of non-AA men succumbed. In the next two eras, the percentage of AA men who had radical prostatectomies increased to 28.5% as compared to an increase of 44.1% in non-AA men. Furthermore, over the 9-year period of the study, the percentage of non-AA men diagnosed with a high Gleason score (>7) went from 9.1% to 8.7%. During this same period, however, the percentage of AA men with high-risk Gleason scores went from 14.5% to 18.4%. On a positive note, the median age at the time of diagnosis in all men decreased during the 9-year period, from 68.4 to 66.4 years and from 67.8 to 64.8 years in non-AA men. This decrease is particularly significant because AA men are known to manifest the disease at earlier ages than other populations. Recurrence rates in all men during the study seemed to decrease, indicating the importance of screening.[31]

In summary, race and ethnicity have been shown to be an independent predictor of whether AA men will continue with an active surveillance (AS) protocol. However, black men who are part of an AS plan progress to treatment faster, regardless of socioeconomic factors and follow-up intensity. Dr. Moul emphasized the importance of screening, especially for those in high-risk groups. He also stressed the need for new molecular markers that are more specific than the PSA marker.

Providing the community activity perspective, Tarrant County Commissioner Roy C. Brooks, an AA and the survivor of PCa, addressed the topic "Healthy Lives Matter: PCa Risk and Preventative Efforts in Tarrant County, Fort Worth, Texas." He shared his life experiences; about how he was diagnosed at an early stage of PCa because of an early screening recommendation by his physician. Ironically, his physician who recommended the screening never followed his own advice and he was diagnosed with a stage-4 ductile PCa. His experiences lead to the development of a program called "Healthy Lives Matter." It started 3 years ago in his precinct in Tarrant County. This program serves about half a million people or approximately one-fourth of the Tarrant County residents. Healthy Lives Matter is an annual event that hosts and promotes PCa education and screening. The purpose of the annual gathering is to inform black men about the importance of PCa screening. This increased awareness enables AA men to know their status and to make essential decisions in choosing life.

PCa is the most commonly diagnosed nonskin cancer and the second leading cause of cancer mortality[32] and one of the most treatable cancers if diagnosed early. Among men who presently live, it is estimated that 1 in 6 will be diagnosed with PCa and 1 in 33 dies as a result of PCa.[32] There are several risk factors associated with the disease such as age, family history, and lower levels of Vitamin D in the blood. Furthermore, dietary choices such as the higher consumption of dairy products and red meats also contribute to the development of diseases. Half of most men are diagnosed at or above the age of 70 years. Moreover, 26% of men diagnosed at the age of 75 years and older have cancer that is identified as being high-risk disease.[33] A history of PCa in father or brother doubles the risk of developing PCa. Studies have shown that AA men have a 1.8 times higher risk of developing PCa than the general population and they are often diagnosed at later stages, with higher mortality rates.

In Tarrant County, cancer rates by race from 2007 to 2011 showed that blacks have the highest incidence and mortality rates of any type of cancer, 646.9 and 289.7 per 100 thousand, respectively. In 2015, it was estimated that there would be 8023 new cancer cases and 2962 cancer deaths in Tarrant County. Early cancer screening and detection in patients is critical in helping them get treatment, in preventing metastasis to the bone and brain, and in increasing survival rates. Screening for PCa can be done with a digital or rectal examination and by monitoring PSA levels.[34,35]

Healthy Lives Matter collaborates with community partners including JPS Health Network, Tarrant County Public Health, North Texas PCa Coalition, Moncrief Cancer Institute, Texas Health Harris Methodist Hospital, Texas Rangers, Cigna, Aetna, and United Healthcare. In the 2016 event, total attendance was 121 and AA were 81%, whites were 5%, Hispanics were 12%, and others were 2%. The majority of attendees were within the age range of 50–59 years. Fort Worth had the highest number of attendees from the 18 cities represented at the event. A risk assessment tool was developed using the combination of risk factors listed above. It consists of 5 categories: 5–10, 11–15, 16–20, 21–25, and 26–30, where a score of 5–10 represents a low risk and a score of 26–30 is considered high risk. A questionnaire was administered to each participant. Then, individual scores were assessed and patients were informed of their risk level. Most men scored between 11 and 15 points. Those with the highest risk (26–30 points) represented the fewest number of participants. According to the results of the PSA test, 86% were normal (<2 ng/ml), 7.5% were borderline (2–4 ng/ml), and 6.5% were abnormal (>4 ng/ml). For the Healthy Lives Matter 2017, the total attendance was 176 men. 79% were AA, 12% were Caucasians, 7% were Hispanics, and 2% were Asians. Most participants were between the ages of 50 and 59 years. The majority scored in the 10–15 risk category, and the lowest scores were in the 25–30-point category. The scores were similar to the results from the previous year. One hundred and thirty-five participants were normal, eight were borderline, and six were abnormal.

Roundtable Discussions

Roundtable discussions were held on various community health and health disparity topics to provide for small group discussions. Each table was assigned a thematic topic. The topics were (1) Decision-Making for testing and treatment (Moderator: Kim Linnear, Komen Foundation Fort Wort), (2) Mi Casa, Su Casa (Moderator: Tracey Willingham, Cancer Care Services), (3) Do Macho men get ill? (Moderator: Chris Hinojosa, Cancer Care Service), (4) Health Literacy and Health Care access for Cancer Patients (Moderator: Hilda Mendoza, Tarrant County Public Healt), (5) Women's Cancer Health Issues (Moderator: Amy Raines-Milenkov, DrPh, UNTHSC), (6) Cancer risks for Children (Moderator: W. Paul Bowman, MD, UNTHSC and Cook Children's Medical Cente), (7) Patient Safety and Economics for Cancer Patients (Moderator: Thomas Diller, UNTHSC), (8) The Role of Nutrition in Cancer Treatment (Moderator: Michelle Cummings, Tarrant County Public Health), and (9) Sleep disturbance and BCa (Moderator: Natasha Williams, NYU School of Medicine).

Colorectal Cancer

The CRC session was chaired by Dr. Harlan Jones, Associate Professor and Director of the Center for Diversity and International Programs at UNTHSC.

Dr. Ajay Goel, Director of Gastrointestinal (GI) Research in Baylor Scott and White Research Institute, Dallas, Texas, presented his work studying the liquid biopsy biomarkers for GI cancers. GI cancers are responsible for 25% of deaths in the western world. CRC remains one of the most prevalent cancers accounting for 600,000 deaths worldwide. CRC stands second in the United States with approximately 58,000 deaths and 175,000 new cases. Dr. Goel's current research focuses on noncoding RNAs (ncRNAs) as liquid biopsy markers and microRNAs (miRNAs) as diagnostic and prognostic signatures in CRC and other GI cancers.[36] ncRNAs were previously referred to as junk RNA even though 90% of the genome actively is transcribed into ncRNAs. ncRNAs play a major role in cellular development and, hence, believed to play an essential role in disease progression. ncRNAs can be characterized into three groups based on nucleotide size. Small ncRNAs (18–30 nucleotides) such as silencing RNA (siRNA) and miRNA are believed to be attractive targets for liquid biopsy biomarkers compared to long ncRNAs (>200 nucleotides). Dr. Goel emphasized the point that for the coming decades, these ncRNAs hold promise in advancing our ability to diagnose GI cancers.

Dr. Goel presented potential advances for early detection of GI cancers. Early-stage detection of colon cancer is curable, but typically, patients are diagnosed at advanced stages. Late detection is attributed to inadequate screening methods for colon cancer. Currently, there are several screening methods, each with their own limitations. For example, the colonoscopy is an invasive method that may deter patients from choosing the procedure. However, noninvasive methods such as the stool test are nonspecific and may therefore lead to false positives. Hence, the implementation of a strategy that involves the analysis of molecular markers that represent genetic and epigenetic alterations associated with CRC is critical. Dr. Goel also explained that different analytes could be examined for molecular markers such as miRNA, exosomes, and circulating tumor cells. from saliva, blood, or stool to examine patient survival. These analytes can also be employed for developing prognostic tools and for developing biomarkers for selecting targeted therapy like personalized medicine. His laboratory is currently working on a novel strategy to monitor disease markers. One promising approach is to utilize liquid biopsy markers to track patient treatment response to a given chemotherapeutic agent. Liquid biopsies have certain advantages. It is noninvasive, reduces patient discomfort, and is cost-effective. The test also affords better sampling because it can overcome tumor heterogeneity. Finally, it is also beneficial for monitoring treatment response.[37]

Dr. Goel also discussed the value of DNA-based liquid biopsy biomarkers. The FDA approved stool and blood tests for CRC like Cologuard from Exact Sciences Corporation, a detectable stool-based test that has a panel of 8–10 markers such as methylated BMP3, NDRG4, and mutant KRAS. The recent blood test detects methylated septin-9 gene, test kit from companies such as Epi proColon 1.0 (Epigenomics, Seattle, Washington), ColoVantage (Quest Diagnostics, Madison, New Jersey), and RealTime mS9 (Abbott Laboratories, Des Plaines, Illinois). Disadvantages of these tests have been that they are expensive and have a low sensitivity for detecting advanced adenomas. Hence, in such a scenario, studies such as those from Dr. Goel's laboratory have the potential to improve health outcomes. Furthermore, he talked about miRNAs as diagnostic and prognostic signatures in CRC. Dr. Goel believes that miRNAs as biomarkers could significantly improve the current Cologuard screening technology. He added that the single-oncogenic miR-21, used as a diagnostic marker, is preferable to using the 8–10 markers of the Cologuard blood test. The test also showed positive results for advanced adenomas and was found to be 80% effective. His laboratory works on a combination of multiple miRNAs such as miR-21, miR-29a, and miR-125b for development of markers to make them more effective. For example, his own research showed that the test specificity and sensitivity increased in combination as compared to single miRNA. Some of these markers could be used as prognostic markers, for example, high tissue and serum miR-21 expression,[38] and high expression of serum miR-885-5p in CRC patients predicts poor overall survival and distant-free survival.[39,40] The most complicated condition in CRC is patient with high-risk stage II and III because guidelines for treating these patients are not clear. Hence, Dr. Goel *et al.* performed the discovery step wherein they developed six mi-RNA classifiers (miR-183, -21, -20a, -139, -145, and -195) to distinguish between high- and low-risk stage II and III CRC, to identify patients who required adjuvant chemotherapy. Using the TCGA database (GC, n = 436, normal = 41) and other datasets, they also identified nine more circulating miRNAs (miR-21, -196a, -146b, -196b, -181b, -181a, -18a, -93, and -335) that could be used as the diagnostic signature for the detection of early gastric cancer. In his concluding remarks, Dr. Goel stated that the expression of ncRNAs is regularly dysregulated in CRC and other GI cancers. The small size of ncRNAs makes them useful for noninvasive, liquid biopsy biomarkers in detecting GI cancers. These clinical studies are aimed at evaluating the sensitivity and specificity of liquid, biopsy biomarkers for their adoption in future clinical practices.

The clinical perspective on CRC was presented by Dr. Milena Gould Suarez who spoke about her approach to improving the CRC mortality rates in Harris County, Texas. Dr. Suarez is an Associate Professor of Medicine

and the Associate Program Director at Baylor College of Medicine in Houston, Texas. In the U. S., CRC is the third most prevalent cancer among both men and women and comes in second regarding cancer mortality.[41,42] However, with proper screening, it is relatively easy to prevent, depending on the stage of cancer at the time of detection.

Several factors contribute to disparities in colon cancer rates. For example, low socioeconomic status (SES) when combined with obesity, smoking, or an unhealthy diet increases the risk of getting CRC.[41] In addition, higher mortality rates are attributed to comorbidities, lack of screening, access to treatment, and follow-up care. In the county where Dr. Suarez practices, there is a racially and ethnically diverse population with one of the highest uninsured and underinsured areas in the United States. As a result, the CRC screening rates are insufficient, resulting in higher mortality rates.[43,44]

Dr. Suarez *et al.* in the Harris Health System assessed their approach to overall patient care. Their goal was to develop and execute a comprehensive program that would encompass a network of health-care establishments to address the medical deficiencies experienced by specific populations in Harris County, Texas. Ultimately, they wanted to develop a system that would improve screening and follow-up care and decrease the prevalence of colorectal, cervical, and BCa in these underserved communities. They established this community network in 2010.

In their community assessment, they identified several areas of medical care that needed improvement. These included system failures such as lack of access to health care and a system that was ill-equipped to determine which individuals required screening. They also considered intervention strategies such as theater outreach, community engagement, and innovative access routes. Harris County providers are working toward overcoming barriers to patient education such as low literacy rates, a diverse population, and the need to accommodate English, Spanish, and the Vietnamese languages. In addition, they must work through these challenges amidst the backdrop of a busy clinic.

Dr. Suarez *et al*. have developed innovative approaches to the issues that plague their county. They have coordinated a variety of approaches that facilitate patient education, access to care, and follow-up. Fecal Immunochemical Test (FIT) is an in-home test to screen for CRC. The team at Baylor Medical Center in Harris County has designed a FIT instruction sheet, developed a FIT hotline, and produced educational videos all in English, Spanish, and Vietnamese. In addition, they have incorporated all of these into the clinic flow, along with special training for nurses. The Baylor Medical team has implemented similar procedures for colonoscopies. The results have been encouraging. FIT-screening rates have increased from 10% in 2010 to 40% in 2017.[45] The innovations and studies designed by Dr. Suarez show a comprehensive way to incorporate patient education into the high-volume environment of medical clinics. Patients are now guided through a CRC model as an integrated part of their clinic visits. The combination of these strategies has brought about a significant increase in the delivery of FIT screening kit, completion, and follow-up.

Dr. Joseph Unger, an Assistant Member at Fred Hutchinson Cancer Research Center and an Affiliate Assistant Professor at the University of Washington, Seattle, WA, USA, spoke about the "Income and Age Disparities in Access to Cancer Clinical Trials: Models, Evidence, and Implication." Clinical trials represent the final step in evaluating the efficacy and effectiveness of new cancer therapies, but <5% of adult cancer patients join these experiments. Unfortunately, there is an enormous gap between the willingness to participate and actual participation. In the clinical trial participation pathway, there may be demographic and socioeconomic disparities.[46] Structural barriers such as access to a clinic are often influenced by the availability of transportation, travel cost, and insurance status. Clinical barriers include trial availability and patient eligibility. Finally, the most common reason for ineligibility is the presence of comorbid conditions. The average number of eligibility criteria is 16% and 60% are related to comorbidity. Physician attitudes may also play a significant role in guiding patient care because physicians may prefer a specific treatment and trial participation may affect physician–patient relationship. Time and effort could be a burden and there are also issues with reimbursement. For patients' attitudes, altruism is a motivation and finding the best treatment for their disease is understandably their primary concern. They may be nervous about participating in trials because of residual distrust of medical science due to past exploitations, like Tuskegee syphilis study for example.[47-49] Fears of many people have reduced due to patient protection and informed consent. The main reason why some patients do not participate in clinical trials is that treatment is randomly assigned. There is no trial available for about half of the patients.

Approximately two-thirds of cancer patients are 65 years and older, but only about 25% of these patients are in clinical trials.[50] A recent study estimated that participation of older patients would approach 60% if protocol exclusions related to organ systems and functional status were relaxed. In another study, which compared income disparities, patients who supplement their Medicare benefits with private insurance participated in greater

numbers than those who relied on Medicare alone. This suggested that the marginal addition of costs associated with trial participation, such as copays and coinsurance, is most likely responsible for patient participation disparities. Clinical trial participation by SES is not well studied because of the lack of patient-level data in NCI-sponsored trials.

In a study conducted using an online web-based platform between 2007 and 2011 using more than 70,000 surveys, income was the only demographic factor that had a statistically significant association with clinical trial participation in multivariable regression. People with an income of <$50,000/year were less likely to participate in clinical trials. Assessing patients' attitudes showed that patients were very concerned about how to pay for clinical trial treatment.[51] More than half (53%) of those who were earning <$20,000/year and 24% of those earning >$100,000/year were concerned about how to pay for clinical trial treatment. There was no evidence that there is a difference between the association of income and clinical trial participation by state. According to the NCI, patients' health-care cost for clinical trials is not appreciably higher than the nontrial care. Cost concerns are much higher in low-income patients and these patients are more sensitive to direct costs (coinsurance and copays) and indirect costs (time off work for extra clinic visits). Ways to address this are to cover all excess costs clinical trial patients, make payments to participants. There should be a careful calibration of the amount of the monetary incentive to avoid undue influence (per US Common Rule for Protection of Human Subjects), which might affect participants' assessment of potential risks or impair their judgment. Although there is little evidence to indicate whether payment inducement leads to undue influence, there is some concern that payments made to patients will create a disproportionate burden of research on low-income patients. On the other hand, offering no monetary incentive has the probability of skewing the subject pool and violating distributive justice. Different payment models have been proposed, which are used to plan how to make payments to the participants. The market model determines the amount needed to pay to recruit the number and type of subjects required for each time frame. Higher payments are made when there is a low intrinsic incentive for participation, a small eligible patient pool, and situations where it is essential to accrue patients quickly. Lower payments are made when there is a high intrinsic incentive for participation.

In the wage-payment model, payment is made to compensate for time spent, contribution to the study, and effort or discomfort the participants might have experienced. The amount paid is based on a standardized hourly wage accompanied by completion bonuses to encourage compliance. Finally, in the reimbursement model, participants are compensated for their actual expenses. It follows the idea that revenue should be neutral for all research participants. One example is the reimbursement for travel, meals, parking, and for time spent away from work. Direct-to-consumer advertising (DTCA) has increased in recent years with a high awareness of oncology-related DTCA among cancer patients. This program targets low-income patients.

Finally, improved participation is needed to accelerate the conduction of clinical trials. A higher percentage of involvement of all demographic and SES groups would ensure trials with more accurate interpretations and results that are accessible to anyone who needs care. Clinical trials offer newest and innovative treatments and all patients should have equal access to these trials.

Conclusions

The 12th annual Texas Conference on Health Disparities was focused on addressing the complexity of different cancers and related health disparities. Some of the basic/translational researchers highlighted the biological functions including metabolomics, genomics, and proteomics studies and discussed how these studies could be used to develop new markers for the diagnosis, prognosis, and treatment of breast, prostate, and CRCs addressing the health disparities. The clinicians highlighted the aggressiveness of the three cancers by discussing their case studies and outlining different tools that can be used for better prognosis and treatment of patients. Furthermore, suggestions were offered throughout the conference on programs, diagnostics, treatments, and incentives to improve the health of minority and uninsured populations. The conference provided a platform for scientists, clinicians, patients, and students to come together and discuss health disparity issues with future implications.

Financial support and sponsorship

This publication was supported in part by the National Institute on Minority Health and Health Disparities of the National Institutes of Health under Award Numbers P20MD006882 and U54MD006882. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Conflicts of interest

There are no conflicts of interest.

References

1. Texas State Office of Rural Health, Office of Rural Affairs, editor. Texas Department of Agriculture: Texas County Designations; 2012.

2. Age-Adjusted Cancer Incidence in Texas, 2010-2014 – Leading Sites by Sex and Race/Ethnicity. Cancer Incidence Leading Sites 2010-2015. Available from: https://www.dshs.texas.gov/tcr/. [Last updated on 2018 Jan 19; Last accessed on 2018 Jan 19].
3. Funded Grants. Available from: http://www.cprit.state.tx.us/funded-grants?program=&entity=&cancersites=Breast&location=Fort+Worth. [Last accessed on 2018 Jan 19].
4. Osteopathic Scholars in Cancer Research. Available from: http://www.cprit.state.tx.us/files/funded-grants/RP170301.pdf. [Last accessed on 2018 Jan 19].
5. Mishra P, Ambs S. Metabolic signatures of human breast cancer. Mol Cell Oncol 2015;2. pii: e992217.
6. Karlstaedt A, Zhang X, Vitrac H, Harmancey R, Vasquez H, Wang JH, *et al.* Oncometabolite d-2-hydroxyglutarate impairs α-ketoglutarate dehydrogenase and contractile function in rodent heart. Proc Natl Acad Sci U S A 2016;113:10436-41.
7. Kernytsky A, Wang F, Hansen E, Schalm S, Straley K, Gliser C, *et al.* IDH2 mutation-induced histone and DNA hypermethylation is progressively reversed by small-molecule inhibition. Blood 2015;125:296-303.
8. Colvin H, Nishida N, Konno M, Haraguchi N, Takahashi H, Nishimura J, *et al.* Oncometabolite D-2-hydroxyglurate directly induces epithelial-mesenchymal transition and is associated with distant metastasis in colorectal cancer. Sci Rep 2016;6:36289.
9. Chandriani S, Frengen E, Cowling VH, Pendergrass SA, Perou CM, Whitfield ML, *et al.* A core MYC gene expression signature is prominent in basal-like breast cancer but only partially overlaps the core serum response. PLoS One 2009;4:e6693.
10. Terunuma A, Putluri N, Mishra P, Mathé EA, Dorsey TH, Yi M, *et al.* MYC-driven accumulation of 2-hydroxyglutarate is associated with breast cancer prognosis. J Clin Invest 2014;124:398-412.
11. DeSantis C, Ma J, Bryan L, Jemal A. Breast cancer statistics, 2013. CA Cancer J Clin 2014;64:52-62.
12. Giuliano AE, Connolly JL, Edge SB, Mittendorf EA, Rugo HS, Solin LJ, *et al.* Breast cancer-major changes in the American Joint Committee on cancer eighth edition cancer staging manual. CA Cancer J Clin 2017;67:290-303.
13. Maisonneuve P, Disalvatore D, Rotmensz N, Curigliano G, Colleoni M, Dellapasqua S, *et al.* Proposed new clinicopathological surrogate definitions of luminal A and luminal B (HER2-negative) intrinsic breast cancer subtypes. Breast Cancer Res 2014;16:R65.
14. Liu J, Deng H, Jia W, Zeng Y, Rao N, Li S, *et al.* Comparison of ER/PR and HER2 statuses in primary and paired liver metastatic sites of breast carcinoma in patients with or without treatment. J Cancer Res Clin Oncol 2012;138:837-42.
15. Goldhirsch A, Wood WC, Coates AS, Gelber RD, Thürlimann B, Senn HJ, *et al.* Strategies for subtypes – Dealing with the diversity of breast cancer: Highlights of the St. Gallen international expert consensus on the primary therapy of early breast cancer 2011. Ann Oncol 2011;22:1736-47.
16. Kozick Z, Hashmi A, Dove J, Hunsinger M, Arora T, Wild J, *et al.* Disparities in compliance with the oncotype DX breast cancer test in the United States: A National Cancer Data Base Assessment. Am J Surg 2017. pii: S0002-9610(17)30570-6.
17. Sreenath TL, Macalindong SS, Mikhalkevich N, Sharad S, Mohamed A, Young D, *et al.* ETS related gene mediated androgen receptor aggregation and endoplasmic reticulum stress in prostate cancer development. Sci Rep 2017;7:1109.
18. Rosen P, Pfister D, Young D, Petrovics G, Chen Y, Cullen J, *et al.* Differences in frequency of ERG oncoprotein expression between index tumors of caucasian and African American patients with prostate cancer. Urology 2012;80:749-53.
19. Zhou CK, Young D, Yeboah ED, Coburn SB, Tettey Y, Biritwum RB, *et al.* TMPRSS2:ERG gene fusions in prostate cancer of West African men and a meta-analysis of racial differences. Am J Epidemiol 2017;186:1352-61.
20. Esgueva R, Perner S, J LaFargue C, Scheble V, Stephan C, Lein M, *et al.* Prevalence of TMPRSS2-ERG and SLC45A3-ERG gene fusions in a large prostatectomy cohort. Mod Pathol 2010;23:539-46.
21. Petrovics G, Li H, Stümpel T, Tan SH, Young D, Katta S, *et al.* A novel genomic alteration of LSAMP associates with aggressive prostate cancer in African American men. EBioMedicine 2015;2:1957-64.
22. Hung CL, Wang LY, Yu YL, Chen HW, Srivastava S, Petrovics G, *et al.* A long noncoding RNA connects c-Myc to tumor metabolism. Proc Natl Acad Sci U S A 2014;111:18697-702.
23. Petrovics G, Zhang W, Makarem M, Street JP, Connelly R, Sun L, *et al.* Elevated expression of PCGEM1, a prostate-specific gene with cell growth-promoting function, is associated with high-risk prostate cancer patients. Oncogene 2004;23:605-11.
24. Rice LJ, Jefferson M, Briggs V, Delmoor E, Johnson JC, Gattoni-Celli S, *et al.* Discordance in perceived risk and epidemiological outcomes of prostate cancer among African American men. Prev Med Rep 2017;7:1-6.
25. Cullen J, Rosner IL, Brand TC, Zhang N, Tsiatis AC, Moncur J, *et al.* A biopsy-based 17-gene genomic prostate score predicts recurrence after radical prostatectomy and adverse surgical pathology in a racially diverse population of men with clinically low- and intermediate-risk prostate cancer. Eur Urol 2015;68:123-31.
26. Jaroff L. The Man's Cancer: Prostate Cancer is Reaching Epidemic Levels in the U.S. This is no Time for Squeamishness. In: Time; 1996.
27. McGinley KF, Tay KJ, Moul JW. Prostate cancer in men of African origin. Nat Rev Urol 2016;13:99-107.
28. Hsieh P. Is President Obama's Prostate Gland More Important Than Yours. In: Forbes Opinion. Forbes Magazine; 2012.
29. Tewari AK, Gold HT, Demers RY, Johnson CC, Yadav R, Wagner EH, *et al.* Effect of socioeconomic factors on long-term mortality in men with clinically localized prostate cancer. Urology 2009;73:624-30.
30. Krishna S, Fan Y, Jarosek S, Adejoro O, Chamie K, Konety B, *et al.* Racial disparities in active surveillance for prostate cancer. J Urol 2017;197:342-9.
31. Xu DD, Sun SD, Wang F, Sun L, Stackhouse D, Polascik T, *et al.* Effect of age and pathologic gleason score on PSA recurrence: Analysis of 2911 patients undergoing radical prostatectomy. Urology 2009;74:654-8.
32. Brawley OW. Prostate cancer epidemiology in the United States. World J Urol 2012;30:195-200.
33. Bechis SK, Carroll PR, Cooperberg MR. Impact of age at diagnosis on prostate cancer treatment and survival. J Clin Oncol 2011;29:235-41.
34. MacKintosh FR, Sprenkle PC, Walter LC, Rawson L, Karnes RJ, Morrell CH, *et al.* Age and prostate-specific antigen level prior to diagnosis predict risk of death from prostate cancer. Front Oncol 2016;6:157.
35. Essand M. Gene therapy and immunotherapy of prostate cancer: Adenoviral-based strategies. Acta Oncol 2005;44:610-27.
36. Rapisuwon S, Vietsch EE, Wellstein A. Circulating biomarkers to monitor cancer progression and treatment. Comput Struct Biotechnol J 2016;14:211-22.
37. Shigeyasu K, Toden S, Zumwalt TJ, Okugawa Y, Goel A. Emerging role of microRNAs as liquid biopsy biomarkers in gastrointestinal cancers. Clin Cancer Res 2017;23:2391-9.
38. Toiyama Y, Takahashi M, Hur K, Nagasaka T, Tanaka K, Inoue Y, *et al.* Serum miR-21 as a diagnostic and prognostic biomarker in colorectal cancer. J Natl Cancer Inst 2013;105:849-59.
39. Hur K, Toiyama Y, Schetter AJ, Okugawa Y, Harris CC, Boland CR, *et al.* Identification of a metastasis-specific MicroRNA signature in human colorectal cancer. J Natl Cancer Inst 2015;107. pii: dju492.

40. Lam CS, Ng L, Chow AK, Wan TM, Yau S, Cheng NS, *et al*. Identification of microRNA 885-5p as a novel regulator of tumor metastasis by targeting CPEB2 in colorectal cancer. Oncotarget 2017;8:26858-70.
41. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2017. CA Cancer J Clin 2017;67:7-30.
42. Haggar FA, Boushey RP. Colorectal cancer epidemiology: Incidence, mortality, survival, and risk factors. Clin Colon Rectal Surg 2009;22:191-7.
43. Liu Z, Zhang K, Du XL. Risks of developing breast and colorectal cancer in association with incomes and geographic locations in texas: A retrospective cohort study. BMC Cancer 2016;16:294.
44. Gupta S, Sussman DA, Doubeni CA, Anderson DS, Day L, Deshpande AR, *et al*. Challenges and possible solutions to colorectal cancer screening for the underserved. J Natl Cancer Inst 2014;106:dju032.
45. Colonoscopy – Patient Education Tools. Available from: https://www.bcm.edu/centers/cancer-center/prevention/educational-resources/patient-education-tools/colonoscopy-education. [Last accessed on 2018 Jan 19].
46. Fisher JA, Kalbaugh CA. Challenging assumptions about minority participation in US clinical research. Am J Public Health 2011;101:2217-22.
47. Corbie-Smith G, Thomas SB, Williams MV, Moody-Ayers S. Attitudes and beliefs of African Americans toward participation in medical research. J Gen Intern Med 1999;14:537-46.
48. Gamble VN. Under the shadow of tuskegee: African Americans and health care. Am J Public Health 1997;87:1773-8.
49. Shavers-Hornaday VL, Lynch CF, Burmeister LF, Torner JC. Why are African Americans under-represented in medical research studies? Impediments to participation. Ethn Health 1997;2:31-45.
50. Murthy VH, Krumholz HM, Gross CP. Participation in cancer clinical trials: Race-, sex-, and age-based disparities. JAMA 2004;291:2720-6.
51. Unger JM, Gralow JR, Albain KS, Ramsey SD, Hershman DL. Patient income level and cancer clinical trial participation: A Prospective survey study. JAMA Oncol 2016;2:137-9.