The Biomedical Research Community: Driving Progress Together

Progress against cancer occurs when individuals in different segments of the biomedical research community work together. Further increasing collaboration among stakeholders will accelerate the pace of lifesaving progress in the future. The stakeholders in the biomedical research community include:

- Health care providers;
- Academic and government researchers from a diverse array of specialties;
- Biotechnology, pharmaceutical, diagnostics, and medical device companies;
- Individual citizen advocates and members of advocacy groups;
- Policy makers;
- Regulators;
- Philanthropic organizations and cancer-focused foundations;
- Federal funding organizations;
- Payers.

American Association for Cancer Research (AACR) Cancer Progress Report 2017
Cancer: A Global Challenge

The number of global deaths from cancer is rising, as is the proportion of deaths that cancer accounts for (6).

In 2005, cancer accounted for 7.5 million of the 53.6 million deaths worldwide, meaning it accounted for 1 in 7 deaths.

In 2015, cancer accounted for 8.8 million of the 55.8 million deaths worldwide, meaning it accounted for almost 1 in 6 deaths.

The devastating impact of cancer will grow significantly in the coming decades if new and more effective approaches to cancer prevention, early detection, and treatment are not developed and effectively implemented.
What Are Cancer Health Disparities?

According to the National Cancer Institute, cancer health disparities in the United States are adverse differences in cancer measures such as incidence (number of new cases), prevalence (number of existing cases), mortality (cancer-related health complications), morbidity (number of deaths), survivorship and quality of life after cancer treatment, burden of cancer or related health conditions, screening rates, and stage at diagnosis that exist between certain segments of the population, including:

- Racial and ethnic minority groups;
- Individuals who lack or have limited health insurance coverage;
- Members of the lesbian, gay, bisexual, and transgender community;
- Individuals with disabilities;
- Individuals of different ancestry;
- Residents in certain geographic locations, including rural areas;
- Refugees or asylum seekers;
- Adolescents and young adults;
- Individuals of low socioeconomic status;
- Immigrants;
- The elderly.
# U.S. Cancer Health Disparities

Great strides have been made in cancer prevention, detection, diagnosis, treatment, and, in some cases, cures. However, not everyone has benefited equally from the advances and adverse differences in numerous cancer measures exist among certain segments of the U.S. population. Some recently identified examples of cancer health disparities are highlighted here:

<table>
<thead>
<tr>
<th>MORE THAN DOUBLE</th>
<th>Black men have a prostate cancer death rate that is more than double that for men of any other racial or ethnic group.</th>
</tr>
</thead>
<tbody>
<tr>
<td>24% MORE LIKELY</td>
<td>Hispanic children are 24 percent more likely to develop leukemia than non-Hispanic children.</td>
</tr>
<tr>
<td>7X</td>
<td>In Union County, Florida, the overall cancer death rate is seven times higher than it is in Summit County, Colorado.</td>
</tr>
<tr>
<td>50% LESS LIKELY</td>
<td>Early-stage ovarian cancer patients of low socioeconomic status are 50 percent less likely to receive recommended care than those of high socioeconomic status.</td>
</tr>
<tr>
<td>MORE THAN 40% MORE LIKELY</td>
<td>Patients with cancer who have Medicaid coverage or no insurance are more than 40 percent more likely to die from their disease than those who have non-Medicaid insurance.</td>
</tr>
<tr>
<td>3X</td>
<td>Women living with a same-sex relationship partner are three times more likely to die from breast cancer than women living with a male spouse or cohabiting relationship partner.</td>
</tr>
<tr>
<td>22% LOWER</td>
<td>Adolescents and young adults (ages 15 to 39) with acute myeloid leukemia have a 5-year relative survival rate that is 22 percent lower than that for children (ages 1 to 14).</td>
</tr>
<tr>
<td>29% LESS LIKELY</td>
<td>Adults who have an intellectual disability are 29 percent less likely to be up to date with colorectal cancer screening recommendations than those without this disability.</td>
</tr>
</tbody>
</table>
Why Do Cancer Health Disparities Exist?

Complex and interrelated factors contribute to U.S. cancer health disparities. The factors may include, but are not limited to, differences and/or inequalities in:

- access to and use of health care;
- genetics;
- physical and mental health;
- treatments received;
- social and economic status;
- cultural beliefs; and
- exposure to environmental cancer risk factors;
- clinical trial participation;
- health literacy.

American Association for Cancer Research (AACR) Cancer Progress Report 2017
What is Basic Research and How Does it Drive Progress against Cancer?

The National Institutes of Health (NIH) defines basic research as “the systematic study directed toward fuller knowledge or understanding of the fundamental aspects of a phenomenon and of observable facts without specific applications toward processes or products of mind.” Basic research, however, has broad implications, and has been fundamental to our understanding and treatment of human diseases including cancer. The NIH spends more than half of its budget supporting basic research. Selected examples of basic research discoveries that have transformed the field of cancer research are:

- **Discovery of DNA and its building blocks (bases) in the 1800s, followed by the groundbreaking discovery of its 3-dimensional structure in 1953, paved the way for understanding genetic mutations, the underlying basis of most cancers.**

- **Understanding the basic molecular biology of DNA replication and cell division led to the development of chemotherapeutics that kill rapidly dividing cancer cells.**

- **Recombinant DNA technology, a concept that drives modern biotechnology, is based entirely upon basic research in bacterial biochemistry.**

- **Development of CRISPR-associated protein-9 nuclease has revolutionized the field of gene editing, and its utility to treat genetic diseases, including cancer, is being investigated.**

American Association for Cancer Research (AACR)
Cancer Progress Report 2017
Genetic and Epigenetic Control of Cell Function

The genetic material of a cell comprises strings of four deoxyribonucleic acid (DNA) units called bases.

DNA bases are organized into genes. The order, or sequence, of the bases provides the code used by the cell to produce the various proteins it needs to function.

The entirety of a person’s DNA is called the genome. Almost every cell in the body contains a copy of the genome. The genome is packaged together with proteins known as histones into structures called chromosomes.

Special chemical marks, called epigenetic marks, on the DNA and histones together determine whether a gene is accessible for reading. The sum of these chemical marks across the entire genome is called the epigenome.

The accessible genes within each cell are read to produce the proteins that ultimately define the function of the cell and the tissue in which the cell resides.
Genetic Mutations

Below are some of the types of genetic mutation known to lead to cancer. Of note, genetic mutations do not always result in cancer.

**Single base changes**
- Some mutations can lead to the generation of altered versions of normal proteins, and these may cause cancer to develop.
- Deletion or insertion of a single base can result in new proteins or loss of protein function, which can lead to cancer.

**Extra copies of genes (gene amplification)**
Higher quantities of certain proteins can result in enhanced cell survival and growth, leading to cancer.

**Large deletions**
Loss of DNA can result in loss of genes necessary to stop or control the growth of cancer.

**Genetic recombination**
Exchange of DNA across different parts of the genome can lead to entirely new proteins that can drive the development of cancer.

**Mutations that alter the epigenome**
Several proteins read, write, or erase the epigenetic marks on DNA or the histones around which it is packaged. Mutations in the genes that produce these proteins can lead to cancer.

American Association for Cancer Research (AACR) Cancer Progress Report 2017
Sources of Genetic Mutations

Cancer initiation and progression are predominantly caused by the accumulation of changes, or mutations, in the genetic material of a cell over time. The primary sources of genetic mutations are as follows:

Five to 10 percent of all new U.S. cancer cases are linked to genetic mutations present in each cell of the body from birth.

Most mutations, however, are acquired during a person’s lifetime.

- Some occur during cell multiplication, and the number of times a cell multiplies increases the chance it will acquire a mutation.

- Some occur as a result of exposure to factors that damage genetic material, such as toxicants in tobacco smoke and ultraviolet (UV) light from the sun.

These factors come together to determine the chance that an individual cell has of acquiring mutations over time. This, in turn, helps determine the overall risk that a person will develop a particular type of cancer, although it is important to note that not all mutations lead to cancer.

American Association for Cancer Research (AACR)
Cancer Progress Report 2017
Cancer Growth: Local and Global Influences

Solid tumors are much more complex than an isolated mass of proliferating cancer cells because cancer initiation, development, and progression are strongly influenced by interactions among cancer cells and numerous factors in their environment. Among the components of the tumor microenvironment are normal parts of the tissue in which the cancer is growing, systemic factors that transiently percolate through the tissue, and cells that are actively recruited to the tissue.

Cancer cells can stimulate the growth of blood and lymphatic vessel networks, which supply the cancer cells with the nutrients and oxygen required for rapid growth and survival, and provide a route for cancer cell escape to distant sites (metastasis).

The matrix of proteins that surrounds the cancer cells can influence cancer formation, metastasis, and other processes.

Systemic factors in the circulation, such as hormones and nutrients, influence the development and growth of cancer.

The immune system can identify and eliminate cancer cells, although in many cases this system is suppressed, permitting the formation and progression of a tumor. However, in some situations of chronic inflammation, the immune system can promote cancer development and progression.

Other tissue-specific tumor-associated cells, such as pericytes, fibroblasts, and astrocytes, can support tumor growth through various mechanisms including stimulating tumor growth, triggering formation of new blood vessels, and enhancing survival of cancer cells.
E-Cigarettes: A Report from the U.S. Surgeon General

Electronic cigarettes (e-cigarettes) are a rapidly emerging form of electronic nicotine delivery system (ENDS) that deliver nicotine, flavorings, and other additives to users via an inhaled aerosol. The increase in e-cigarette use among youth and young adults has become a public health concern and prompted the U.S. Surgeon General to issue a report that offers a list of goals intended to minimize the public health threat posed by these products.

Goal 1. First, Do No Harm | Include e-cigarettes in policies and programs related to conventional cigarette smoking while educating the public about the health risks using evidence-based messages.

Goal 2. Provide Information about the Dangers of E-Cigarette Use among Youth and Young Adults | Educate parents, teachers, and coaches as well as health professionals about the risks of e-cigarette use among youth and young adults.

Goal 3. Continue to Regulate E-Cigarettes at the Federal Level to Protect Public Health | Implement FDA regulatory authority over the manufacturing, marketing, and distribution of e-cigarettes.

Goal 4. Promote Programs and Policies at the State and Local Levels to Prevent E-Cigarette Use among Youth and Young Adults | Identify best strategies to implement population-level regulations to reduce e-cigarette use among youth and young adults; include e-cigarettes in smoke-free indoor air policies; restrict youth access to retailers; establish packaging requirements.

Goal 5. Curb Advertising and Marketing That Encourage Youth and Young Adults to Use E-Cigarettes | Restrict advertising and marketing that cater to the younger generation.


American Association for Cancer Research (AACR) Cancer Progress Report 2017
# Enhancing Tobacco Control through FDA Regulation

The U.S. Food and Drug Administration (FDA) has had the authority to regulate tobacco products since passage of the 2009 Family Smoking Prevention and Tobacco Control Act. While the agency exercised regulatory authority over some of these products, such as cigarettes, others remained unregulated—until now. In 2016, the FDA extended its authority to cover all tobacco-based products. However, legal challenges raised by the vaping and tobacco industry have put some aspects of this deeming rule in jeopardy. The rule:

<table>
<thead>
<tr>
<th>Permits FDA regulation of vaporizers, vape pens, cigars, hookah pens, hookah pipes, e-cigarettes, e-pipes, and all other electronic nicotine delivery systems, as well as future tobacco products not yet on the market.</th>
<th>Prohibits the distribution of free samples.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Requires a premarket review process and authorization of new tobacco products that reviews manufacturers' claims and requires the disclosure of ingredients and reporting of harmful or potentially harmful components.</td>
<td>Defines content and size of warning labels and requires additional warnings for cigar packaging.</td>
</tr>
<tr>
<td>Prohibits the sale of tobacco products to individuals under the age of 18 and requires the display of health warnings in advertisements and on tobacco and tobacco-related products.</td>
<td>Defines establishments that mix or prepare e-liquids or create or modify aerosolizing apparatus for direct sale to consumers as tobacco product manufacturers that are subject to regulation as manufacturers.</td>
</tr>
</tbody>
</table>

*American Association for Cancer Research (AACR) Cancer Progress Report 2017*
Reduce Your Risk for Cancers Linked to Being Overweight or Obese, Being Inactive, and/or Consuming a Poor Diet

Research from the World Cancer Research Fund International shows that about one-fifth of all U.S. cancers and one-third of the most common types of cancer diagnosed in the United States are attributable to being overweight or obese, being inactive, and/or eating poorly. As such, among their recommendations are the following:

- Be as lean as possible without becoming underweight, because 14 types of cancer have been causally linked to being obese or overweight.
- Be physically active for at least 30 minutes every day, because regular physical activity can decrease risk for certain cancers.
- Limit consumption of energy-dense foods (foods high in fats and/or added sugars and/or low in fiber) and avoid sugary drinks, because these contribute to weight gain.
- Eat more of a variety of vegetables, fruits, whole grains, and beans, because these foods have a low energy density and, therefore, promote healthy weight.
- Limit intake of red meat and avoid processed meat (e.g., hot dogs, bacon, and sausages) because these foods can increase risk for colorectal cancer.
- If consumed at all, limit alcoholic drinks, because alcohol consumption can increase risk for six types of cancer: breast, colorectal, esophageal, liver, stomach, and mouth/throat cancers.

Source: Research has been reviewed and found to support cancer prevention recommendations
American Association for Cancer Research (AACR)
Cancer Progress Report 2017
## Physical Activity Guidelines

The U.S. Department of Health and Human Services recommends the following minimum physical activity levels to improve the nation’s health; see [http://www.health.gov/paguidelines/guidelines/summary.aspx](http://www.health.gov/paguidelines/guidelines/summary.aspx).

### For children and adolescents

- Sixty minutes or more of physical activity such as running daily.
- Muscle- and bone-strengthening exercises such as push-ups at least three days per week.

### For adults

- All adults should avoid inactivity; some physical activity is better than none.
- At least 150 minutes per week of moderate-intensity activity such as a brisk walk or 75 minutes per week of vigorous-intensity activity such as running.
- Moderate- or high-intensity muscle-strengthening activities two or more days per week.

### For specific populations

- Older adults, those who are pregnant, and/or those with disabilities should consult their physicians and the modified guidelines.
- Cancer survivors should consult their physicians and follow modified guidelines adapted for their specific cancers and treatments.

American Association for Cancer Research (AACR) Cancer Progress Report 2017
Ways to Protect Your Skin

To reduce your risk of the three main types of skin cancer—basal cell carcinoma, squamous cell carcinoma, and melanoma—the Centers for Disease Control and Prevention recommends the following measures:

- seek shade and limit time in the sun, especially during peak sun hours (10:00 a.m. to 4:00 p.m.);
- wear clothing that covers your arms and legs; some clothing is designed to provide protection from the sun;
- wear a wide-brimmed hat;
- wear wrap-around sunglasses;
- apply the recommended amount of a sunscreen that provides protection against UVA and UVB rays and that is rated sun protection factor (SPF) 15 or higher at least every 2 hours and after swimming, sweating, and towelling off; and
- avoid indoor tanning with UV devices like sunlamps, sunbeds, and tanning booths.

American Association for Cancer Research (AACR)
Cancer Progress Report 2017
## Preventing or Eliminating Infection with the Four Main Cancer-causing Pathogens

<table>
<thead>
<tr>
<th>PATHOGEN</th>
<th>WAYS TO PREVENT INFECTION</th>
<th>WAYS TO ELIMINATE OR TREAT INFECTION</th>
<th>U.S. RECOMMENDATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Helicobacter pylori</em></td>
<td>None available</td>
<td>Treatment with a combination of antibiotics and a proton-pump inhibitor can eliminate infection</td>
<td>CDC recommends testing and treatment for people with active or a documented history of gastric or duodenal ulcers, low-grade gastric MALT lymphoma, or early gastric cancer that has been surgically treated</td>
</tr>
</tbody>
</table>
| HBV | • HBV vaccination  
• Avoid behaviors that can transmit infection (e.g., injection drug use and unsafe sex) | Treatment of those chronically infected with antiviral drugs rarely eliminates infection but does slow virus multiplication; this slows the pace at which liver damage occurs and thereby reduces risk for liver cancer | • Vaccination part of childhood immunization schedule since 1998  
• USPSTF recommends screening high-risk individuals—those from countries with high rates of HBV infection, HIV-positive persons, injection drug users, household contacts of HBV-infected individuals, and men who have sex with men—for HBV infection |
| HCV | Avoid behaviors that can transmit infection (e.g., injection drug use and unsafe sex) | Treatment with any of several antiviral drugs can eliminate infection | CDC and USPSTF recommend screening those born from 1945 to 1965 for HCV infection |
| HPV | • Three FDA-approved vaccines  
• Practice safe sex, although this may not fully protect against infection | None available | CDC recommends HPV vaccination for:  
• boys and girls age 11 or 12  
• women up to age 26 and men up to age 21 who did not receive the vaccine or complete the course as preschool |

CDC, Centers for Disease Control and Prevention; HBV, hepatitis B virus; HCV, hepatitis C virus; HPV, human papillomavirus; MALT, mucosa-associated lymphoid tissue; USPSTF, U.S. Preventive Services Task Force. Adapted from [10].

Updated HPV Vaccination Recommendations

13 strains of HPV can cause cancer: HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 66.

3 Although there are three FDA-approved HPV vaccines, only one (Gardasil 9) is currently being distributed in the United States.

Gardasil 9
- Protects against infection with HPV6, 11, 16, 18, 31, 33, 45, 52, and 58.
- FDA approved in 2014 for
  - preventing anal, cervical, vaginal, and vulvar cancers and precancers, as well as genital warts.
  - vaccination of females ages 9 to 26 and males ages 9 to 15.

The U.S. Centers for Disease Control and Prevention (CDC) and the Advisory Committee on Immunization Practices (ACIP) announced updated guidelines for HPV vaccination in October, 2016. According to the new recommendations:
- Two doses of HPV vaccine, given at least 6 months apart, are now recommended for adolescents younger than age 15 (except immunocompromised persons), rather than three doses.
- Three doses of HPV vaccine are still recommended for teenagers and young adults ages 15 to 26 and for people with weakened immune systems.

The updated recommendations are based on recent clinical data showing that, in younger adolescents, two doses of the vaccine trigger an immune response equivalent to that produced by three doses among adolescent girls and young women.

American Association for Cancer Research (AACR) Cancer Progress Report 2017
# Cancer Screening

## Benefits of Screening

**Reduced cancer incidence.** Screening tests can detect precancerous lesions. Removal of the lesions can reduce, or even eliminate, an individual's risk of developing the screened cancer at that site.

**Reduced incidence of advanced disease.** Screening tests that detect cancers at an early stage of development can reduce the individual's risk of being diagnosed with the screened cancer at a stage when it has spread to other parts of the body.

**Reduced cancer mortality.** Diagnosis at an early stage of disease can increase the likelihood that a patient can be successfully treated, which thereby reduces the individual’s risk of dying from the screened cancer.

## Potential Risks of Screening

**Adverse events.** Screening tests are medical procedures; thus, they carry some risk. However, the chance that an adverse event will occur during a screening test recommended by the U.S. Preventive Services Task Force or a professional society is low.

**Anxiety.** Screening individuals who are not at high risk of disease can cause unnecessary anxiety during the waiting period for the test results.

**False-positive test results.** Not all individuals who have a positive screening test result have the screened cancer. The rates of false-positive test results vary depending on the test but are generally low; a false-positive test result can result in additional unnecessary medical procedures, treatments, and anxiety.

**False-negative test results.** Not all individuals who have a negative screening test result are free from the screened cancer. The rates of false-negative test results are generally low, but a false-negative test result can lead to missed opportunities for early treatment.

**Overdiagnosis and overtreatment.** Not all precancers or cancers detected by screening will go on to cause symptoms and threaten life. Overdiagnosis, as this is called, can lead to overtreatment, which may carry its own risks and costs. The rates of overdiagnosis and overtreatment vary among screening tests and will require more longitudinal studies to elucidate and quantify.
Cancers for Which Population-level Screening Has Been or Is Being Performed

**BREAST CANCER**

Screening mammogram: Uses X-rays to image the breast. The information generated by the procedure can be stored on film (a conventional mammogram) or electronically (a digital mammogram).

In most cases, the image is 2-dimensional but some machines generate 3-dimensional images in a process called breast tomosynthesis.

Can detect breast cancers that cannot be felt. These cancers can be at any stage of development, but the aim of screening is to find them at the earliest possible stage.

**CERVICAL CANCER**

Pap test: Samples cervical cells, which are analyzed under a microscope to look for abnormalities.

Can detect precancerous or cancerous cervical lesions, but the aim of screening is to find them at the earliest possible stage.

HPV test: Detects the presence of certain cervical cancer-causing types of human papillomavirus (HPV).

Does not directly detect precancerous or cancerous cervical lesions, but identifies people for whom follow-up is recommended.

**COLORECTAL CANCER**

Stool tests: Same test for the presence of red blood cells in stool samples. Others test for both red blood cells and certain genetic mutations linked to colorectal cancer.

Do not directly detect colorectal precancerous lesions or cancers, but identify people for whom further testing is recommended.

**LUNG CANCER**

Low-dose CT scan: Uses low doses of X-rays to image the lungs.

Can detect lung cancers that are not causing symptoms. These cancers can be at any stage of development, but the aim of screening is to find them at the earliest possible stage.

**PROSTATE CANCER**

PSA test: Measures the level of the protein prostate-specific antigen (PSA) in blood.

Does not directly detect prostate cancer, but the blood level of PSA is often elevated in men with prostate cancer, which identifies men for whom further testing is recommended.
The U.S. Preventive Services Task Force (USPSTF) rigorously evaluates data regarding the benefits and potential risks of cancer screening tests to make evidence-based recommendations about the routine use of these tests. As of July 31, 2017, the USPSTF had evaluated data and made decisions for 11 types of cancer. Of note, the USPSTF is currently reviewing its recommendations for cervical cancer, ovarian cancer, pancreatic cancer, and prostate cancer screening and may revise them if deemed necessary.

The USPSTF recommends population-level screening of certain individuals for:
- breast cancer
- cervical cancer
- colorectal cancer
- lung cancer

The USPSTF recommends against population-level screening of average-risk individuals with no signs or symptoms of:
- ovarian cancer
- pancreatic cancer
- testicular cancer
- and thyroid cancer

The USPSTF considers there is insufficient evidence to assess the balance of benefits and harms of screening average-risk adults with no signs or symptoms of:
- bladder cancer
- oral cancer
- and skin cancer

For more information about the USPSTF decisions see:
http://www.uspreventiveservicestaskforce.org

American Association for Cancer Research (AACR)
Cancer Progress Report 2017
## Consensus among Cancer Screening Recommendations

The U.S. Preventive Services Task Force (USPSTF) and many professional societies have evidence-based recommendations about the use of cancer screening tests. Here, we highlight consensus, as of July 31, 2017, among cancer screening recommendations from the USPSTF, the American Cancer Society (ACS), the National Comprehensive Cancer Network (NCCN), the American College of Physicians (ACP), the American College of Obstetrics and Gynecology (ACOG), and the American Urological Association (AUA). Not all of the professional societies have recommendations for every cancer screening test.

### Breast Cancer

There is consensus among the ACOG, ACS, NCCN, and USPSTF that women ages 50–74 who are at average risk for breast cancer should have regular screening mammograms. However, there is variability about whether this should be done every year or every other year.

### Cervical Cancer

- There is consensus among the ACOG, ACS, ACP, and USPSTF that:
  - average-risk women younger than 21 should not be screened;
  - average-risk women ages 21–29 should have a Pap test every 3 years;
  - average-risk women ages 30–65 should have either a Pap test every 3 years or a Pap test and HPV testing every 5 years; and
  - women older than 65 should not be screened if they have previously had regular screenings with normal results and are not otherwise at high risk for cervical cancer.

### Colorectal Cancer

- There is consensus among the ACS, ACP, NCCN, and USPSTF that:
  - adults ages 50–75 who are at average risk for colorectal cancer should be screened; and
  - adults ages 50–75 should consult with their healthcare providers to choose the test that is right for them.

Some professional societies recommend certain approaches over others. The overall message, however, is that using any one of the approved tests is better than not being screened.

### Lung Cancer

There is consensus among the ACS, ACP, and USPSTF that screening with low-dose computed tomography should be limited to adults ages 55–79 who are at high risk for lung cancer because they have smoked at least one pack of cigarettes per day for 30 years, or the equivalent (two packs per day for 15 years, etc.), and who currently smoke or have quit within the past 15 years.

The USPSTF recommends annual screening for these individuals, whereas the ACS and ACP recommend these individuals talk to a physician about the benefits and potential harms of screening before deciding if it is right for them.

### Prostate Cancer

There is consensus among the ACS, ACP, and AUA that men ages 55–69 who are at average risk for prostate cancer talk to a physician about the benefits and potential harms of PSA testing before deciding if screening is right for them.

The USPSTF is finalizing new recommendations and is considering a recommendation that would be aligned with those of the ACS, ACP, and AUA.

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**To find out more about cancer screening recommendations see:**
- [https://www.uspreventiveservicestaskforce.org](https://www.uspreventiveservicestaskforce.org)
- [https://www.cancer.org](https://www.cancer.org)
- [https://www.acr.org](https://www.acr.org)
- [https://www.acponline.org](https://www.acponline.org)
- [https://www.acog.org](https://www.acog.org)
- [https://www.nccn.org](https://www.nccn.org)

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*American Association for Cancer Research (AACR) Cancer Progress Report 2017*
How Do I Know If I Am at High Risk for Developing an Inherited Cancer?

According to the National Cancer Institute, some of the factors to consider are whether, in your family, there is one or more of the following:

- several close blood relatives with the same type of cancer, such as a mother, daughter, and sisters with breast cancer;
- members diagnosed with cancers at younger ages than usual, such as colon cancer in a 20-year-old;
- one or more members who have more than one type of cancer, such as a female relative with both breast and ovarian cancer;
- one or more members with cancers in both of a pair of organs, such as both eyes, both kidneys, or both breasts;
- members with a type of cancer usually occurring in the opposite sex, such as breast cancer in a man.

American Association for Cancer Research (AACR)
Cancer Progress Report 2017
Interpreting Genetic Tests

Genetic testing is a type of medical test that looks for changes, or mutations, in a person’s DNA. Some individuals with a family or personal history of cancer decide to undergo genetic testing to determine whether they have inherited a genetic mutation that predisposes them to cancer. Many make this decision in consultation with a health care professional trained in genomics but some decide to use a direct-to-consumer test. Because of the complexities of direct-to-consumer tests, both the FDA and Federal Trade Commission recommend involving a health care professional in any decision to use these tests, as well as to interpret the results.

Interpreting the results of genetic tests can be challenging and it is important to remember that not everyone who inherits a cancer-predisposing mutation will develop cancer. One of the challenges is that the effects of a genetic mutation on the risk of developing cancer are not always known. These mutations are often called “variants of unknown significance.” Determining whether these variants are inconsequential or important in driving cancer is an area of intensive research investigation. One approach being undertaken involves sharing of genetic test results. By pooling test results and clinical data obtained at institutions around the world to generate large data sets, it should be possible to gain new insight into the frequency and consequences of these variants.

This approach is being used by the BRCA Exchange of the Global Alliance for Genomics and Health to advance our understanding of the genetic basis of breast cancer, ovarian cancer, and other diseases. As of July 31, 2017, the publicly available database contained 18,952 unique BRCA1/2 variants. This should provide an invaluable resource given that it is estimated that BRCA variants of unknown significance occur in 10 percent to 20 percent of BRCA tests, which are among the most common genetic tests performed given that mutations in the genes BRCA1 and BRCA2 account for 5 percent to 10 percent of breast cancer cases in U.S. women.

For more information on the BRCA Exchange go to http://brcaexchange.org.
American Association for Cancer Research (AACR) Cancer Progress Report 2017
Disparities in Cancer Screening

There are disparities in adherence to United States Preventive Services Task Force (USPSTF) cancer screening recommendations among certain segments of the U.S. population. These disparities, which highlight the need for new public policies to increase cancer screening uptake among disadvantaged segments of the U.S. population, include the following:

- **32% MORE LIKELY** Whites are 32 percent more likely to be up to date with colorectal cancer screening than American Indians/Alaska Natives.

- **19% MORE LIKELY** Women in the highest income bracket are 19 percent more likely to be up to date with cervical cancer screening than women in the lowest income bracket.

- **MORE THAN 2X** Women who have private health insurance are more than twice as likely to be up to date with breast cancer screening than women who are uninsured.

- **31% MORE LIKELY** Colorectal cancer screening uptake varies by U.S. state, with those in Massachusetts 31 percent more likely to be up to date with screening than those in Wyoming.

- **12% MORE LIKELY** Straight women are 12 percent more likely to be up to date with cervical cancer screening than gay women.

- **2X** Foreign-born women in the U.S. are twice as likely to have never had a mammogram than U.S.-born women.

*American Association for Cancer Research (AACR) Cancer Progress Report 2017*
Supporting Early-Career Investigators

A strong and diverse pipeline of early-career investigators is vital if we are to continue to accelerate the pace of progress against cancer. To cultivate this pipeline we need robust, sustained, and predictable funding increases for the National Institutes of Health, as well as federal, state, philanthropic, and private funding programs. In this regard, the American Association for Cancer Research (AACR) recently launched the AACR NextGen Grants for Transformative Cancer Research with support from Bayer, the Breast Cancer Research Foundation, Incyte Corporation, and Takeda Oncology. Through this program the AACR is helping:

**Kivanc Birsoy, PhD**, identify how cell nutrients can be targeted for therapy for hard-to-treat cancers;

**Sidi Chen, PhD**, develop new ways to identify the genes that fuel liver cancer growth and response to treatment;

**Hani Goodarzi, PhD**, investigate how certain RNA structures can influence colon cancer progression and metastasis;

**Andrew C. Hsieh, MD**, use multidisciplinary approaches to enhance our understanding of the complex cellular processes that lead to the production of cancer-driving proteins;

**Sophia Y. Lunt, PhD**, elucidate how pancreatic cancer cells use energy to support tumor growth and metastasis;

**Costas Andreas Lyssiotis, PhD**, determine how cells in the tumor microenvironment communicate with pancreatic cancer cells and promote their survival;

**Paul A. Northcott, PhD**, deepen our understanding of the molecular basis of recurrent childhood medulloblastoma;

**Nikhil Wagle, MD**, improve our understanding of why breast cancer cells become resistant to molecularly targeted therapeutics that block the function of CDK4/6 proteins.

For more information about the research being conducted by these early-career investigators see www.AACR.org/Funding/PAGES/NEXTGEN-GRANT-RECIPIENTS.ASPX

*American Association for Cancer Research (AACR) Cancer Progress Report 2017*
**Therapeutic Development**

- **Target validation.** Potential therapeutic targets identified in discovery research are confirmed to play a causative role in a given disease.

- **Target to hit.** Large numbers of chemical or biological agents are screened to identify molecules that "hit" the target.

- **Hit to lead.** Positive hits are further tested to determine which bind the target with the most specificity.

- **Lead optimization.** The properties of the lead compound are refined to enhance potency and drug availability and to reduce side effects.

- **Preclinical testing.** Cellular and animal models are used to test for effectiveness of the optimized lead, identify any potential toxicity issues, and determine an optimal starting dose for clinical or "first-in-human" testing. The final compound is called the clinical candidate.

- **Investigational new drug (IND).** Prior to clinical testing, one or more clinical candidates are submitted to the FDA for approval to be used in clinical trials.

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American Association for Cancer Research (AACR) Cancer Progress Report 2017
Disparities in Clinical Trial Participation

If we are to ensure that investigational anticancer therapeutics are safe and effective for everyone who will use them if they are approved, it is vital that the participants in the clinical trials testing the agents represent the entire population who may use them. Despite this knowledge, several segments of the population have been found to be underrepresented in clinical trials. Examples of these disparities in clinical trial participation include the following:

- The elderly (age 65 or older) accounted for about two-thirds of patients with breast, lung, colorectal, and prostate cancer, but only one-third of participants in clinical trials testing treatments for these four types of cancer in one recent study.
- African-Americans account for about 20 percent of new multiple myeloma cases but just 10 percent of the participants involved in the clinical trials testing daratumumab (Darzalex).

Why Do They Exist?

As with disparities in cancer burden, there are many complex and interrelated factors that contribute to disparities in clinical trial participation. The factors may include, but are not limited to, differences or inequalities in:

- Health insurance status;
- Eligibility criteria;
- Cultural beliefs; and
- Social and economic status;
- Site at which cancer care is received;
- Health literacy.

Given that a significant proportion of the U.S. population falls into one or more risk categories, it is important that research into these issues continues. Only with new insights will we develop and implement interventions that will ensure that participants in cancer treatment clinical trials appropriately represent all the people who will use the agents if they are approved.

American Association for Cancer Research (AACR) Cancer Progress Report 2017
Using Radiation in Cancer Care

**Radiation Therapy**

- Radiotherapy is the use of high-energy rays (e.g., gamma rays and X-rays) or particles (e.g., electrons, protons, and carbon nuclei) to control or eliminate cancer.
- Radiotherapy works chiefly by damaging DNA, leading to cell death.

**Uses of Radiotherapy**

- **Curative** radiotherapy seeks to completely eliminate a cancer, particularly small cancers, as well as locally advanced cancers as part of combination therapy.
- **Neoadjuvant** radiotherapy is used to reduce or control a cancer so that it can be subsequently treated by a different method such as surgery.
- **Adjuvant** radiotherapy seeks to eliminate any remaining cancer following prior treatment.
- **Palliative** radiotherapy is used to reduce or control symptoms of disease when cure by another method is not possible.

**Types of Radiotherapy**

- **Particle therapy** uses protons or carbon ions rather than X-rays as the source of energy. In contrast to X-rays that pass through the body, losing energy and causing damage to the noncancerous tissues through which they pass, these heavier particles deposit most of their energy in the target. In this manner, particle therapy can deliver higher doses with less damage to surrounding tissue. Although of great interest, proton facilities are much more expensive than traditional facilities and the overall benefit to the patient is still being determined.
- **Brachytherapy** places small radioactive sources in or next to the tumor either temporarily or permanently.
- **External beam radiotherapy** encompasses several types of radiotherapy that direct radiation at the tumor from outside the body. It is the most common form of radiotherapy. Electrons and photons (X-rays) are the most common sources of radiation in external beam radiotherapy.
- **Radioisotope therapy** involves systemic ingestion or infusion of radioisotopes, for example, iodine-131 to treat thyroid cancer or yttrium-90 ibritumomab (Zevalin) to treat non-Hodgkin lymphoma.
Companion Diagnostics

The effective use of anticancer therapeutics targeting particular cancer-driving molecular abnormalities often requires tests called companion diagnostics. Companion diagnostics:

- are stringently tested for accuracy, sensitivity, and fidelity;
- are regulated by the U.S. Food and Drug Administration;
- accurately match patients with the most appropriate therapy;
- allow patients to receive a treatment to which they are most likely to respond; and
- allow patients identified as very unlikely to respond to forgo treatment with the therapeutic and thus be spared any adverse side effects.
How Immunotherapeutics Work

The way in which different immunotherapeutics unleash a patient’s immune system to fight cancer varies:

Some release the brakes on the natural cancer-fighting power of the immune system, for example, avelumab (Bavencio) and durvalumab (Imfinzi).

STOP

Some increase the killing power of the immune system by providing more cancer-targeted immune cells called T cells; these are called adoptive T-cell therapies, for example the CAR T-cell therapy CTL019. For more information on these immunotherapeutics see the AACR Cancer Progress Report 2015.

Some enhance the cancer-killing power of the immune system by triggering cancer-fighting T cells; these are called therapeutic cancer vaccines, for example, sipuleucel-T (Provenge).

Some flag cancer cells for destruction by the immune system, for example, daratumumab (Darzalex) and elotuzumab (Empliciti), which were highlighted in the AACR Cancer Progress Report 2016.

Some boost the killing power of the immune system by enhancing T-cell function, for example, interleukin-2 (Aldesleukin).

FUNCTION

Some comprise a virus that preferentially infects and kills cancer cells, releasing molecules that trigger cancer-fighting T cells; these are called oncolytic virotherapeutics, for example, talimogene laherparepvec (T-Vec; Imlycig), which was highlighted in the AACR Cancer Progress Report 2016.

American Association for Cancer Research (AACR) Cancer Progress Report 2017
Accelerated Approval

The accelerated approval program is one of four evidence-based strategies used by the U.S. Food and Drug Administration (FDA) to expedite the assessment of therapeutics for life-threatening diseases such as cancer.

Accelerated approval is based on assessing the effect of a therapeutic at an earlier stage than usual by using a surrogate endpoint. A surrogate endpoint is a marker, such as a radiographic image showing tumor shrinkage, that is thought to predict clinical benefit, which is defined as prolongation of survival or improved quality of life. The surrogate endpoint is not itself a measure of clinical benefit.

Any therapeutic approved through this program must undergo additional clinical testing to verify that it does provide the anticipated clinical benefit. If the confirmatory trial shows that the therapeutic does provide clinical benefit, then the FDA grants traditional approval. If the confirmatory trial does not show that the therapeutic provides clinical benefit, the FDA has the option of removing the therapeutic from the market.

*American Association for Cancer Research (AACR)*
*Cancer Progress Report 2017*
Life after a Cancer Diagnosis in the United States

When an individual becomes a cancer survivor, his or her life is changed irrevocably. Cancer survivors often face serious and persistent adverse outcomes, including physical, emotional, psychosocial, and financial challenges as a result of the cancer diagnosis and treatment.

Among the challenges experienced from the time from diagnosis to the end of initial treatment are:

- choosing a physician(s) and treatment facility;
- choosing among a variety of treatment options; and
- managing adverse side effects of cancer and cancer treatment, many of which persist long term.

Many challenges experienced by cancer survivors begin during cancer treatment and continue long term, but others can appear months or even years later. These long-term and late effects include, but are not limited to:

- bone density loss (osteoporosis);
- cognitive impairment, sometimes known as "chemo brain";
- diagnosis with a new form of cancer(s);
- distress, which can interfere with a person's ability to cope effectively with cancer and its treatment;
- fatigue that is severe and often not relieved by rest;
- fear of cancer recurrence;
- heart damage (cardiotoxicity);
- infertility;
- lung (pulmonary) damage;
- lymphedema: swelling, most often in the arms or legs, that can cause pain and problems in functioning;
- pain;
- premature aging;
- recurrence of original cancer;
- sexual dysfunction.

Although all cancer survivors face challenges, survivors of cancer diagnosed from ages 0 to 19, during childhood and adolescence, are particularly at risk for severe long-term and late effects. The Children's Oncology Group's "Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers" were developed to help characterize and enhance the lifelong follow-up care of individuals who were diagnosed with cancer as children, adolescents, or young adults. For more information, see http://survivorshipguidelines.org/.
What Is Palliative Care?

Palliative care is specialized care that provides an extra layer of support to patients with serious illnesses such as cancer and their families.

It is not the same as hospice care, because it can be given throughout a patient’s experience with cancer, beginning at diagnosis and continuing through treatment, follow-up, survivorship, and end-of-life care.

It can be given in addition to cancer treatment or to those with no curative treatment options; palliative care given near the end of life is usually referred to as hospice care.

Palliative care addresses many of the challenges that can affect quality of life after a cancer diagnosis, including:

- emotional challenges such as anxiety and depression;
- physical symptoms and adverse effects of the disease and its treatment, such as pain, nausea, vomiting, fatigue, difficulty sleeping, and loss of appetite;
- practical challenges such as navigating the health care system; and
- spiritual challenges.

American Association for Cancer Research (AACR)
Cancer Progress Report 2017
Helping Patients with Cancer through Psycho-oncology Research

Healthcare practitioners working in the field of psycho-oncology, including psychiatrists, psychologists, and nurses, are dedicated to addressing the behavioral, emotional, psychological, and social challenges faced by patients with cancer. Examples of recent psycho-oncology clinical trials investigating new approaches to helping patients with cancer follow:

- **A psychoeducational intervention** comprising a psychoeducational booklet and three individual telephone-based psychotherapeutic sessions with a psychologist effectively reduced stress and fear of cancer recurrence among survivors of melanoma.

- **A psychosocial intervention** called Attention and Interpretation Modification for Fear of Breast Cancer Recurrence, which consisted of eight personalized treatment sessions, reduced health worries among survivors of breast cancer.

- Treatment with the **psychedelic drug psilocybin** led to clinically significant reductions in depression and anxiety as well as improved quality of life.

- **A meaning-centered group psychotherapy intervention**, comprising eight group sessions led by a psychiatrist, clinical psychologist, or social worker, resulted in improved spiritual well-being and quality of life as well as reduced depression, hopelessness, desire for hastened death, and physical symptom distress among patients with advanced cancer.

- **A web-based cognitive rehabilitation program** called insight, which uses adaptive exercises to improve cognition through speed and accuracy of information processing, improved perceived cognitive function and quality of life and reduced depression, fatigue, and stress among adult cancer survivors who reported having chemo brain.

*American Association for Cancer Research (AACR) Cancer Progress Report 2017*
Moving toward Minimally Invasive Testing

Liquid biopsy refers to the collection and analysis of biofluids, such as blood or urine. In oncology it primarily involves the capture and analysis of cells, lipid-encapsulated sacs called exosomes, or free DNA shed by tumors into the blood. For example, a blood sample, rather than a biopsy of the tumor tissue itself, could be used to analyze genomic alterations in a patient’s cancer. Currently, many liquid biopsy platforms are being developed and tested. The major advantages compared to traditional tissue biopsies are:

- Liquid biopsies have the potential to be safer, quicker, more convenient, and better representative of tumor heterogeneity than a typical biopsy.
- Liquid biopsies provide minimally invasive ways to repeatedly sample the genome of different tumor lesions to evaluate whether a cancer is responding to treatment or becoming treatment resistant and, if it is developing resistance, determine what treatment might be the most appropriate next option.

Ongoing research will continue to evaluate the clinical utility of these approaches.

American Association for Cancer Research (AACR)
Cancer Progress Report 2017
Charting the Future of Cancer Health Disparities Research

In 2015, representatives from four leading cancer organizations—the American Association for Cancer Research (AACR), the American Cancer Society (ACS), the American Society of Clinical Oncology (ASCO), and the National Cancer Institute (NCI)—began to meet to discuss the state of health disparities in the United States. The resulting position statement provides specific recommendations to improve the way disparities research is conducted and disseminated. The key recommendations aim to drive progress in five areas:

- Defining and improving measures and tools for cancer disparities research.
- Advancing knowledge of biologic and environmental determinants of cancer incidence disparities.
- Enhancing our understanding of the biologic, environmental, and system-level determinants of postdiagnosis survival to address cancer survival disparities.
- Advancing community engagement in cancer research and throughout the cancer care continuum.
- Redesigning clinical trials to acknowledge and address cancer disparities.

American Association for Cancer Research (AACR)  
Cancer Progress Report 2017
Building Blocks of Further Progress against Cancer

To accelerate the pace of progress against cancer, we must:

- Prioritize and increase federal funding for biomedical research.
- Support crosscutting initiatives to advance progress against cancer.
- Support regulatory science initiatives.
- Develop and train the biomedical research workforce of tomorrow.
- Support policies that advance patient-centered research and care.

American Association for Cancer Research (AACR) Cancer Progress Report 2017
Turning Back the Clock

In his first budget proposal to Congress, President Trump proposed drastic and devastating cuts of $7.2 billion, or 20 percent, to the budget for the National Institutes of Health (NIH). This request would take funding for the agency back to levels not seen in more than 15 years and reduce the number of available grants by several thousand. If these cuts were enacted, a recent analysis predicted:

- Nearly 90,000 jobs nationwide would be lost.
- More than $15 billion in economic activity would be lost.
- No U.S. state would be spared from the negative impact of this dramatic reduction in federal funding, with 13,581 jobs predicted to be lost in California alone.

American Association for Cancer Research (AACR)
Cancer Progress Report 2017
Working Together to Implement the Beau Biden Cancer Moonshot

At the White House on December 13, 2016, President Obama signed the 21st Century Cures Act into law. The legislation created an NIH Innovation Fund that provides $4.8 billion over 10 years in targeted, annual appropriations to three research initiatives, one of which is the Beau Biden Cancer Moonshot. Over seven fiscal years, beginning in fiscal year (FY) 2017, the Cancer Moonshot is to receive $1.8 billion through the NIH Innovation Fund. The first installment of $300 million was appropriated to the National Cancer Institute (NCI) in December 2016. The Beau Biden Cancer Moonshot is now under way thanks to the infusion of funding and the thoughtful recommendations set forth by the NCI Blue Ribbon Panel (BRP) in its September 2016 report. The BRP recommendations are:

- A network for direct patient engagement
- A cancer immunotherapy clinical trials network
- Therapeutic target identification to overcome resistance
- A national cancer data ecosystem for sharing and analysis
- More research into fusion oncoproteins in pediatric cancer
- Symptom management research
- Implementation of evidence-based approaches in prevention and early detection
- A retrospective analysis of biospecimens from patients treated with standard of care
- Generation of human tumor atlases
- The development of new enabling cancer technologies

Implementation teams aligned with the BRP recommendations have been organized to both identify ways to fund Cancer Moonshot-related research, and consider appropriate partnerships with foundations, academia, professional societies, and the private sector. Specifically, these teams are responsible for:

- Discussing approaches and developing initiatives for FY 2018 and FY 2019 that will achieve the goals of the BRP recommendation for which the team is responsible;
- Seeking input from the cancer research community, the BRP and its working groups, and NCI advisory committees through workshops, listening sessions, webinars, and other means; and
- Providing oversight and coordination of the funded initiatives associated with the BRP recommendation for which the team is responsible.

For more information on the Beau Biden Cancer Moonshot see https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative/implementation.

American Association for Cancer Research (AACR) Cancer Progress Report 2017
The Aims of the FDA Oncology Center of Excellence

The FDA Oncology Center of Excellence (OCE) brings together regulatory scientists and reviewers with oncology expertise to support an integrated approach to driving progress against cancer. The goals of the OCE include:

- Ensuring that the patient perspective is considered in the regulatory decision-making process through a Patient-Focused Drug Development program.
- Encouraging novel clinical trial designs.
- Modernizing the eligibility criteria of cancer clinical trials by enrolling patients who reflect the real-world population, such as allowing more older adults to enroll.
- Striving for “excellence” within the OCE by collaborating externally with academia, industry, patient groups, and professional societies with the goal of expedited, risk-benefit ratio balanced drug development.

American Association for Cancer Research (AACR)
Cancer Progress Report 2017
Supporting the Future of Cancer Research

The Next Generation Researchers Initiative was announced by the NIH earlier this year, with the aim of bolstering support for early-stage and mid-career investigators and addressing challenges they face as they begin and sustain independent research careers. With an expressed commitment to doing more to ensure a strong pipeline of researchers, the NIH plans a multipronged approach to boost the number of scientists at these stages that are supported by NIH grants. The initiative will make additional funds available to do the following:

- **Extend the payline** for early stage investigators to 25 percent;
- **Extend the payline** for mid-career investigators who are principal investigators and about to lose all NIH funding; and,
- **Identify “rising stars”** who are seeking their second research project grant (RPG) but just missed the payline.

The NIH estimates that this initiative will require $210 million in funding for the first year, and $1.1 billion over five years. Therefore, this is an initiative that is dependent on robust and sustained funding increases for the NIH over the next several years.

*American Association for Cancer Research (AACR) Cancer Progress Report 2017*
Revisions to the Common Rule

The regulations for federally funded research on human subjects, referred to as the Common Rule, were updated in January 2017. The updates, which aim to enhance safeguards for individuals who participate in cancer and other biomedical research while making it easier for scientists to conduct lifesaving research on samples provided by these individuals, include provisions that allow for:

Use of broad but simple consent from patients regarding the storage, maintenance, and secondary research use of identifiable private information and biospecimens.

Collaborative research being undertaken across multiple institutions to be conducted under a single Institutional Review Board.

Most of the updates will become effective in January 2018, except for provisions related to cooperative research, which become effective in January 2020.

American Association for Cancer Research (AACR)
Cancer Progress Report 2017