Taming Cancer
Past, Present and Future

Sam Makhoul, MD
CARTI
Little Rock, Arkansas
May 9, 2024
Conflicts of Interest

• None
Representative Fred Allen

From the 86th General Assembly, Regular Session in 2007 - Act 1171
AN ACT TO MAKE AN APPROPRIATION TO THE UNIVERSITY OF ARKANSAS FOR MEDICAL SCIENCES FOR THE WITNESS PROJECT AND THE UNIVERSITY CENTERS FOR EXCELLENCE IN DEVELOPMENTAL DISABILITIES; AND FOR OTHER PURPOSES.

From the 87th General Assembly, Regular Session in 2009 - Act 75
AN ACT TO REQUIRE HEALTH BENEFIT PLANS TO PROVIDE PROSTATE CANCER SCREENING FOR MEN FORTY (40) YEARS OF AGE AND OVER; AND FOR OTHER PURPOSES.

From the 87th General Assembly, Regular Session in 2009 - Act 280
AN ACT TO ENHANCE THE EXPERTISE OF THE CERVICAL CANCER TASK FORCE; TO REDEFINE THE FOCUS OF THE CERVICAL CANCER TASK FORCE; AND FOR OTHER PURPOSES.

From the 88th General Assembly, Regular Session in 2011 - Act 830
AN ACT TO AUTHORIZE THE CREATION AND ISSUANCE OF THE PROSTATE CANCER AWARENESS SPECIAL LICENSE PLATE; AND FOR OTHER PURPOSES.
From the 91st General Assembly, Regular Session in 2017 - Act 516
AN ACT TO UPDATE THE COLORECTAL CANCER PREVENTION, EARLY DETECTION, AND TREATMENT ACT OF 2009; AND FOR OTHER PURPOSES.

From the 92nd General Assembly, Regular Session in 2019 - Act 1045
AN ACT TO CREATE THE ARKANSAS BLUE RIBBON PANEL ON PEDIATRIC CANCER RESEARCH; AND FOR OTHER PURPOSES.

From the 92nd General Assembly, Regular Session in 2019 - Act 655
AN ACT TO UPDATE THE COLORECTAL CANCER PREVENTION, EARLY DETECTION, AND TREATMENT ACT; AND FOR OTHER PURPOSES.

From the 94th General Assembly, Regular Session in 2023 - Act 429
AN ACT CONCERNING COVERAGE FOR BIOMARKER TESTING FOR EARLY DETECTION AND MANAGEMENT FOR CANCER DIAGNOSES; AND FOR OTHER PURPOSES.

From the 94th General Assembly, Regular Session in 2023 - Act 66
AN ACT TO ENHANCE COVERAGE OF PROSTATE CANCER SCREENINGS BY HEALTH BENEFIT PLANS; AND FOR OTHER PURPOSES.
The Black Box Era

1982

The Targeted therapy Era

2003

The Genomic Era

2011

The Immunotherapy Era

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Cancer Progress Report 2023
SECTION I

The Past
Apollo 11 Moon Landing: July 20, 1969

“One step for [a] man, one giant leap for mankind”
Neil Armstrong
The dogma

• One cause

• One disease

• One treatment
Early Results

- Rous Sarcoma Virus (Peyton Rous)

- 1960’s: cure of choriocarcinoma (Min Chiu Li)
  - Maintenance chemotherapy (Methotrexate)

- 1968: cure of acute lymphblastic leukemia at St. Jude’s in Memphis (Donald Pinkel)
  - High dose combination chemotherapy
  - Intrathecal chemotherapy
  - Cranial irradiation
  - Maintenance chemotherapy

- 1968: cure of disseminated Hodgkin’s disease (Vincent De Vita)
  - Combination chemotherapy (MOPP)
The Pragmatics

• The war on cancer is the conquest of “inner space”…
  Mary Lasker
• The iron is hot and this is the time to pound without cessation
  Sidney Farber
• A major hindrance to cancer effort has been a chronic, severe shortage of funds…
  Solomon Garb
December 9th, 1969

Mr. Nixon:

You can cure cancer.

A new President needs new policies.

1. RESIGN, Mr. President. Or have the courage to say to the public:
   "I have been wrong. I shall resign."

2. URGE new anti-cancer research.
   ~ Mr. President, when you entered the White House in January, you pledged to make the War on Cancer your top priority. Now it is time to deliver on that promise.

Mr. President, as you well know, cancer is the second leading cause of death in America. It costs the country billions of dollars each year in medical expenses and lost productivity. The United States spends more on cancer research and treatment than any other country in the world, yet we have not made significant progress in curing this disease.

We urge you to take immediate action to increase funding for cancer research and to appoint a Cabinet-level position to oversee efforts to find a cure. The American public is counting on you to lead in the fight against cancer, and we are grateful for your commitment to make this a priority.

Sincerely,

[Signature]

[Name]

CITIZENS COMMITTEE FOR THE CONQUEST OF CANCER
Mr. Nixon: You can cure cancer

• If prayers are heard in Heaven, this prayer is heard the most: “Dear God, please. Not cancer.”
• Still, more than 318,000 Americans died of cancer last year.
• This year, Mr. President, you have it in your power to begin to end this curse.
• As you agonize over the Budget, we beg you to remember the agony of the 318,000 Americans. And their families
• We ask a better perspective, a better way to allocate our money. To save hundreds of thousands of lives each year
Mr. Nixon: You can cure cancer

• Dr. Sidney Farber, Past President of the American Cancer Society, believes: “We are so close to a cure for cancer. We lack only the will and the kind of money and comprehensive planning that went into putting a man on the moon.”

• Why don’t we try to conquer cancer by America’s 200th birthday?

• If you fail us, Mr. President, this will happen:
  • One in six Americans now alive, 34,000,000 people, will die of cancer unless new cures are found.
  • One in four Americans now alive, 51,000,000 people, will have cancer in the future.

• We simply cannot afford this.
The skeptics

• Cancer is not an island waiting in isolation for a crash program to wipe it out. It is in no way comparable to a moon shot.
  Philip Lee

• An all-out effort at this time would be like trying to land a man on the moon without knowing Newton’s laws of gravity
  Sol Spiegelman

• Doing “relevant” research is not necessarily doing “good” research…In particular, we must reject the notion that we will be lucky... instead we will be witnessing a massive expansion of well-intentioned mediocrity
  James Watson
The Signature of The National Cancer Act December 23, 1971
NATIONAL CANCER ACT
SECTION 404 (a) (1)

The Director shall “collect, analyze and disseminate information...useful in the prevention, diagnosis, and treatment of cancer, including the establishment of an international cancer research data bank...for cancer research undertaken in any country for the use of any person involved in cancer research in any country.”

11/83

Cancer Crusade
THE STORY OF THE NATIONAL CANCER ACT OF 1971
RICHARD A. RETTIG
Early Failures …

• Millions of dollars were poured into the virus research program, but NO viruses were found

• Several millions were spent on large trials comparing different cytotoxics with modest yield

• Basic Research was pushed to the periphery
... and early successes

- 1982: The discovery of the first oncogene; $ras$
  Weinberg, Barbacid and Wigler

- 1986: the discovery of the first tumor suppressor gene: $Rb$
  Friend, Weinberg and Dryja

- Triumph of the somatic mutation hypothesis
SECTION II
THE STATUS OF CANCER IN THE US IN 2024
Cancer Status 2024

1991

33%
Reduction in Overall Cancer Death Rate

2020

3.8 Million Lives Saved

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Cancer Progress Report 2023
43% Reduction In Breast Cancer Death Rate

1989

2020

460K Fewer Cancer Deaths

©American Association for Cancer Research® (AACR) Cancer Progress Report 2023
5-YEAR RELATIVE SURVIVAL RATE
(All cancers combined)

85%  2012-2018

58%  mid-1970s

86%  2012-2018

68%

Children (Ages 0-14)  Adolescents (Ages 15-19)

©American Association for Cancer Research® (AACR)
Cancer Progress Report 2023
2022
18+ MILLION SURVIVORS
(5.4% OF THE POPULATION)

1971
3 MILLION SURVIVORS
(1.4% OF THE POPULATION)

©American Association for Cancer Research® (AACR)
Cancer Progress Report 2023
Cancer Status 2024

In the United States, patients with cancer have collectively gained nearly 14 million years of life since 1980 because of NCI-funded clinical trials.
Cancer Statistics in 2024

• 2 million Americans will be diagnosed with cancer

• 611,720 will die of cancer

• Over 57% of all cancers will occur in the 18% of the population older than 65

• Spending on cancer care in the US has surpassed $209 billion in 2020

• Annual out-of-pocket spending on cancer care estimated at $16 billion
The Burden of Cancer is not Distributed Equally Among Americans
Social Determinants of Health

RACISM • DISCRIMINATION • SEGREGATION

STRUCTURAL INEQUITIES AND SOCIETAL INJUSTICES

Socioeconomic
Education, Income, Employment

Clinical
Health care access, health care quality

Environmental
Air, water quality, Housing, Transportation, Community safety

Cultural
Health beliefs, Health-related attitudes

Behavioral
Diet, Tobacco use, Excess body weight, Physical inactivity

Psychosocial
Stress, Mental health, Isolation

SOCIAL DETERMINANTS
OF HEALTH

CANCER HEALTH DISPARITIES

Lack of Diversity in Cancer Research and Care Workforce

ADVERSE HEALTH OUTCOMES

Adapted from ©American Association for Cancer Research® (AACR) Cancer Progress Report 2023
Survival Depends on the Type and Stage of Cancer

• Breast and prostate cancers have excellent 5-year survival when confined to the organ (99% and 100%, respectively)

• If breast or prostate cancer have metastasized to distant organs, 5-year survival is 31% and 34%, respectively

• 5-year survival for liver and pancreatic cancers remain dismal (23% and 13%, respectively)
The Incidence of Certain Cancers is still Rising

- Pancreatic cancer
- Cervix cancer
- Uterine cancer
- Early onset colorectal cancer (+1.3% a year between 2001 and 2018)
WHAT IS CANCER?
The Central Dogma in Genetics

DNA → Transcription → mRNA → Translation → Proteins → Post Translational changes → Function
Cancer is a Genetic and Epigenetic Disease Promoted by a Special Micro-Environment

- DNA alterations (germline or somatic)
- Changes of the epigenetic markings
- Alterations of the transcription of the mRNA
- Alterations of proteins synthesis and energy metabolism
- Aided by a permissive environment
Inherited Cancer Risk

Cancers of the Brain and the Nervous System
- Basal cell nevus syndrome (PTCH1, PTCH2, SUFU)
- Familial glioma-melanoma syndrome (CDKN2A)
- Familial adenomatous polyposis (APC)
- Neurofibromatosis type I and type II (NF1 and NF2)
- Brain tumor polyposis type I (MLH1, PM2)
- Brain tumor polyposis type II (APC)
- von Hippel-Lindau syndrome (VHL)

Eye
- Retinoblastoma predisposition syndrome (RBP)

Thyroid
- Multiple endocrine neoplasia 2 (RET, MEN2)
- Cowden syndrome (PTEN)
- MYH-associated polyposis (MUTYH)

Liver
- Peutz-Jeghers syndrome (STK11/LKB1)

Kidney
- von Hippel-Lindau syndrome (VHL)
- Wilms tumor (WT1)

Ovarian
- Breast-ovarian cancer syndrome (BRCA1, BRCA2)
- Peutz-Jeghers syndrome (STK11/LKB1)

Uterine
- Hereditary leiomyomatosis and renal cell cancer (FH1)
- Peutz-Jeghers syndrome (STK11/LKB1)

Blood cancers
- Leukemia; Lymphoma; Myelodysplastic syndrome
  - Ataxia telangiectasia (ATM)
  - Inherited bone marrow failure syndromes, such as Fanconi’s anemia and telomere syndromes (FANCC, FANC, FANCB, FANC, BRCA1, TERT, TERCI)
  - Li-Fraumeni syndrome (TP53)
  - Hereditary myeloid malignancy syndromes, such as familial AML/acute myeloid leukemias (RUNX1, GATA2, CEBPA, ETV6, DD7A1, ANKRD26, ATG12B/65KIP)

Bone
- Retinoblastoma predisposition syndrome (RBP)
- Li-Fraumeni syndrome (TP53)

Breast
- Cowden syndrome (PTEN)
- Breast-ovarian cancer syndrome (BRCA1, BRCA2)
- Li-Fraumeni syndrome (TP53)

Gastric
- MYH-associated polyposis (MUTYH)
- Diffuse gastric and intestinal type breast cancer syndrome (CDH1)

Pancreas
- Breast-ovarian cancer syndrome (BRCA1, BRCA2)
- Familial atypical multiple mole-melanoma syndrome (CDKN2A)
- Hereditary pancreatic tumors/ familial pancreatic cancer (PRSS1, SPINK1)
- Multiple endocrine neoplasia 1 (MEN1)
- Peutz-Jeghers syndrome (STK11/LKB1)

Colorectal
- Lynch syndrome (EPCAM, MSH2, MSH6, PMS2)
- MYH-associated polyposis (MUTYH)
- Familial adenomatous polyposis (APC)

Skin
- Familial atypical multiple mole-melanoma syndrome (CDKN2A)
- Familial glioma-melanoma syndrome (CDKN2A)
- Multiple endocrine neoplasia 1 (MEN1)
- Xeroderma pigmentosum (XPD, XPF, XPA)
- Basal cell nevus syndrome (PTCH1, PTCH2, SUFU)

All cancers
- Bloom syndrome (BLM)

Adapted from ©American Association for Cancer Research (AACR) Cancer Progress Report 2023
Somatic Mutations and Tumor Heterogeneity

- Normal Cell
- Tumor Population 1
- Tumor Population 2
- Clonal Mutation (Exists in all cancer cells)
- Subclonal Mutations (Exist in a subset of cancer cells)
Oncogenes: Gain of function

Tumor suppressor genes: Loss of function

Resistance to apoptosis

Functional immortality
The Hallmarks of Cancer
Each Patient's Cancer is Unique

• Sequencing of genomes, transcriptomes, epigenomes, and proteomes of individual cells is now possible

• One of the most important insights gleaned from this knowledge is that each patient’s cancer is unique
SECTION III
Prevention
# Cancer Risk Factors

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobacco</td>
<td>20%</td>
</tr>
<tr>
<td>Obesity</td>
<td>20%</td>
</tr>
<tr>
<td>Sedentary life-style</td>
<td>5%</td>
</tr>
<tr>
<td>Infections</td>
<td>5%</td>
</tr>
<tr>
<td>Occupational factors</td>
<td>5%</td>
</tr>
<tr>
<td>Familial cancer</td>
<td>5 - 10%</td>
</tr>
<tr>
<td>Alcohol</td>
<td>3%</td>
</tr>
<tr>
<td>Reproductive factors</td>
<td>3%</td>
</tr>
<tr>
<td>Environmental pollution</td>
<td>2%</td>
</tr>
<tr>
<td>Age</td>
<td>?</td>
</tr>
<tr>
<td>Racial and educational disparity</td>
<td>?</td>
</tr>
</tbody>
</table>
Modifiable Cancer Risks

- Tobacco Smoking: 20% of U.S. Cancer Cases in Adults Age >30
- Excess Body Weight: 10%
- Alcohol Consumption: 7%
- Ultraviolet Radiation Exposure: 6%
- Poor Diet: 4%
- Pathogenic Infections: 3%
- Physical Inactivity: 2%

Adapted from ©American Association for Cancer Research® (AACR) Cancer Progress Report 2023
Eliminate Tobacco

• Nearly 20% of all cancer cases and 30 percent of all cancer-related deaths are caused by tobacco products.

• E-cigarettes can deliver nicotine, an extremely addictive substance that is harmful to the developing brain, at similar levels as traditional cigarettes.

• e-cigarettes still expose individuals to toxic chemicals that can damage DNA and trigger inflammation.
Beyond the Lungs: Cancers Caused by Smoking Tobacco

**UROGENITAL SYSTEM**
- Kidney
- Ureter
- Bladder
- Ovary*
- Uterine Cervix

*Certain subtypes of ovarian cancer

**HEAD AND NECK**
- Nasal Cavity
- Nasopharynx
- Oral Cavity
- Oropharynx
- Hypopharynx
- Larynx

**DIGESTIVE SYSTEM**
- Esophagus
- Stomach
- Liver
- Pancreas
- Colon

**LUNG AND BRONCHUS**

**HEMATOPOIETIC SYSTEM**
- Acute Myeloid Leukemia

Adapted from ©American Association for Cancer Research* (AACR) Cancer Progress Report 2023
Tobacco Use in the US, 1900-2005

*Age-adjusted to 2000 US standard population.

Maintain a Healthy Weight, Eat a Healthy Diet, and Stay Active

• Among U.S. adults, the rate of obesity from 2017 to 2020 was 41.9%

• Obesity among children and teens (2 to 19 years of age), increased 400% in the past five decades (from 5% in the 1970s to approximately 19.7% during the period from 2017 to 2020)

• Weight loss interventions are effective in reducing or eliminating the risk of cancers associated with obesity

• 25% of Americans met the minimum amount of aerobic and muscle-strengthening exercise in 2020
Reasons to Maintain a Healthy Weight and Stay Active

- Cancers associated with OBESITY
- Cancers associated with PHYSICAL ACTIVITY
- Cancers associated with BOTH

- Meningioma
  - Certain types of Head and neck cancer
  - Adenocarcinoma
    - Subtype of esophageal cancer
  - Postmenopausal Breast cancer

- Thyroid cancer

- Lung cancer

- Liver cancer

- Gallbladder cancer

- Bladder cancer

- Ovarian cancer

- Endometrial cancer

- Stomach cancer

- Pancreatic cancer

- Kidney cancer

- Colorectal cancer

- Prostate cancer

- Multiple myeloma

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Physical Activity Guidelines

Incorporation of regular physical activity into daily life is one of the most important steps people can take to improve their health, including reducing cancer risk. The recommended level of physical activity varies depending on age and preexisting medical conditions.

**AEROBIC ACTIVITY**

- **Pre-school aged children** (2-5 years): Should be encouraged to move and engage in active play at all levels of intensity throughout the day.
- **Pregnant women**: 150 minutes per week
- **Adolescents** (Under 18 years): 60 minutes per day
- **Adults** (18-64 years): 150 minutes moderate intensity per week or 75 minutes vigorous intensity per week
- **Older adults** (65+ years): 2+ days per week

**STRENGTH TRAINING**

- **Pre-school aged children** (2-5 years): 2 days per week
- **Pregnant women**: 3 days per week
- **Adolescents** (Under 18 years): 2+ days per week
- **Adults** (18-64 years): 2+ days per week
- **Older adults** (65+ years): 2+ days per week

**AEROBIC ACTIVITY**

Cardiovascular exercise that gets your heart pumping

- **Moderate intensity**: Includes activities in which one can still talk without pausing for breaths, such as:
  - Walking
  - Pushing lawnmower
  - Water aerobics
  - Pickle ball

- **Vigorous intensity**: Includes activities during which it is hard to speak more than a few words before catching breath, such as:
  - Running
  - Swimming fast
  - Cycle fast or on hilly terrain

**STRENGTH TRAINING**

Includes activities which work muscles and core by doing repetitions or sets of movements, such as:

- Yoga
- Martial arts
- Tai chi
- Pilates
- Lifting weights
- Using resistance equipment

Cancer survivors should consult their physicians and follow modified guidelines adapted for their personal health, specific cancers, and treatment.

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Barriers that may prevent individuals from being physically active

• Cost
• Access to fitness facilities
• Lack of green spaces
• Family obligations
• Geographic disparities
Eliminate Nutritional Risks

• Poor diet
  o Processed foods
  o No fresh fruits or vegetables
  o Sugar-sweetened beverages

• Poor diet is responsible for the development of about 5% of all cancers

• Food insecurity, Food deserts

• Alcohol consumption increases the risk of
  o Head and neck cancer
  o Esophageal squamous cell carcinoma
  o Breast
  o Colorectal
  o Liver
  o Stomach cancers
Guidelines for Alcohol Consumption

The U.S. Department of Agriculture and U.S. Department of Health and Human Services, Dietary Guidelines for Americans, 2020-2025, do not recommend that individuals who do not drink alcohol start drinking for any reason. There are also some people who should not drink at all, such as those who are pregnant or might be pregnant; are under the legal age for drinking; have certain medical conditions or are taking certain medications that can interact with alcohol; and if they are recovering from an alcohol use disorder or if they are unable to control the amount they drink.

If adults age 21 and older choose to drink alcoholic beverages, drinking less is better for health than drinking more. The guidelines recommend:

**IF ALCOHOL IS CONSUMED, IT SHOULD BE DONE IN MODERATION.**

**Moderate drinking**

≤ 1 drink per day for women

≤ 2 drinks per day for men

The following are reference beverages that are one alcoholic drink-equivalent:

- 12 fl oz of regular beer (5% alcohol)
- 5 fl oz of wine (12% alcohol)
- 1.5 fl oz of 80 proof distilled spirits (40% alcohol)

Only by adults of legal drinking age

**ACCORDING TO THE NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM:**

**Heavy drinking**

≥ 3 drinks on any day or ≥ 7 drinks per week for women

≥ 4 drinks on any day or ≥14 drinks per week for men

**Binge drinking**

≥ 4 drinks within 2 hours for women

≥ 5 drinks within 2 hours for men

**Excessive alcohol consumption**

Includes binge drinking, heavy drinking, and any drinking by pregnant women or those under 21 years of age.
Ways to Protect Your Skin

To reduce the risk of three main types of skin cancer—basal cell carcinoma, squamous cell carcinoma, and melanoma—the U.S. 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 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 sunscreen before going outside (even on slightly cloudy or cool days); it takes about 1 ounce to fully cover the body. Look for sunscreen that is SPF 30 or higher, offers "broad-spectrum" protection, and is water resistant. Sunscreen should be applied 15 minutes prior to going outside.

Avoid indoor tanning with UV devices such as sunlamps, sunbeds, and tanning booths.
Globally, infections are responsible of 18% of all cancer

<table>
<thead>
<tr>
<th>Infection</th>
<th>Cancer Sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>EBV</td>
<td>HD, NHL, stomach, H&amp;N</td>
</tr>
<tr>
<td>HBV/HCV</td>
<td>HCC</td>
</tr>
<tr>
<td>H. Pylori</td>
<td>Stomach cancer</td>
</tr>
<tr>
<td>HIV</td>
<td>NHL, Kaposi’s</td>
</tr>
<tr>
<td>HPV</td>
<td>Cervical, anogenital, H&amp;N</td>
</tr>
</tbody>
</table>
SECTION IV

Screening
What Can Cancer Screening Find and What Can Be Done?

**INCREASING TIME AND NUMBER OF MUTATIONS**

<table>
<thead>
<tr>
<th>TIME</th>
<th>Normal</th>
<th>Precancerous Lesion</th>
<th>STAGE I</th>
<th>STAGE II</th>
<th>STAGE III</th>
<th>STAGE IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIME</td>
<td></td>
<td></td>
<td>Localized</td>
<td>Early Locally Advanced</td>
<td>Late Locally Advanced</td>
<td>Metastasized</td>
</tr>
<tr>
<td></td>
<td>Nothing abnormal detected. Continue routine screening.</td>
<td>Remove precancerous lesion to prevent cancer development.</td>
<td>Cancer is detected at an early stage. Treat as appropriate for the type of cancer and the exact stage of disease at diagnosis.</td>
<td>Cancer is detected at a late stage. Treat as appropriate for the type of cancer and the exact stage of the disease at diagnosis.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Adapted from ©American Association for Cancer Research® (AACR) Cancer Progress Report 2023
# Lifetime Probability of Developing Cancer, Men, 2003-2005*

<table>
<thead>
<tr>
<th>Site</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>All sites†</td>
<td>1 in 2</td>
</tr>
<tr>
<td>Prostate</td>
<td>1 in 6</td>
</tr>
<tr>
<td>Lung and bronchus</td>
<td>1 in 13</td>
</tr>
<tr>
<td>Colon and rectum</td>
<td>1 in 18</td>
</tr>
<tr>
<td>Urinary bladder‡</td>
<td>1 in 27</td>
</tr>
<tr>
<td>Melanoma§</td>
<td>1 in 39</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>1 in 45</td>
</tr>
<tr>
<td>Kidney</td>
<td>1 in 57</td>
</tr>
<tr>
<td>Leukemia</td>
<td>1 in 67</td>
</tr>
<tr>
<td>Oral Cavity</td>
<td>1 in 72</td>
</tr>
<tr>
<td>Stomach</td>
<td>1 in 90</td>
</tr>
</tbody>
</table>

* For those free of cancer at beginning of age interval.
† All Sites exclude basal and squamous cell skin cancers and in situ cancers except urinary bladder.
‡ Includes invasive and in situ cancer cases
§ Statistic for white men.

### Lifetime Probability of Developing Cancer, Women, US, 2003-2005*

<table>
<thead>
<tr>
<th>Site</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>All sites†</td>
<td>1 in 3</td>
</tr>
<tr>
<td>Breast</td>
<td>1 in 8</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>1 in 16</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>1 in 20</td>
</tr>
<tr>
<td>Uterine corpus</td>
<td>1 in 40</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>1 in 53</td>
</tr>
<tr>
<td>Urinary bladder‡</td>
<td>1 in 84</td>
</tr>
<tr>
<td>Melanoma§</td>
<td>1 in 58</td>
</tr>
<tr>
<td>Ovary</td>
<td>1 in 72</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1 in 75</td>
</tr>
<tr>
<td>Uterine cervix</td>
<td>1 in 145</td>
</tr>
</tbody>
</table>

* For those free of cancer at beginning of age interval.
† All Sites exclude basal and squamous cell skin cancers and in situ cancers except urinary bladder.
‡ Includes invasive and in situ cancer cases
§ Statistic for white women.

Evidence-based Interventions to Increase Adherence to Cancer Screening

According to the Centers for Disease Control and Prevention (CDC), evidence-based interventions are strategies that improve delivery of cancer screening and increase the number of people screened.

Below are recent examples of some of the evidence-based interventions that have been shown to increase cancer screening adherence among eligible individuals:

**Combining tailored educational material with patient navigation**
An interactive video of tailored messages about cancer screening followed by a phone call with a patient navigator increased adherence to routine screening for breast, cervical, and colorectal cancers six times among women living in rural areas.

**Mailing self-collection sample kits**
Mailing human papillomavirus self-collection kits to women eligible for cervical cancer screening nearly doubled the screening uptake.

**Using digital interventions**
Using telemedicine as well as Internet- and mobile device-based technologies to help make informed decisions resulted in a 1.5 times increase in the completion rate for colorectal cancer screening.

**Implementing public health campaigns**
Clinics that participated in the Colorectal Cancer Control Program of CDC and applied a combination of three or more evidence-based interventions increased the uptake of colorectal cancer screening by five percentage points.
New Frontiers in Cancer Screening

• Artificial Intelligence for Early Detection of Cancers
  o Al-assisted colonoscopy detected 21 percent more polyps
  o Al-driven medical devices
    ▪ ProstatID and SKOUT improved detection of prostate cancer using MRI

• Moving Toward Minimally Invasive Cancer Screening
  o Liquid biopsy for Multi-Cancer Early Detection (MCED) test
  o Possibility of screening for many cancer types simultaneously and potentially with high specificity
    ▪ Promising
    ▪ Too early to tell
SECTION V

TREATMENT
The Pillars of Cancer Treatment

- Surgery: Ancient Times-Present
- Radiotherapy: 1890s-Present
- Cytotoxic Chemotherapy: 1940s-Present
- Molecularly Targeted Therapy: 1990s-Present
- Immunotherapy: 1990s-Present

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Progress was made in all diagnostic & treatment modalities

• Surgery
  • Minimally invasive surgery (robotic)
  • Organ conservation surgery
  • Sentinel lymph node biopsy
  • Plastic surgery

• Radiation therapy
  • Stereotactic radiation therapy
  • Intensity modulated XRT

• Advances in supportive care
  • Antiemetics
  • Growth factors
  • Bone modifying agents
  • Pain management
Improve the visibility of cancer

• Visualizing Lung and Ovarian Cancers More Precisely During Surgery
  o In December 2022, the FDA approved pafolacianine (Cytalux)
    ▪ A folate receptor–targeted fluorescent agent
    ▪ A targeted molecular imaging agent
    ▪ It illuminates lung cancers and enhances surgeons' ability to see cancer in real time as they operate
Improve our visibility of cancer

- Visualizing Lung Cancers More Precisely During Surgery
  - In December 2022, the FDA approved pafolacianine (Cytalux)
    - A folate receptor–targeted fluorescent agent
    - The first and only targeted molecular imaging agent
    - It illuminates lung cancers and enhances surgeons' ability to see cancer in real time as they operate

- Magnetic Resonance Imaging (MRI)-guided radiotherapy (MRgRT) for the treatment of prostate cancer

- PSMA theranostic
  - To see
  - And to treat (Pluvicto)
Progress in Systemic Therapy

• Multiple chemotherapy regimens were developed for all cancers

• Targeted or biologic therapies
  • Based on our new understanding of the biology of cancer (The Cancer Genome Atlas)
  • Fundamental heterogeneity of cancers even within the same organ
    • Molecular classification of cancer
    • Opportunity for personalized therapy

• Targeting Cancers Based on a Common Genetic Feature, Not Tissue of Origin
Agnostic to the Tissue of Origin Drugs

• BRAF targeting
  o Melanoma
  o Colon cancer
  o Brain tumors

• HER2 targeting
  o Breast cancer
  o Colon cancer
  o Gastric cancer

• Antibody drug conjugate
  o Trastuzumab Dxd
  o Sacituzumab Dxd

• MSI high
  o Immunotherapy
Therapeutic Development

**TARGET VALIDATION**
Potential targets identified by discovery science are confirmed to play a causal role in disease development.

**DRUG SCREENING**
Large numbers of chemical or biological agents are screened to identify and validate molecules that hit the target.

**LEAD IDENTIFICATION**
Agents that hit the target are evaluated to determine which ones bind the target with the greatest specificity and have the most promising medicinal properties.

**LEAD OPTIMIZATION**
The characteristics of lead compounds are optimized to enhance potency and drug-like properties, and to reduce side effects by enhancing specificity.

**PRECLINICAL TESTING**
Optimized lead compound(s) are tested in cell-based and animal models for effectiveness, potential toxicity, optimal starting dose, and dosing schedule for clinical or “first-in-human” testing. The final compound(s) are considered to be clinical candidate(s).

**INVESTIGATIONAL NEW DRUG**
One or more clinical candidates are generated through good manufacturing practices and assessed in rigorous good laboratory practice studies before submission to the U.S. Food and Drug Administration for approval for use in clinical trials.

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Molecularly based drug design

• Combination targeted therapy
  • BRAR and MEK inhibitors in melanoma

• Targeting the microenvironment
  • The tumor vasculature
  • Breaking down the tumor collagen

• Harnessing the immune system

• Modifiable chemotherapeutics, e.g., with “on” and “off” switches, that are selectively delivered to tumors while sparing healthy tissue
TYPES OF CANCER IMMUNOTHERAPY

- T-cell engaging bispecific antibodies
- Oncolytic viruses
- Vaccines
- CAR T cells
- Checkpoint inhibitors
- Cytokines
- Antibody-dependent cellular cytotoxicity promoting antibodies
Going Deep with Immune Checkpoint Inhibitors

**FDA-APPROVED AS OF 2023**

- **Hodgkin lymphoma**
  - nivolumab and pembrolizumab
- **Non-Hodgkin lymphoma**
  - pembrolizumab
- **Lung**
  - atezolizumab, durvalumab, cemiplimab-rwlc, nivolumab, pembrolizumab and combination of ipilimumab and nivolumab, tremelimumab and durvalumab
- **Mesothelioma**
  - nivolumab and combination of ipilimumab and nivolumab
- **Liver**
  - atezolizumab, pembrolizumab and combination of ipilimumab and nivolumab, tremelimumab and durvalumab
- **Bile duct**
  - durvalumab
- **Bladder**
  - atezolizumab, avelumab, nivolumab, and pembrolizumab
- **Cervical**
  - pembrolizumab
- **Endometrial**
  - pembrolizumab and dostarlimab-gxly
- **Head & neck**
  - nivolumab and pembrolizumab
- **Esophageal**
  - nivolumab and pembrolizumab
- **Breast**
  - pembrolizumab
- **Gastric**
  - pembrolizumab and nivolumab
- **Kidney**
  - avelumab, nivolumab, pembrolizumab, and combination of ipilimumab and nivolumab
- **Colorectal**
  - nivolumab and combination of ipilimumab and nivolumab
- **Melanoma**
  - atezolizumab, ipilimumab, nivolumab, pembrolizumab, relatlimab-mbbw+nivolumab and combination of ipilimumab and nivolumab
- **Merkel cell carcinoma**
  - avelumab and pembrolizumab, relatilimab-dlwr
- **Cutaneous squamous cell carcinoma**
  - cemiplimab-rwlc and pembrolizumab
- **Basal cell carcinoma**
  - cemiplimab-rwlc

Solid tumors that are microsatellite instability-high or mismatch repair-deficient
- pembrolizumab, dostarlimab-gxly
- Solid tumors that are tumor mutational burden-high
- pembrolizumab

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Common Side Effects of Immune Checkpoint Inhibitors

**NEUROLOGIC**
- Guillain-Barré syndrome
- Myasthenia gravis
- Neuropathy

**OCULAR**
- Ocular toxicity

**ENDOCRINE**
- Adrenal insufficiency
- Diabetes
- Hypophysitis
- Thyroiditis/hypothyroidism

**ORAL**
- Xerostomia

**RESPIRATORY**
- Persistent wheezing/coughing
- Pneumonitis

**CARDIOVASCULAR**
- Myocarditis

**DERMATOLOGIC**
- Dermatitis
- Mucositis
- Pruritus
- Vitiligo

**GASTROINTESTINAL**
- Celiac disease
- Colitis/diarrhea
- Esophagitis
- Hepatitis
- Pancreatic insufficiency

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New Frontiers in Cancer Research

- Innovative technologies are enabling a deeper understanding of cancer at a single cell and single molecule level
- Modulating the human microbiome
- Artificial intelligence
- Wearable technologies
- Combinations of immunotherapies and targeted therapies
Challenges

• Disparity in access to health care services
  o Minorities
  o Under/uninsured
  o Marginalized groups

• Limited public funds for research

• Limited investment in screening and prevention

• Limited enrollment of patients in clinical trials

• Lack of patient diversity on clinical trials
Summary

• Primary prevention remains the most cost-effective method to decrease cancer mortality
• Screening leads to early detection of cancer and decreases cancer mortality
• Advancement in multidisciplinary and individualized treatment decreases morbidity and improve survival
• The genomic era ushers in the beginning of true personalized cancer management
  o Every patient is unique
  o Every cancer is unique
Are we going to eradicate cancer?

• NO
  • Cancer will always exist

• Yes
  • We will be able to prevent many cancers and will find drugs that either control or eradicate good number of cancers after they happen; we are already doing it...
Questions
The Hallmarks of Cancer

- Spread to other parts of the body
- Multiply limitlessly
- Increase blood vessel formation toward tumor
- Evade the immune system
- Increase nutrient and oxygen supply to the tumor
- Escape cell death
- Grow uncontrollably
- Accumulate changes in the genetic material

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Every cancer is unique