



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.



RESEARCH

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

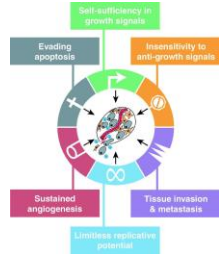
AN ACT TO ENHANCE **COVERAGE OF PROSTATE CANCER SCREENINGS** BY HEALTH BENEFIT PLANS; AND FOR OTHER PURPOSES.

The Black Box Era



1982

The Targeted therapy Era



2003

The Genomic Era



2011

The Immunotherapy Era



2022

18+
MILLION
SURVIVORS
(5.4% OF THE POPULATION)



1971

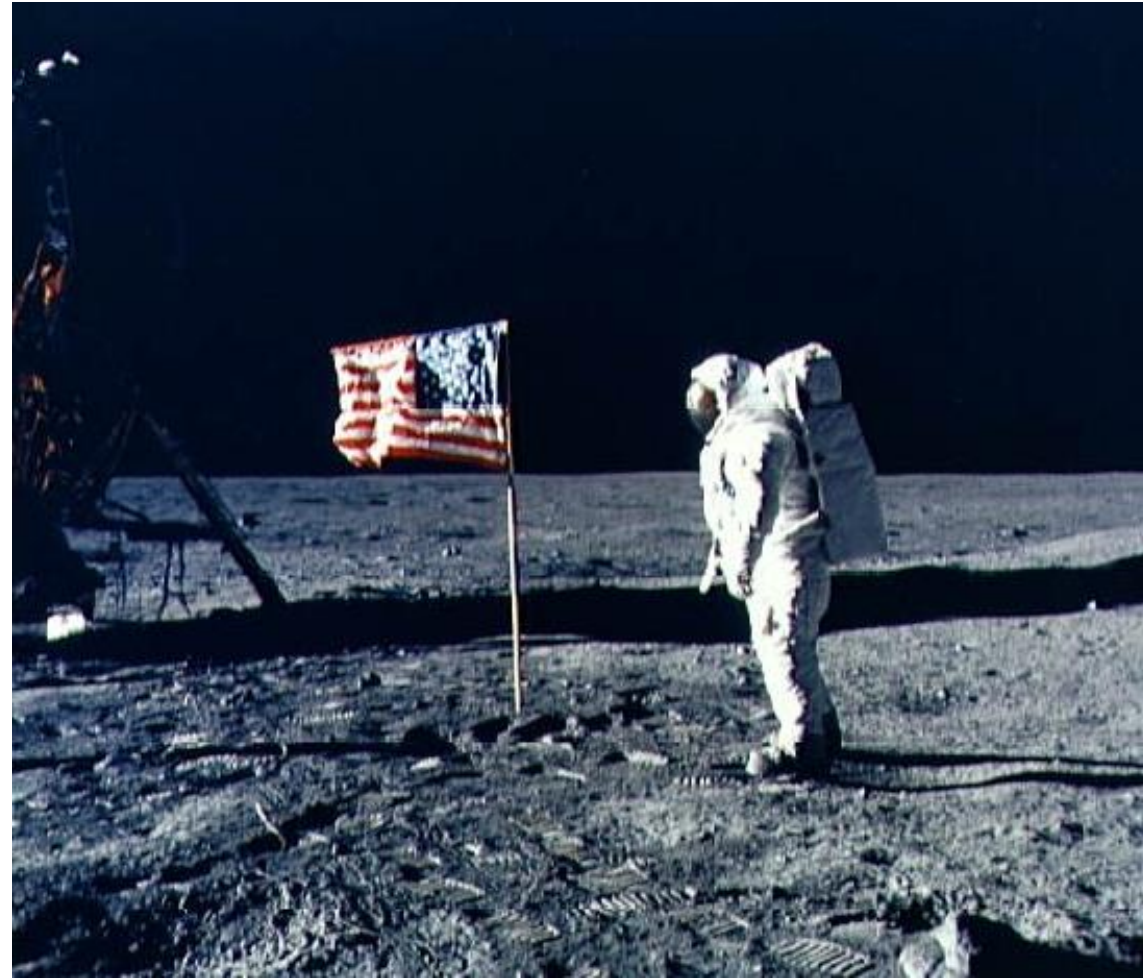
3 MILLION
SURVIVORS
(1.4% OF THE POPULATION)

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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 lymphoblastic 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



Mary Lasker

CURE for CANCER A National Goal

By SOLOMON GARB, M.D., M.A.C.P.
Professor of Microbiology, Associate Professor
of Community Medicine and Medical Practice,
University of Toronto, Ontario, Canada

 FRANKLIN PUBLISHING COMPANY, INC.
NEW YORK

Solomon Garb



Sidney Farber



Mr. Nixon:

You can

cure

cancer



December 9th, 1969

If prayers are heard in Heaven, this prayer is heard first:

"Dear God, please. Not cancer!"
Still, more than 325,000 Americans died of cancer last year.

This year, Mr. President, you have it in your power to begin to end this crime.

As you agonize over the Budget, we beg you to remember the agony of those 325,000 Americans. And their families.

We urge you to remember also that we spend more each day on military matters than each year on cancer research. And, last year, more than 21 times as much on space research as on cancer research.

We ask a better perspective, a better way to allocate our money to save hundreds of thou-

sands of lives each year.

America can do this. There is not a doubt in the minds of our top cancer researchers that the final answer to cancer can be found.

Already, 4 out of about 200 types of cancer can be cured with drugs. And if other drugs will cause temporary remission in 17 other types of 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?

What a holiday that would be! Cancer could be then where smallpox, diphtheria and polio

are today—almost nonexistent.

If you fail us, Mr. President, this will happen: One in six Americans now alive, 54,000,000 people, will die of cancer unless new cures are found.

One in four Americans now alive, 52,000,000 people, will have cancer in the future.

We simply cannot afford this.

Our nation has the money on one hand and the skills on the other. We must, under your leadership, put our hands together and get this thing done.

Surely, the war against cancer has the support of 100% of the people. It is a war in which we lost 21 times more lives last year than we lost in Viet Nam last year. A war we can win and pay the service heroes men in our debt.

To the public, cancer patients, their friends and relatives:

Write or urge the President, urging him to put more funds behind cancer research. Or, please use this coupon.

Dear Mr. Nixon:
Cancer research needs more funds. Please provide these in your 1970 budget. Please.

NAME _____
ADDRESS _____
CITY _____ STATE _____ ZIP _____

Mail this coupon to: The President
The White House
Washington, D.C.

CITIZENS COMMITTEE FOR THE CONQUEST OF CANCER
888 United Nations Plaza, New York, N.Y., Belmont Gch, M.D., Emmett Potts, Co-chairman



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

Nixon Signs \$1.6 Billion Cancer Bill, Names Man to Head Fight

WASHINGTON (UPI)—President Nixon today signed into law a \$1.6 billion program to find a cure for

the act was "a milestone in the long and difficult effort to find the causes and cures of cancer."
"This law is

Cancer Crusade



THE STORY
OF THE NATIONAL
CANCER ACT OF 1971

RICHARD A. RETTIG

Early Failures ...

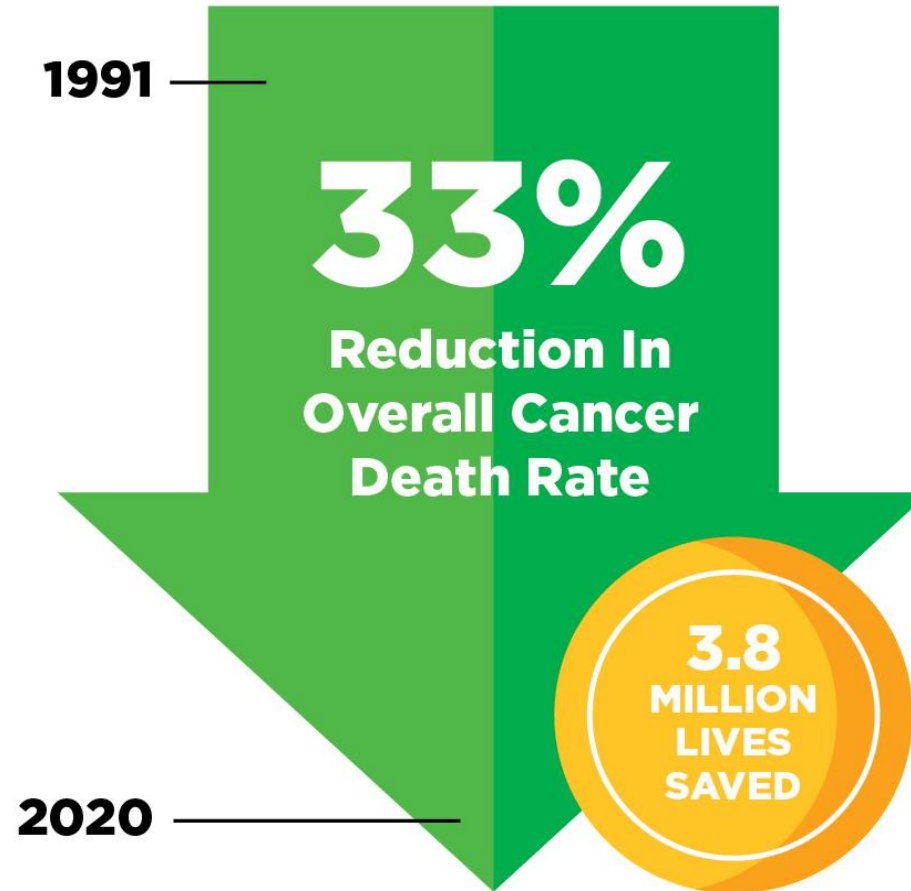
- Millions of dollars were poured into the virus research program, but NO viruses were found
- Several millions were spent on large trials comparing different cytotoxics with modest yield
- Basic Research was pushed to the periphery

... 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



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Cancer Progress Report 2023

1989

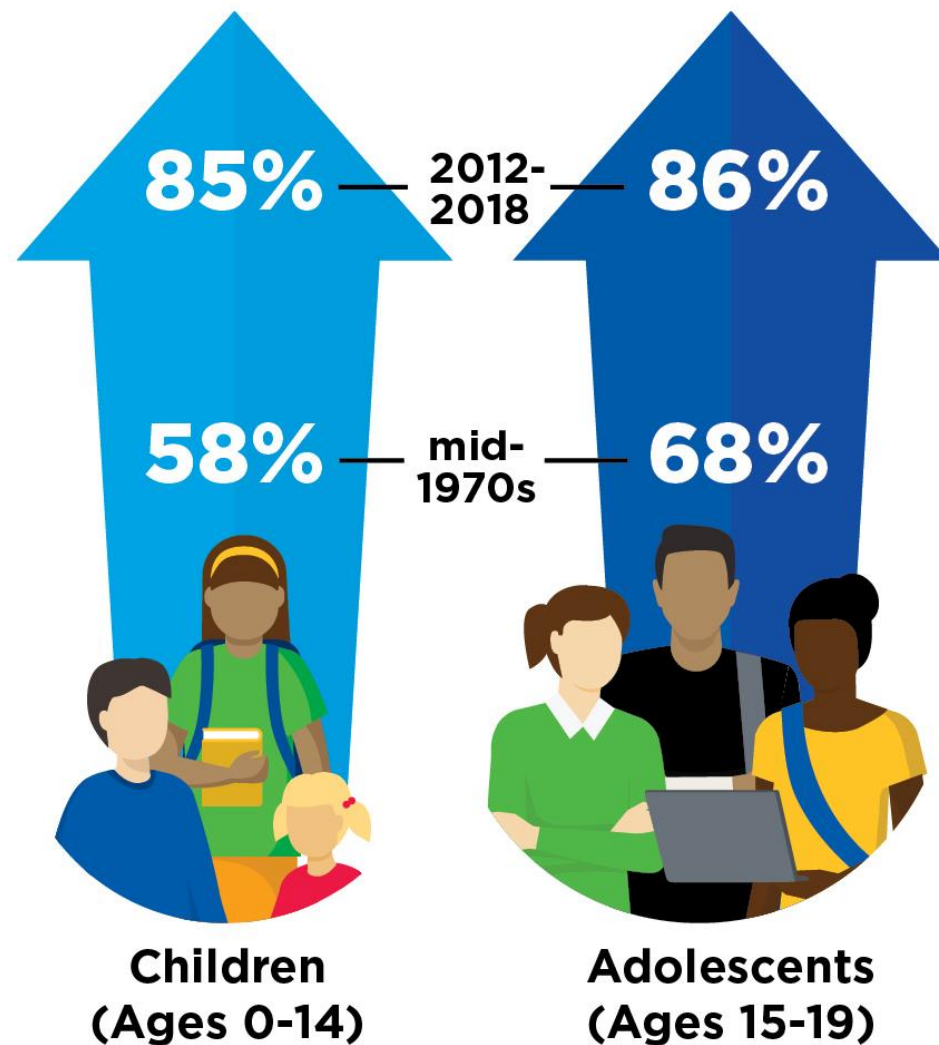
43%

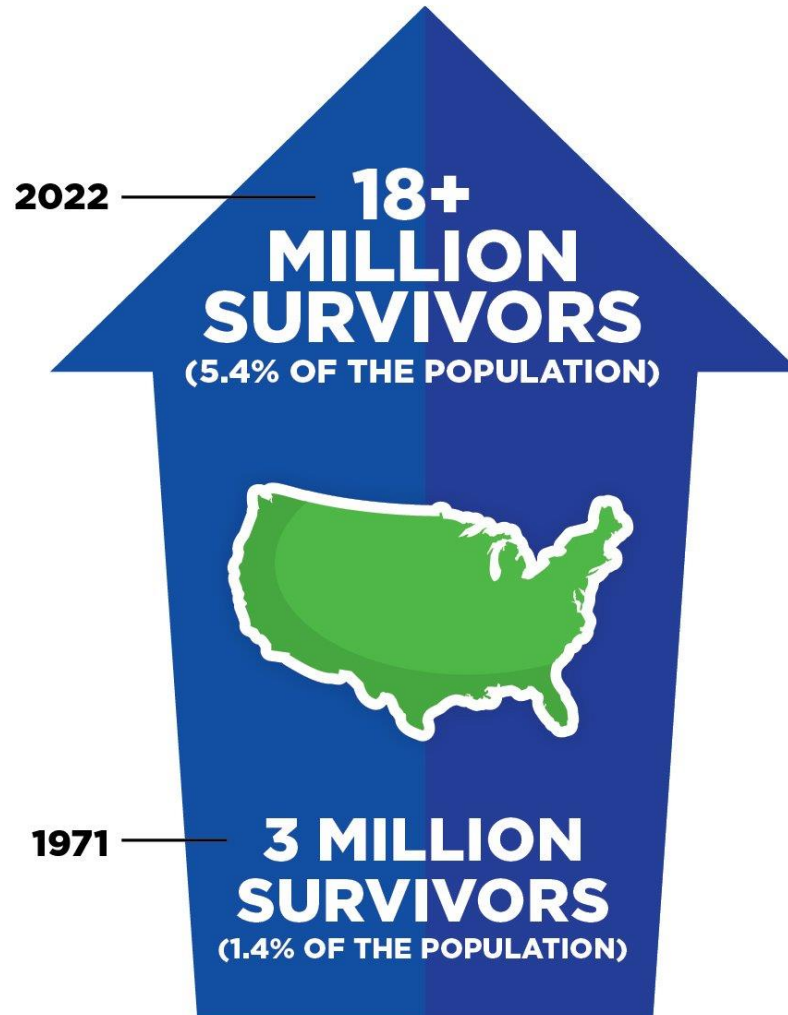
Reduction In
Breast Cancer
Death Rate

2020

460K
FEWER
CANCER
DEATHS

5-YEAR RELATIVE SURVIVAL RATE (All cancers combined)





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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

<p>Individuals belonging to certain ancestry, racial or ethnic minority populations</p> 	<p>Individuals of low socioeconomic status</p> 	<p>Individuals who lack or have inadequate health insurance coverage</p> 
<p>Residents in certain geographic locations, including rural areas</p> 	<p>Individuals belonging to sexual and gender minorities</p> 	<p>Immigrants, refugees, or asylum seekers</p> 
<p>Individuals with disabilities</p> 	<p>Adolescents and young adults</p> 	<p>Older adults</p> 

Social Determinants of Health



Survival Depends on the Type and Stage of Cancer

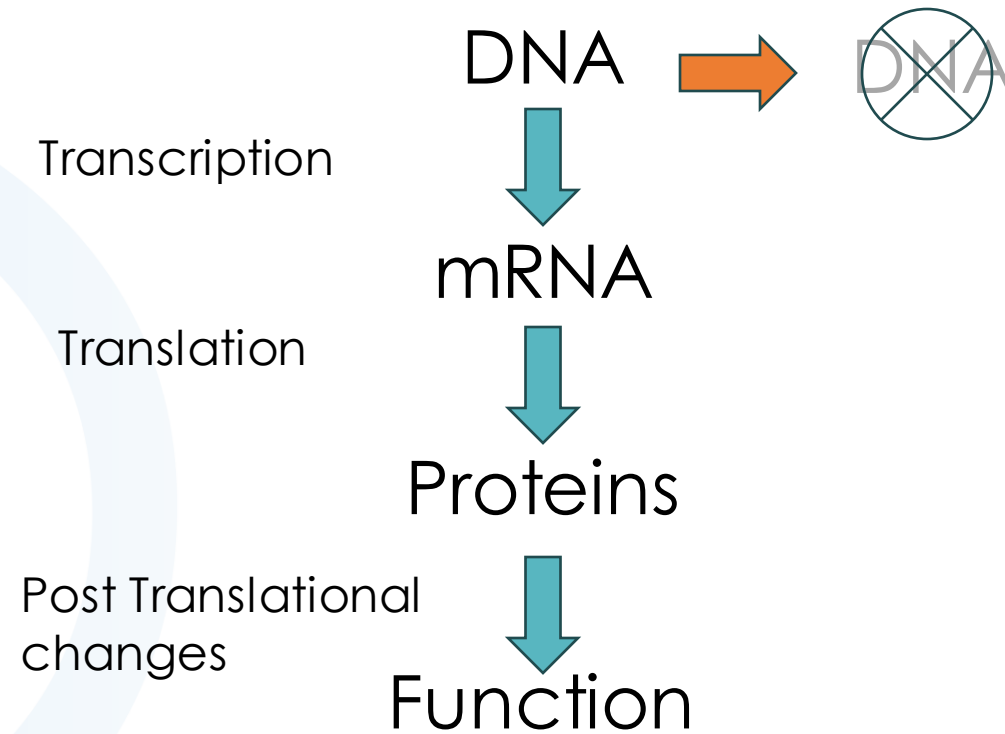
- Breast and prostate cancers have excellent 5-year survival when confined to the organ (99% and 100%, respectively)
- If breast or prostate cancer have metastasized to distant organs, 5-year survival is 31% and 34%, respectively
- 5-year survival for liver and pancreatic cancers remain dismal (23% and 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?

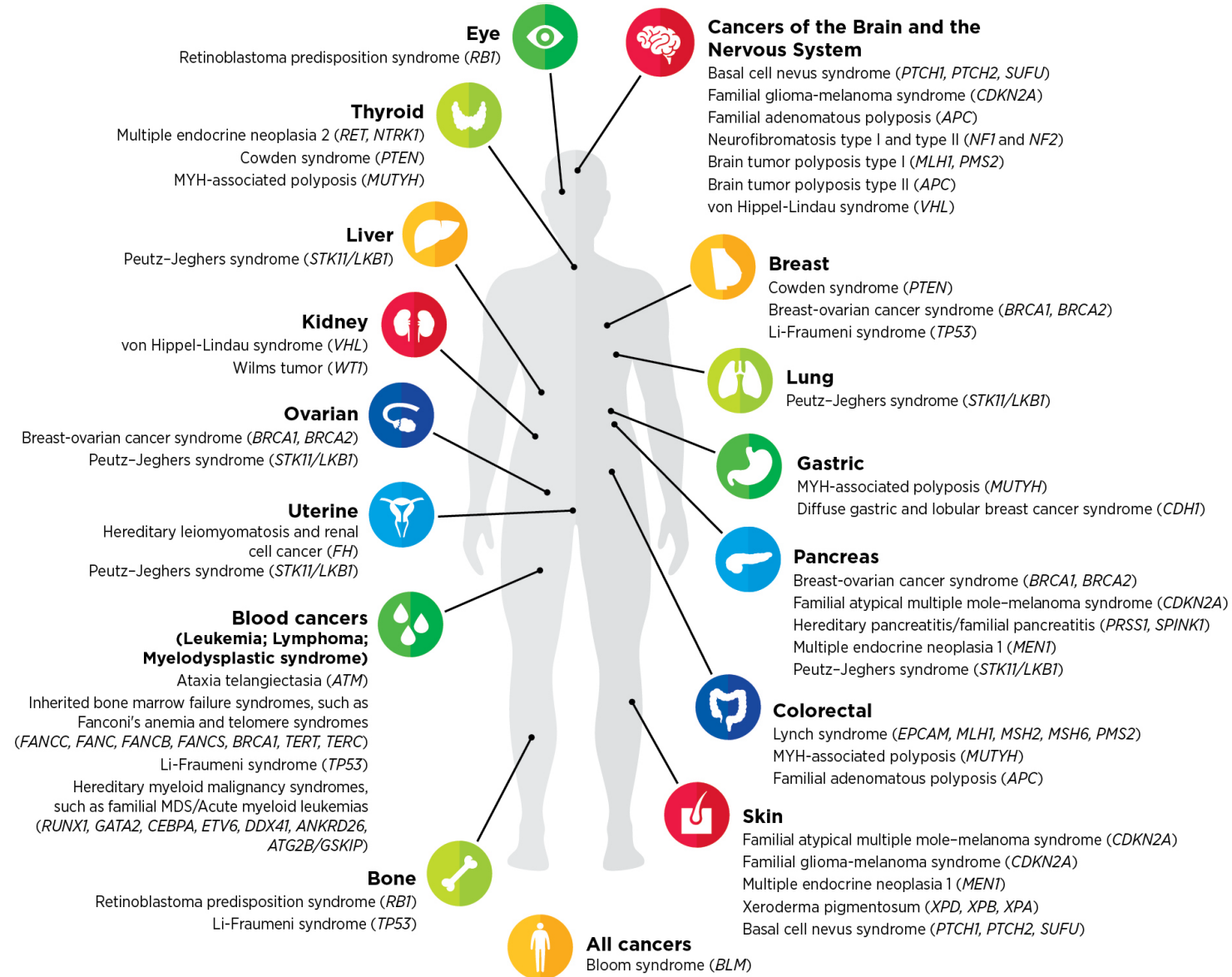
The Central Dogma in Genetics



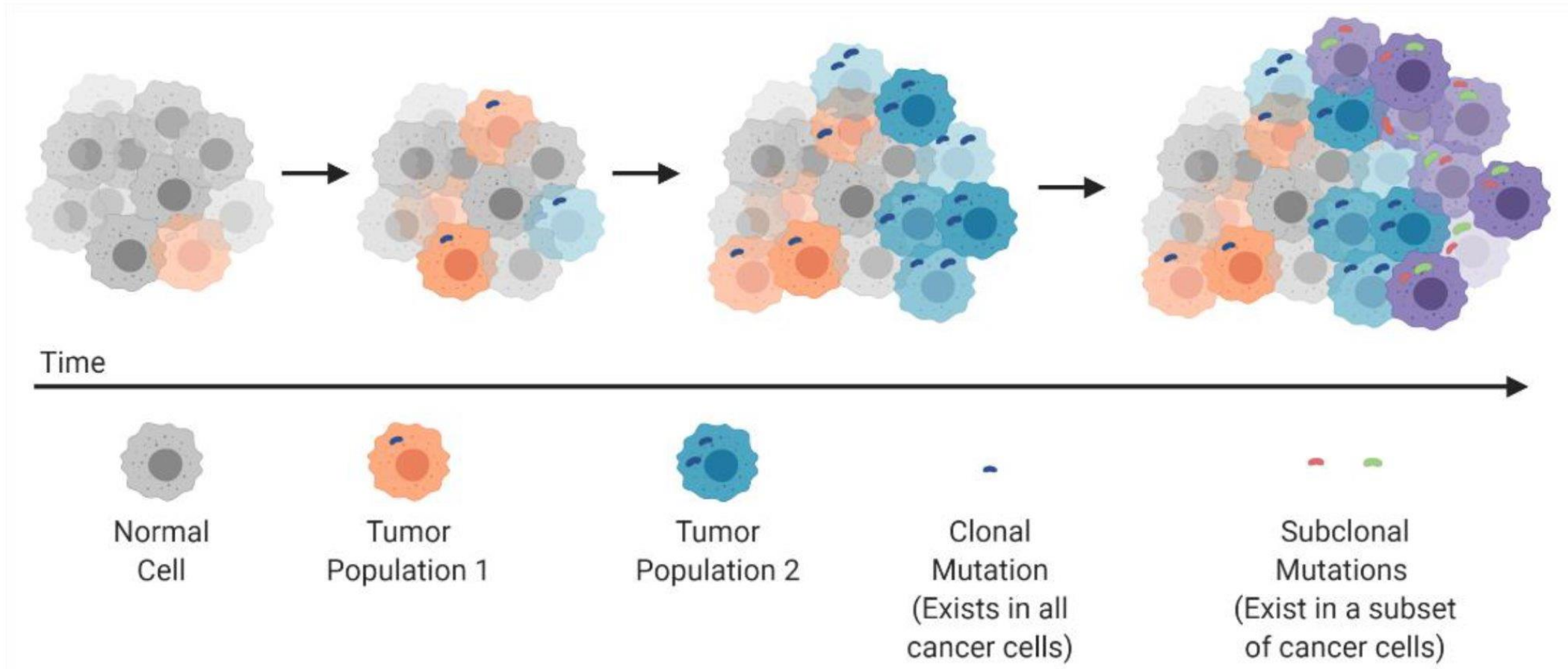
Cancer is a Genetic and Epigenetic Disease Promoted by a Special Micro-Environment

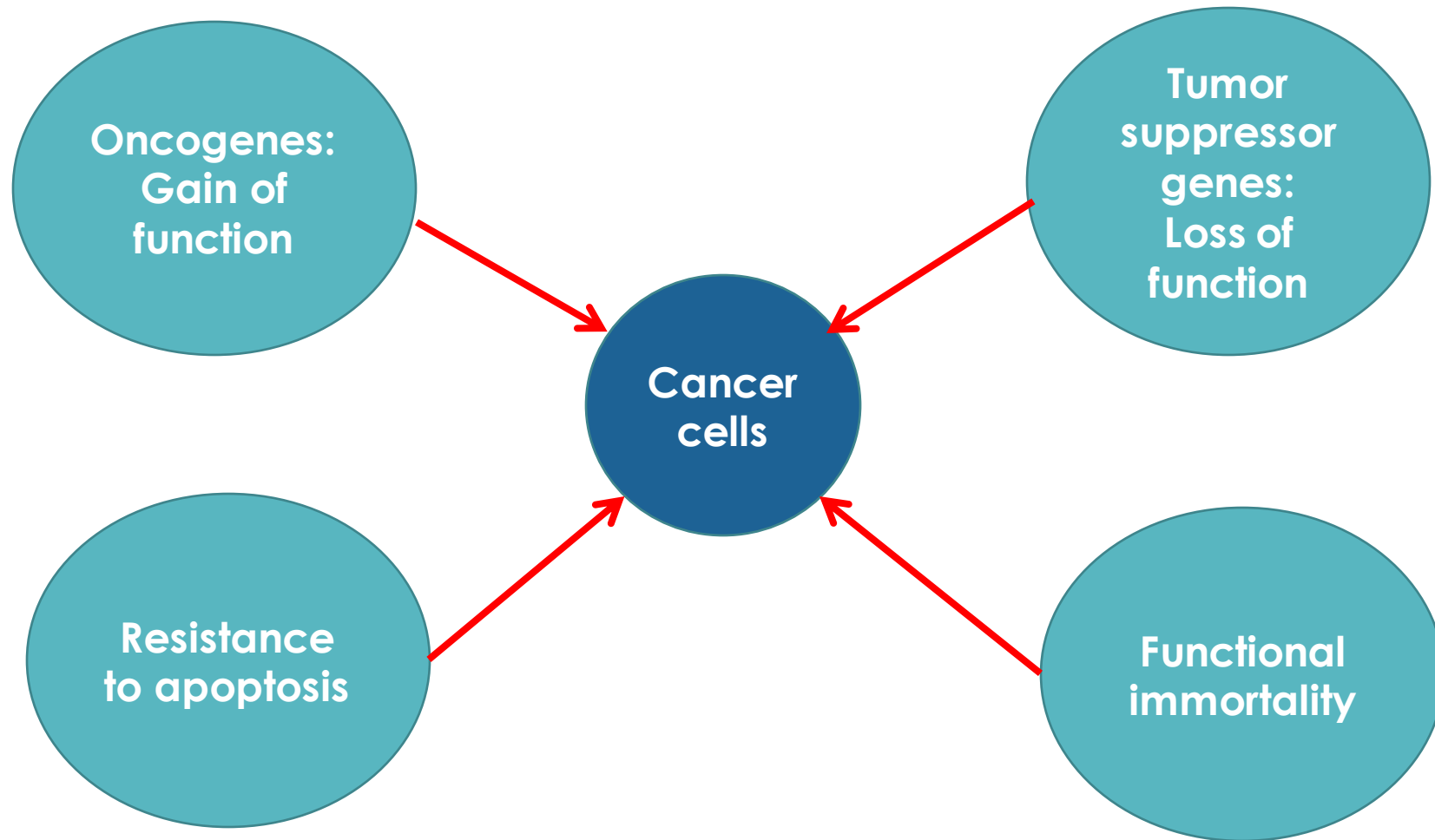
- DNA alterations (germline or somatic)
- Changes of the epigenetic markings
- Alterations of the transcription of the mRNA
- Alterations of proteins synthesis and energy metabolism
- Aided by a permissive environment

Inherited Cancer Risk

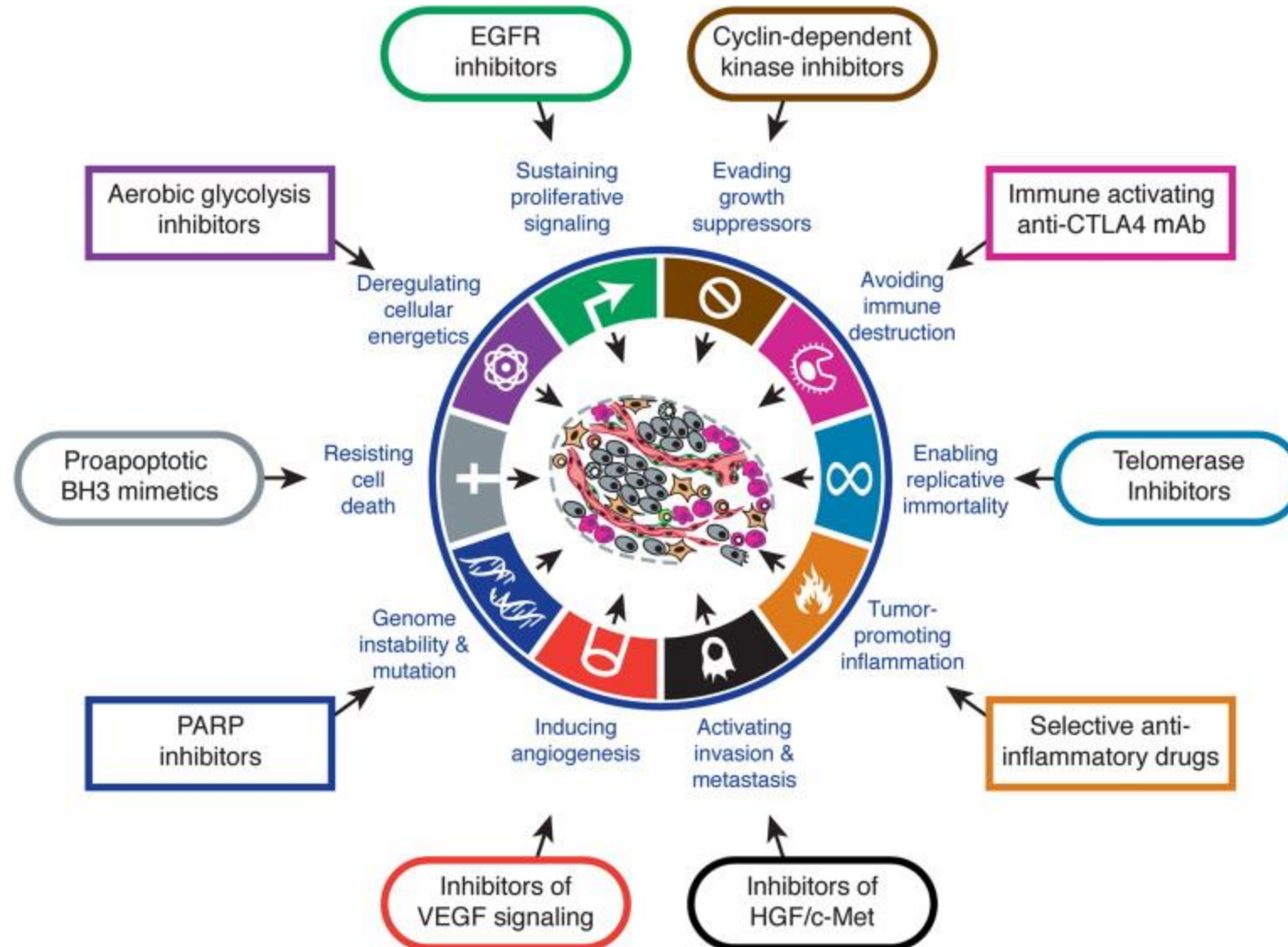


Somatic Mutations and Tumor Heterogeneity





The Hallmarks of Cancer

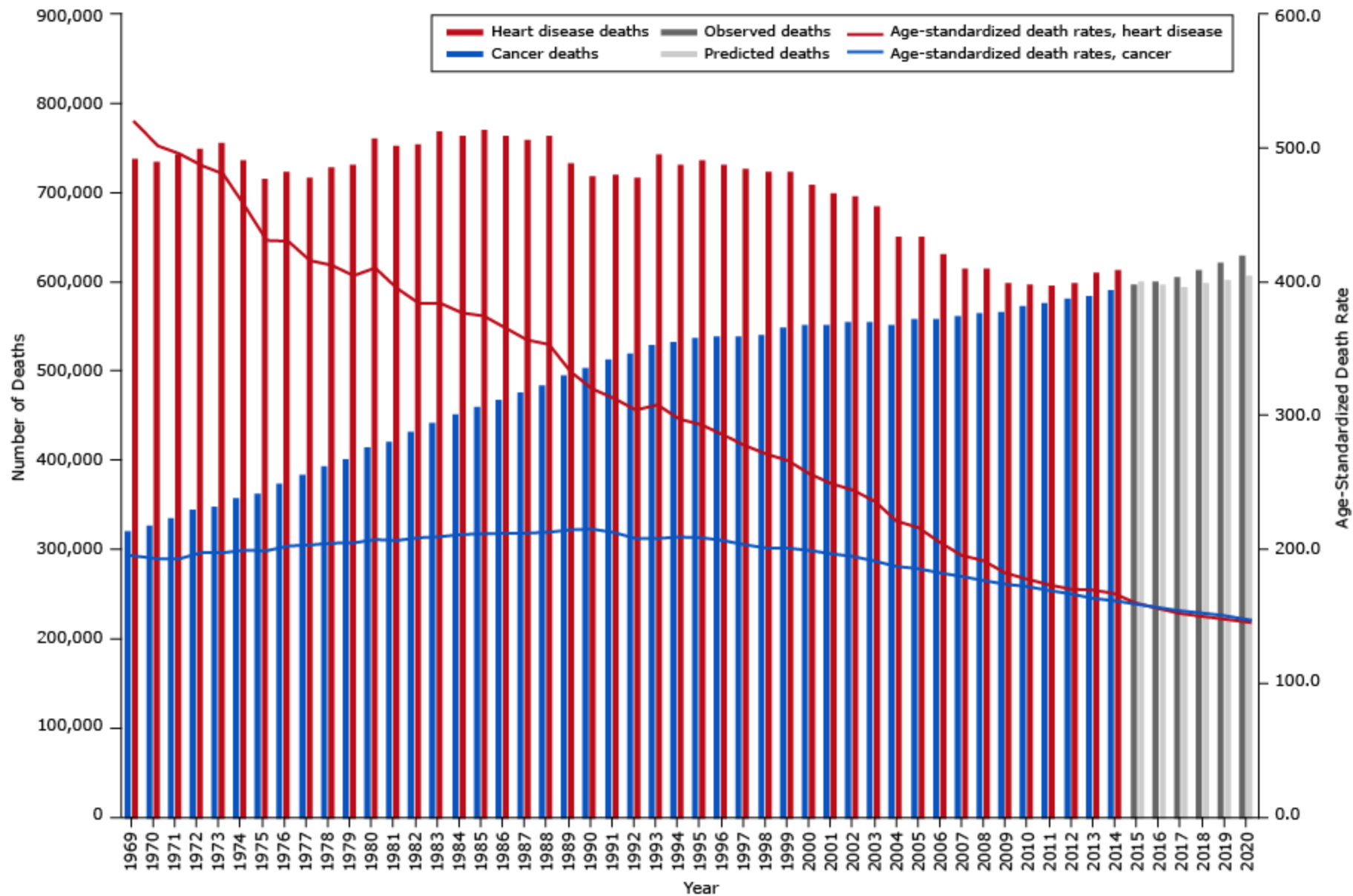


Each Patient's Cancer is Unique

- 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

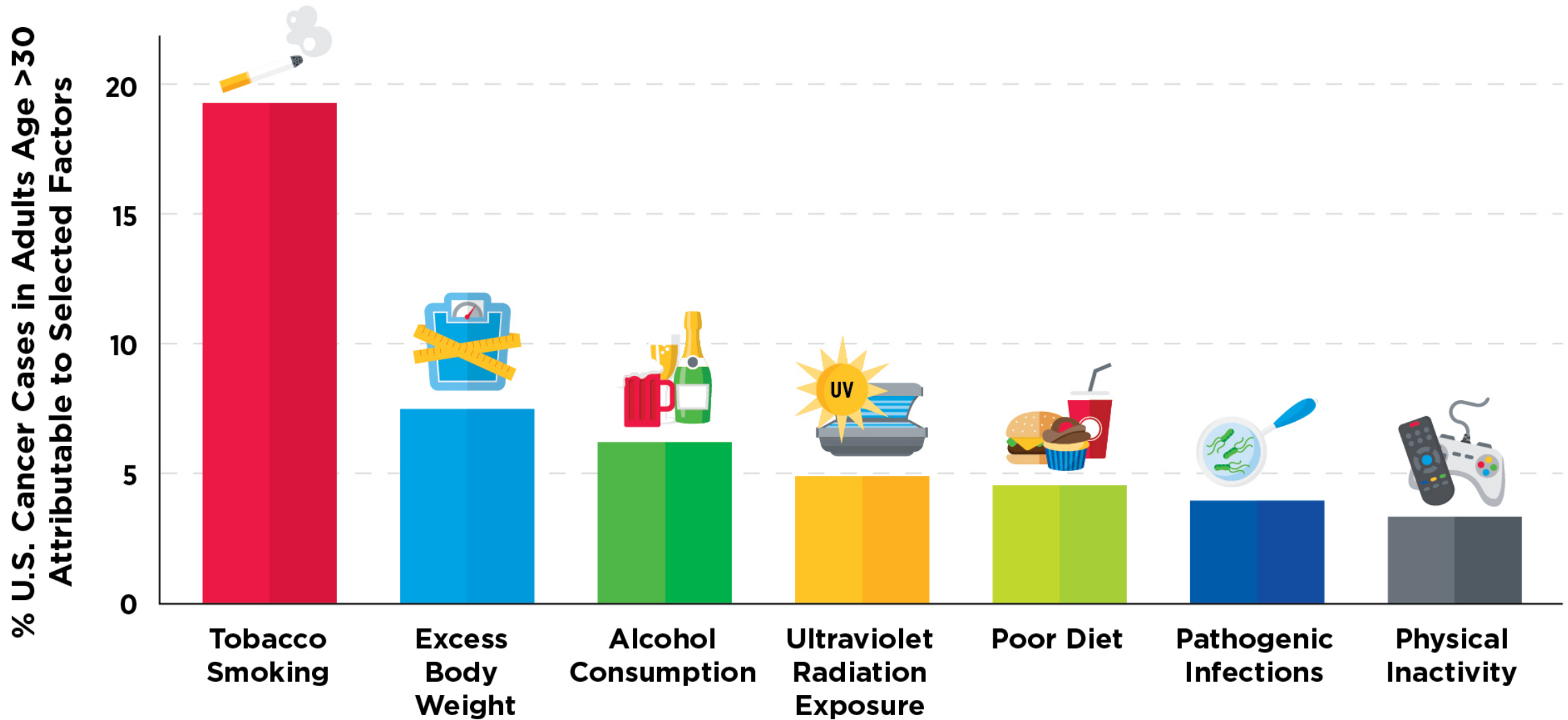
Prevention



Cancer Risk Factors

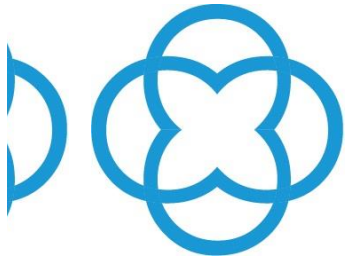
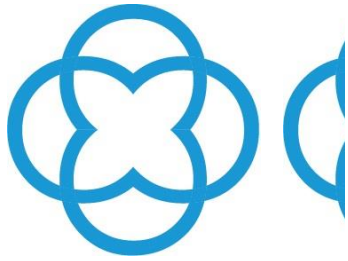
Tobacco	20%
Obesity	20%
Sedentary life-style	5%
Infections	5%
Occupational factors	5%
Familial cancer	5 - 10%
Alcohol	3%
Reproductive factors	3%
Environmental pollution	2%
Age	?
Racial and educational disparity	?

Modifiable Cancer Risks



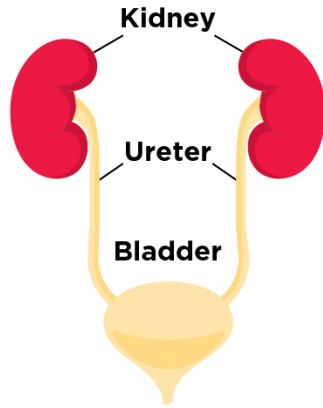
Eliminate Tobacco

- 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

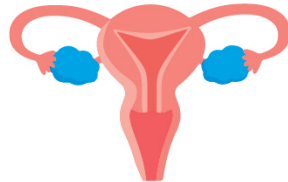


Beyond the Lungs: Cancers Caused by Smoking Tobacco

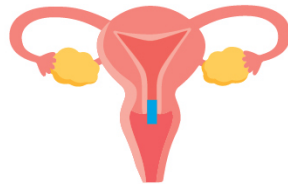
UROGENITAL SYSTEM



Ovary*



Uterine Cervix



*Certain subtypes of ovarian cancer

HEAD AND NECK



Nasal Cavity



Nasopharynx



Oral Cavity



Oropharynx



Hypopharynx



Larynx

DIGESTIVE SYSTEM

Esophagus



Stomach

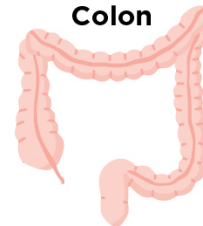
Liver



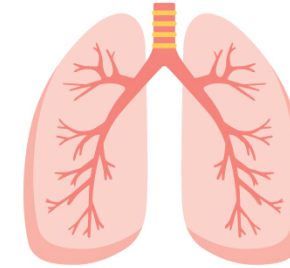
Pancreas



Colon

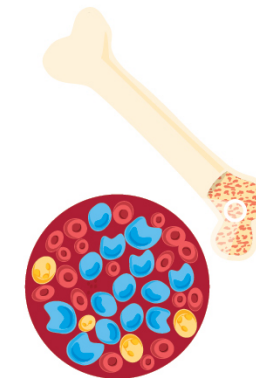


LUNG AND BRONCHUS



HEMATOPOIETIC SYSTEM

Acute Myeloid Leukemia



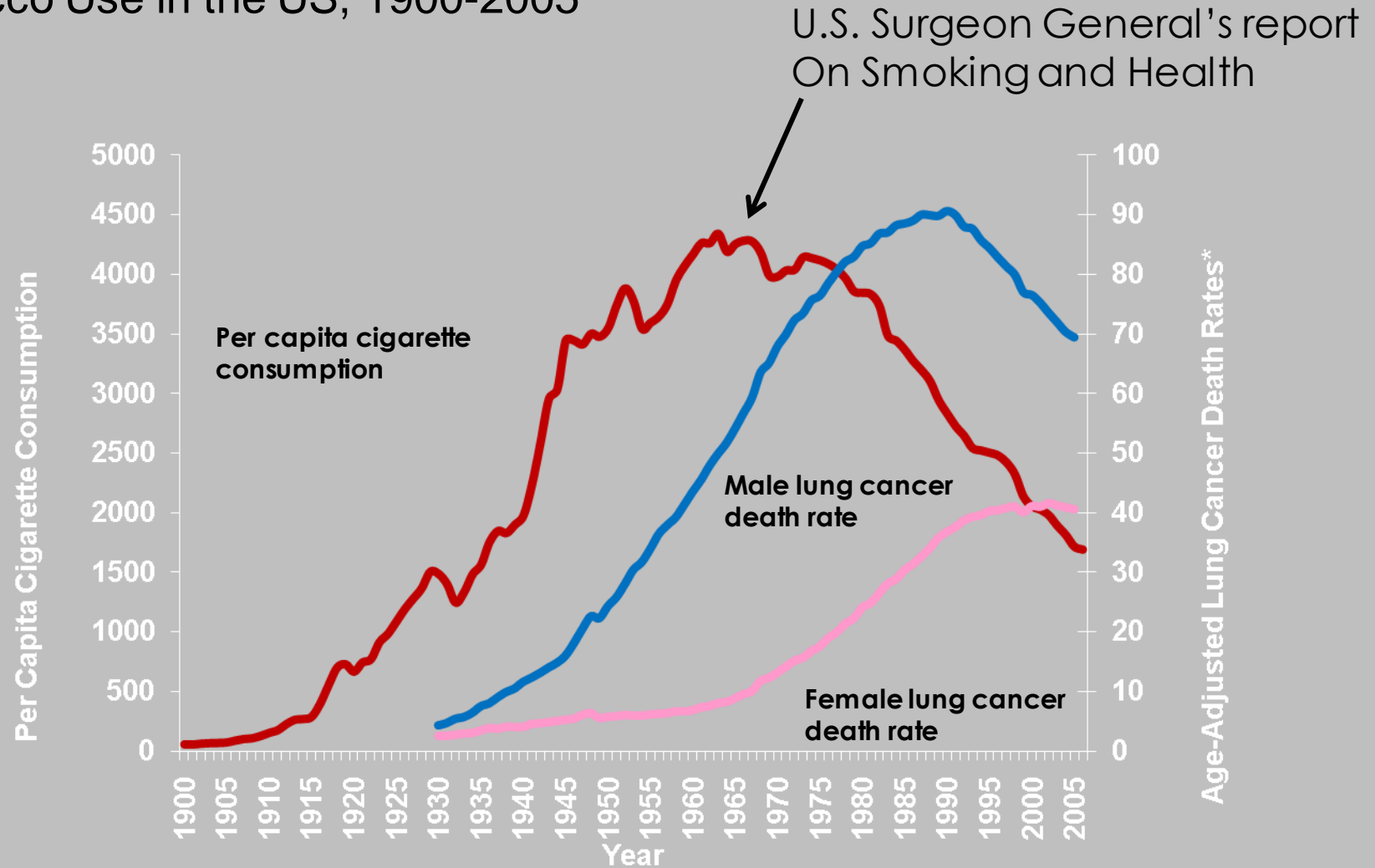
1965
42%



**Cigarette
Smoking
Rates Among
U.S. Adults**

11.5%
2021

Tobacco Use in the US, 1900-2005



*Age-adjusted to 2000 US standard population.

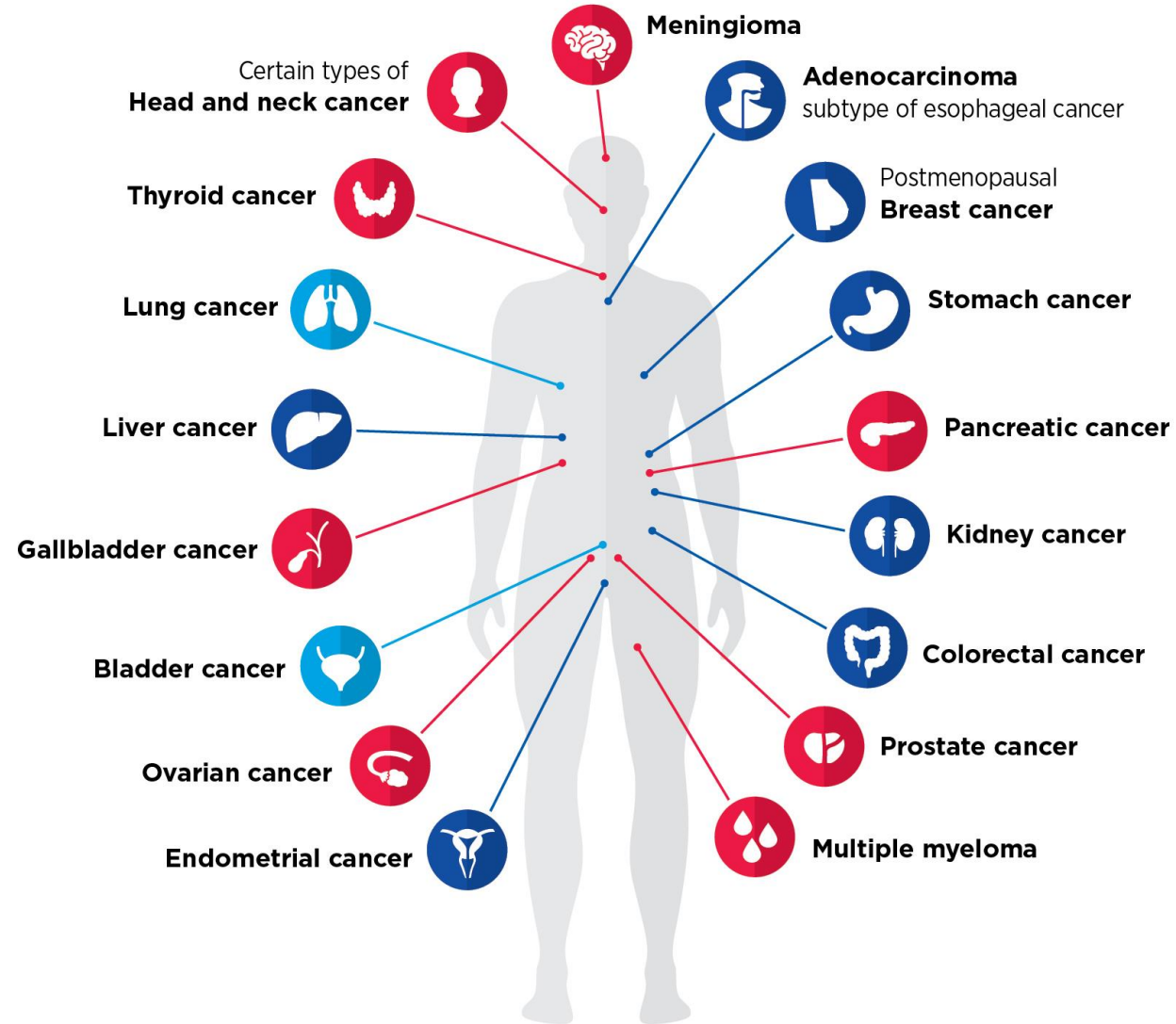
Source: Death rates: US Mortality Data, 1960-2005, US Mortality Volumes, 1930-1959, National Center for Health Statistics, Centers for Disease Control and Prevention, 2006. Cigarette consumption: US Department of Agriculture, 1900-2007.

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**



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.

	 PRE-SCHOOL AGED CHILDREN (3-5 years)	 PREGNANT WOMEN	 ADOLESCENTS (Under 18 years)	 ADULTS (18-64 years)	 OLDER ADULTS (65+ years)
Should be encouraged to move and engage in active play at all levels of intensity throughout the day.	AEROBIC ACTIVITY				
	150 minutes per week	60 minutes per day	150 minutes moderate intensity per week or 75 minutes vigorous intensity per week		
	STRENGTH TRAINING				
	2 days per week	3 days per week	2+ days per week	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

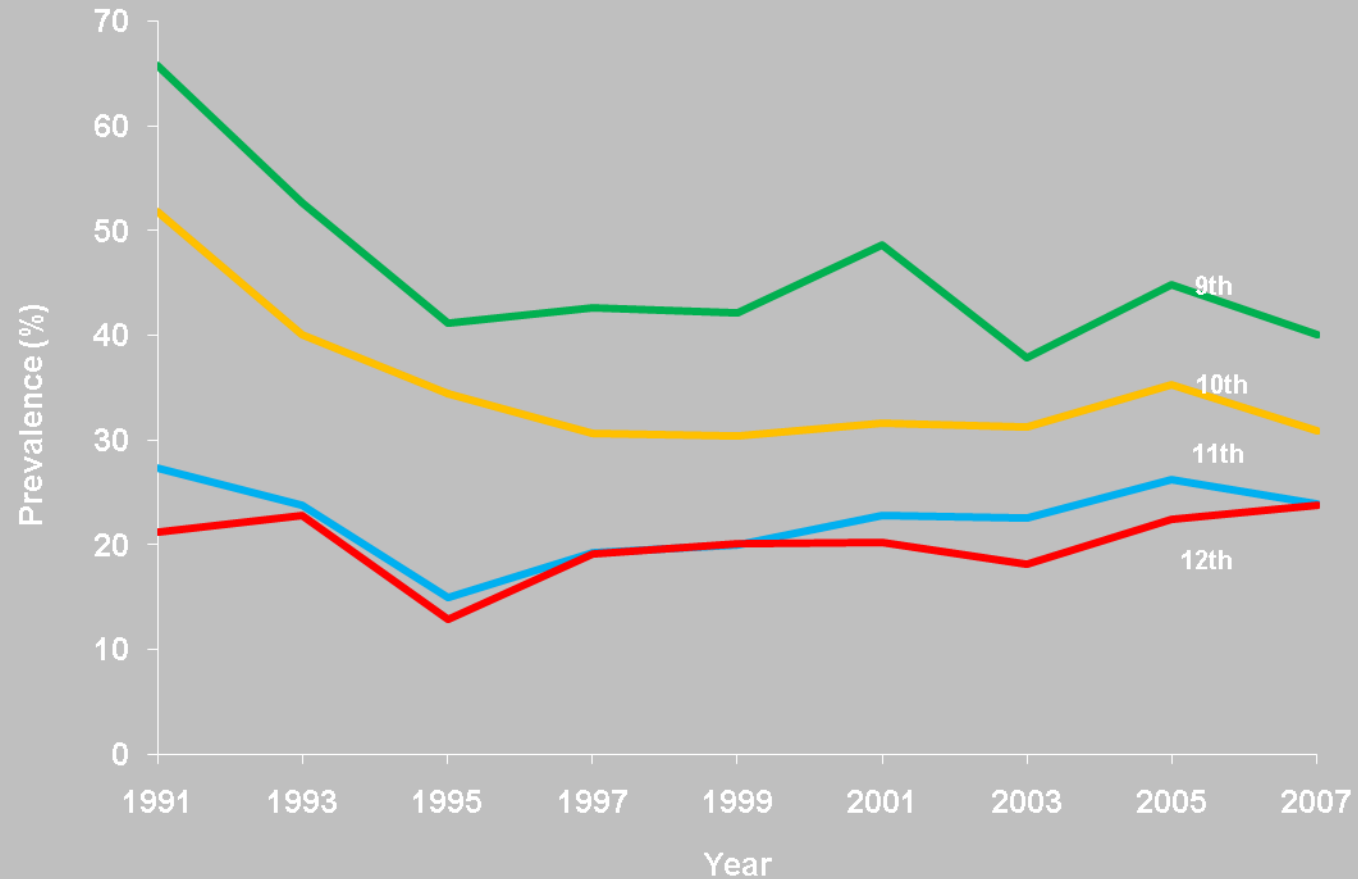
Includes activities which work muscles and core by doing repetitions or sets of movements, such as:



- 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.

Trends in Prevalence (%) of High School Students Attending PE Class Daily, by Grade, US, 1991-2007



Source: **Source: Youth Risk Behavior Surveillance System, 1991, 1995, 1997, 1999, 2001, 2003, 2005, 2007 National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, 2008.**

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
 - Processed foods
 - No fresh fruits or vegetables
 - 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
 - Head and neck cancer
 - Esophageal squamous cell carcinoma
 - Breast
 - Colorectal
 - Liver
 - Stomach cancers

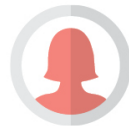
Guidelines for Alcohol Consumption

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

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

Excessive alcohol consumption

Includes **binge drinking**, **heavy drinking**, and **any drinking** by **pregnant women** or those **under 21** years of age.

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)



Protect Skin from UV Exposure

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**.



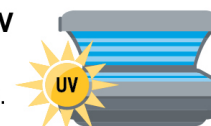
Wear **wrap-around sunglasses**.



Apply the recommended amount of a **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

- EBV
 - HD, NHL, stomach, H&N
- HBV/HCV
 - HCC
- H.Pylori
 - Stomach cancer
- HIV
 - NHL, Kaposi's
- HPV
 - Cervical, anogenital, H&N

SECTION IV

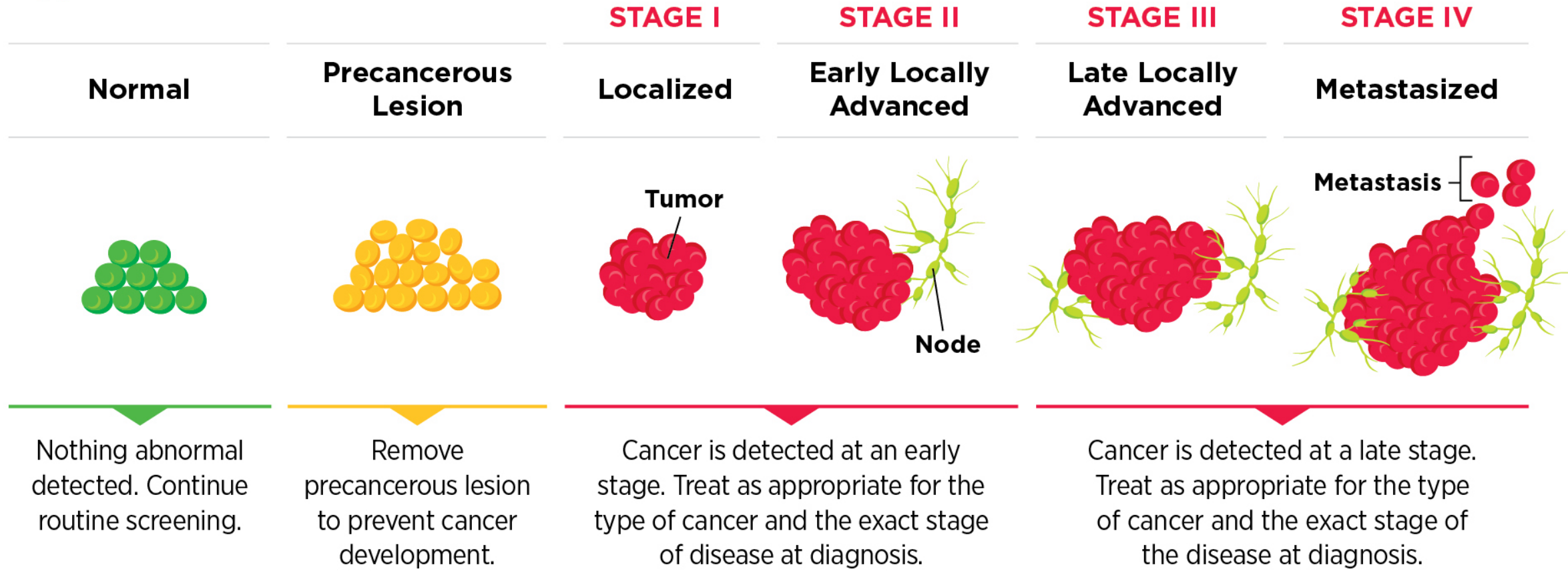
Screening

What Can Cancer Screening Find and What Can Be Done?

INCREASING TIME AND NUMBER OF MUTATIONS



TIME



Lifetime Probability of Developing Cancer, Men, 2003-2005*

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

* 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.

Source: DevCan: Probability of Developing or Dying of Cancer Software, Version 6.3.0 Statistical Research and Applications Branch, NCI, 2008. <http://srab.cancer.gov/devcan>

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

Site	Risk
All sites†	1 in 3
Breast	1 in 8
Lung & bronchus	1 in 16
Colon & rectum	1 in 20
Uterine corpus	1 in 40
Non-Hodgkin lymphoma	1 in 53
Urinary bladder‡	1 in 84
Melanoma§	1 in 58
Ovary	1 in 72
Pancreas	1 in 75
Uterine cervix	1 in 145

* 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.

Source: DevCan: Probability of Developing or Dying of Cancer Software, Version 6.3.0 Statistical Research and Applications Branch, NCI, 2008. <http://srab.cancer.gov/devcan>

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.

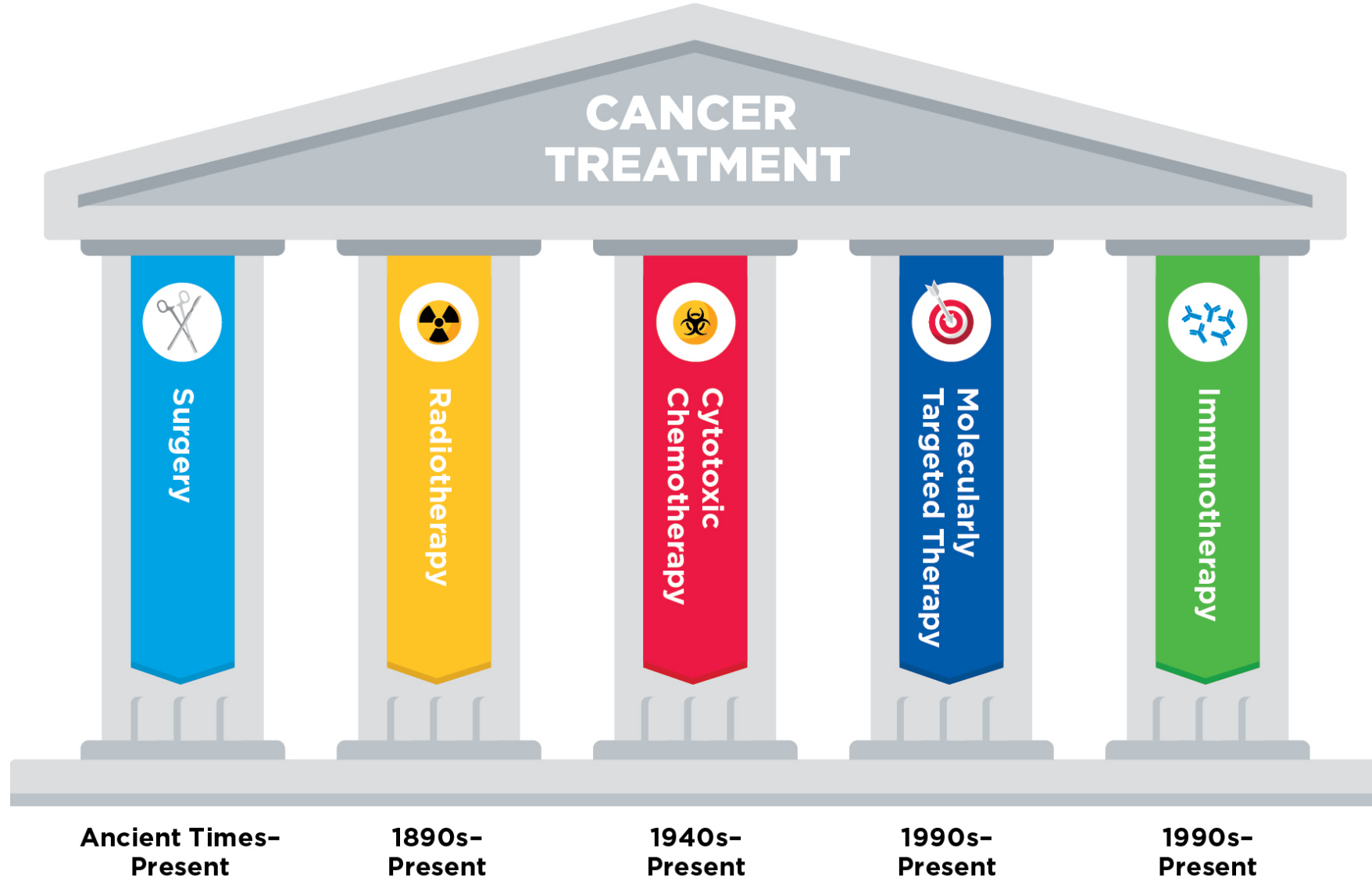
New Frontiers in Cancer Screening

- Artificial Intelligence for Early Detection of Cancers
 - AI-assisted colonoscopy detected 21 percent more polyps
 - AI-driven medical devices
 - ProstatID and SKOUT improved detection of prostate cancer using MRI
- Moving Toward Minimally Invasive Cancer Screening
 - Liquid biopsy for Multi-Cancer Early Detection (MCED) test
 - Possibility of screening for many cancer types simultaneously and potentially with high specificity
 - Promising
 - Too early to tell

SECTION V

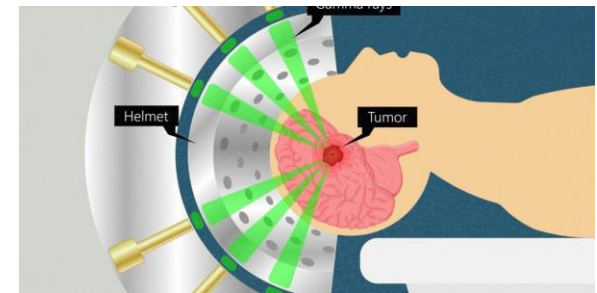
TREATMENT

The Pillars of Cancer Treatment



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

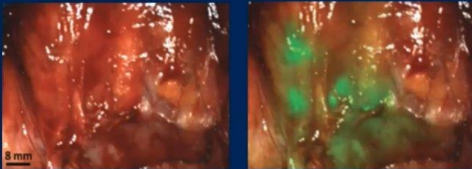
- Visualizing Lung and Ovarian Cancers More Precisely During Surgery
 - In December 2022, the FDA approved pafolacianine (Cytalux)
 - A folate receptor–targeted fluorescent agent
 - A targeted molecular imaging agent
 - It illuminates lung cancers and enhances surgeons' ability to see cancer in real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

Pafolacianine Sodium Injection (OTL38)¹
fluorescence imaging agent leveraging tumor-specific overexpression of folate receptor alpha in ovarian cancer^{2,3}

Folic acid analog conjugated to indole cyanine green-like dye

Internalized by FR expressing cells (97% of ovarian cancers²)

Visualized with near-infrared imaging system



EleVision™ IR (Medtronic)

Spectrum® (Quest Medical Imaging)

1. Pafolacianine sodium injection (OTL38) is an investigational product. It is not approved in any country of the world for any use or indication.
2. Hoogstraal CE, et al. Clin Cancer Res. 2016; Apr 15;22(12):2929-38. 3. Markert S, et al. Anticancer Res. 2008 Nov Dec;28(12A):2657-72.

Presented By: **Janos L. Tanyi, MD, PhD** #ASCO21 Content of this presentation is the property of the author, licensed by ASCO. Permission required for reuse.

2021 ASCO ANNUAL MEETING

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

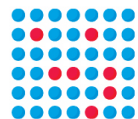
- BRAF targeting
 - Melanoma
 - Colon cancer
 - Brain tumors
- HER2 targeting
 - Breast cancer
 - Colon cancer
 - Gastric cancer
- Antibody drug conjugate
 - Trastuzumab Dxd
 - Sacituzumab Dxd
- MSI high
 - Immunotherapy

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.

5K-10K
compounds



5-10 years

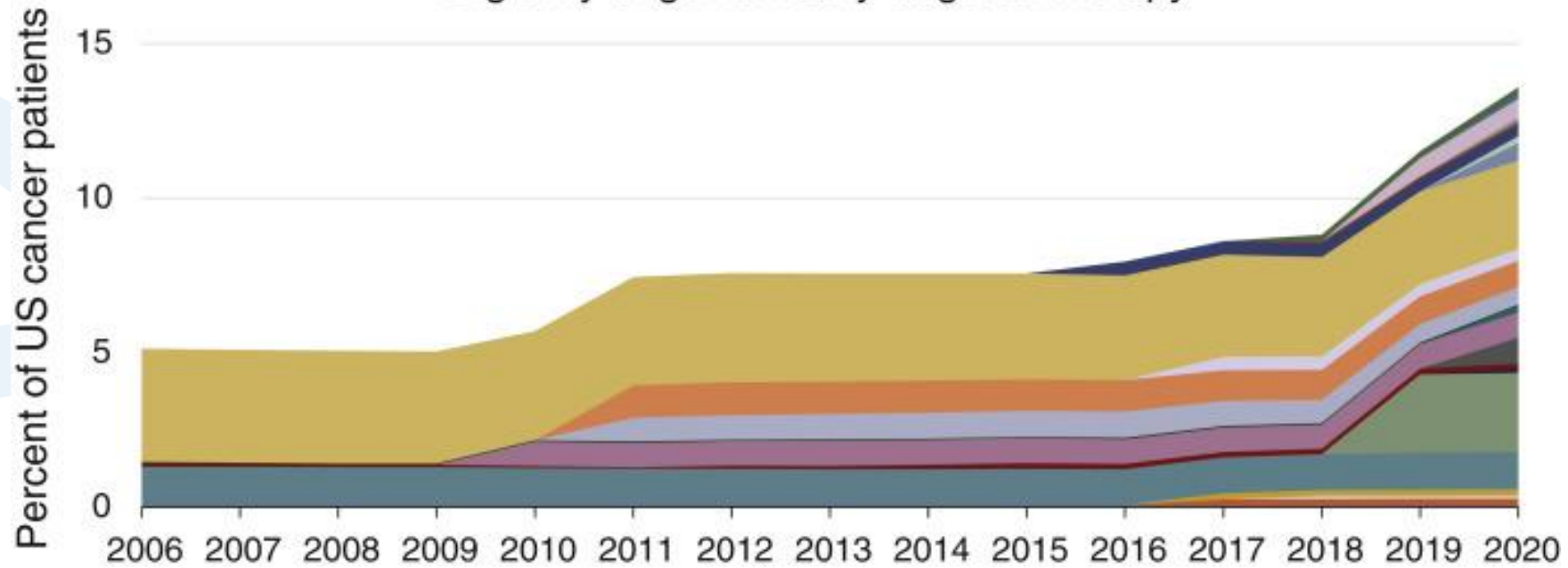


1-5
compounds

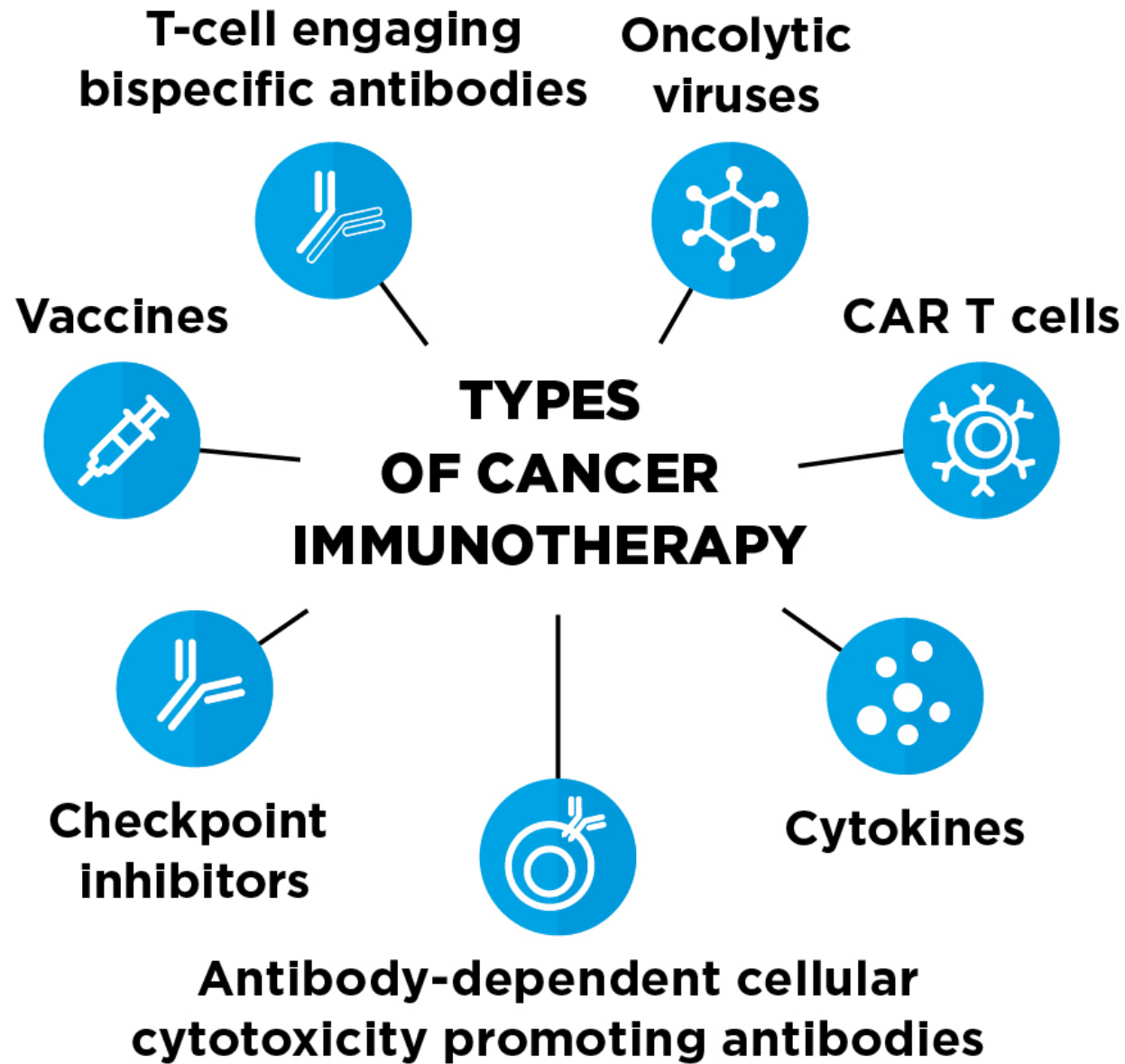
Molecularly based drug design

- 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

Eligibility of genomically targeted therapy

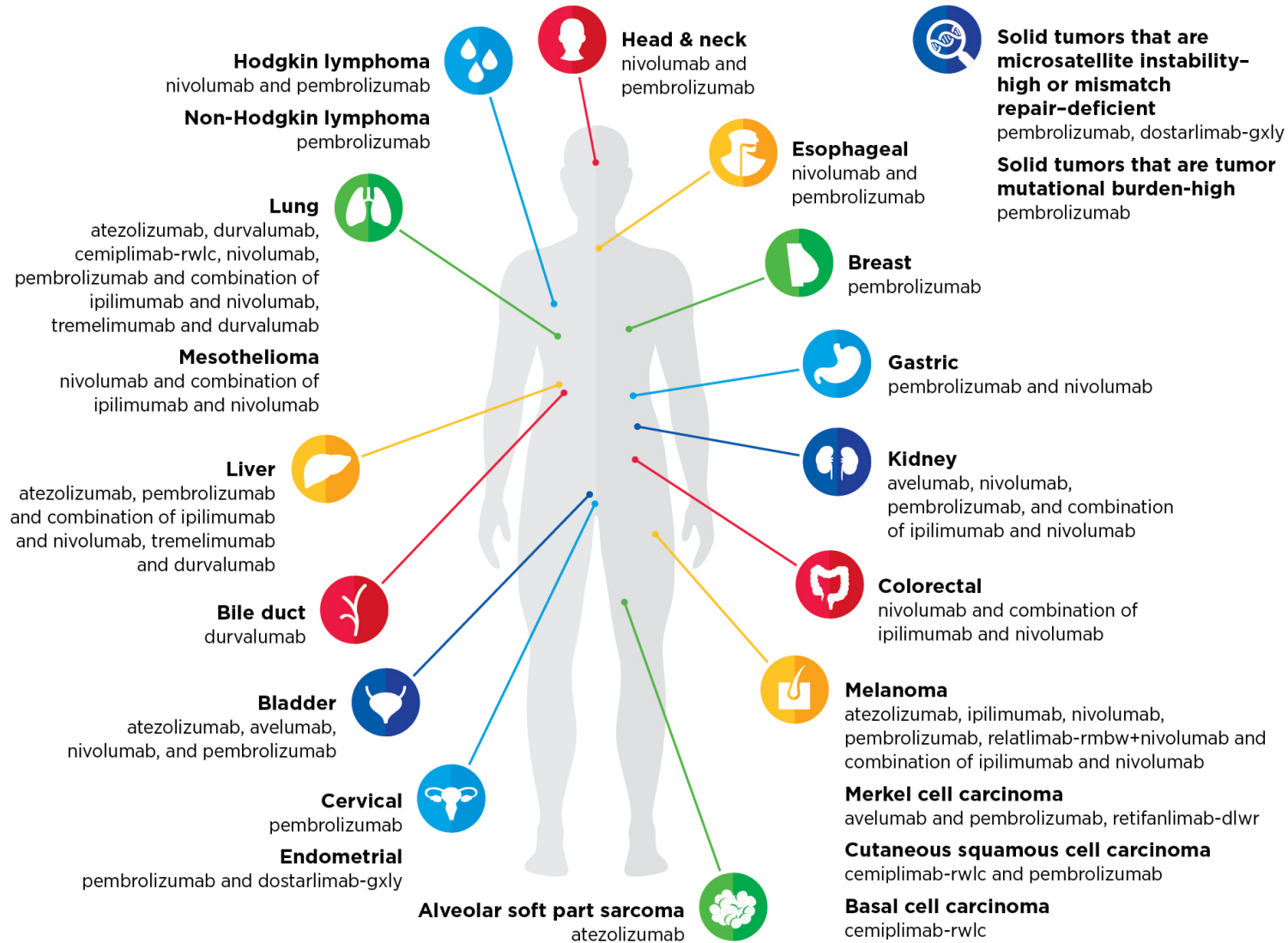


- ALL *Ph+*
- AML *IDH1*
- Breast *HER2*
- Cholangiocarcinoma *FGFR2*
- CRC *BRAF*
- Gastric *PDGFRA*
- Melanoma *BRAF V600*
- NSCLC *BRAF*
- NSCLC *MET*
- NSCLC *ROS1*
- Thyroid *RET*
- Follicular *EZH2*
- Hypereosinophilic syndrome *FIP1L1-PDGFR α*
- AML *FLT3*
- AML *IDH2*
- Breast *PIK3CA*
- CML *Ph+*
- Gastric *HER2*
- GIST
- NSCLC *ALK*
- NSCLC *EGFR*
- NSCLC *RET*
- Thyroid *BRAF*
- Urothelial *FGFR*
- Solid tumors *MSI/MMR*

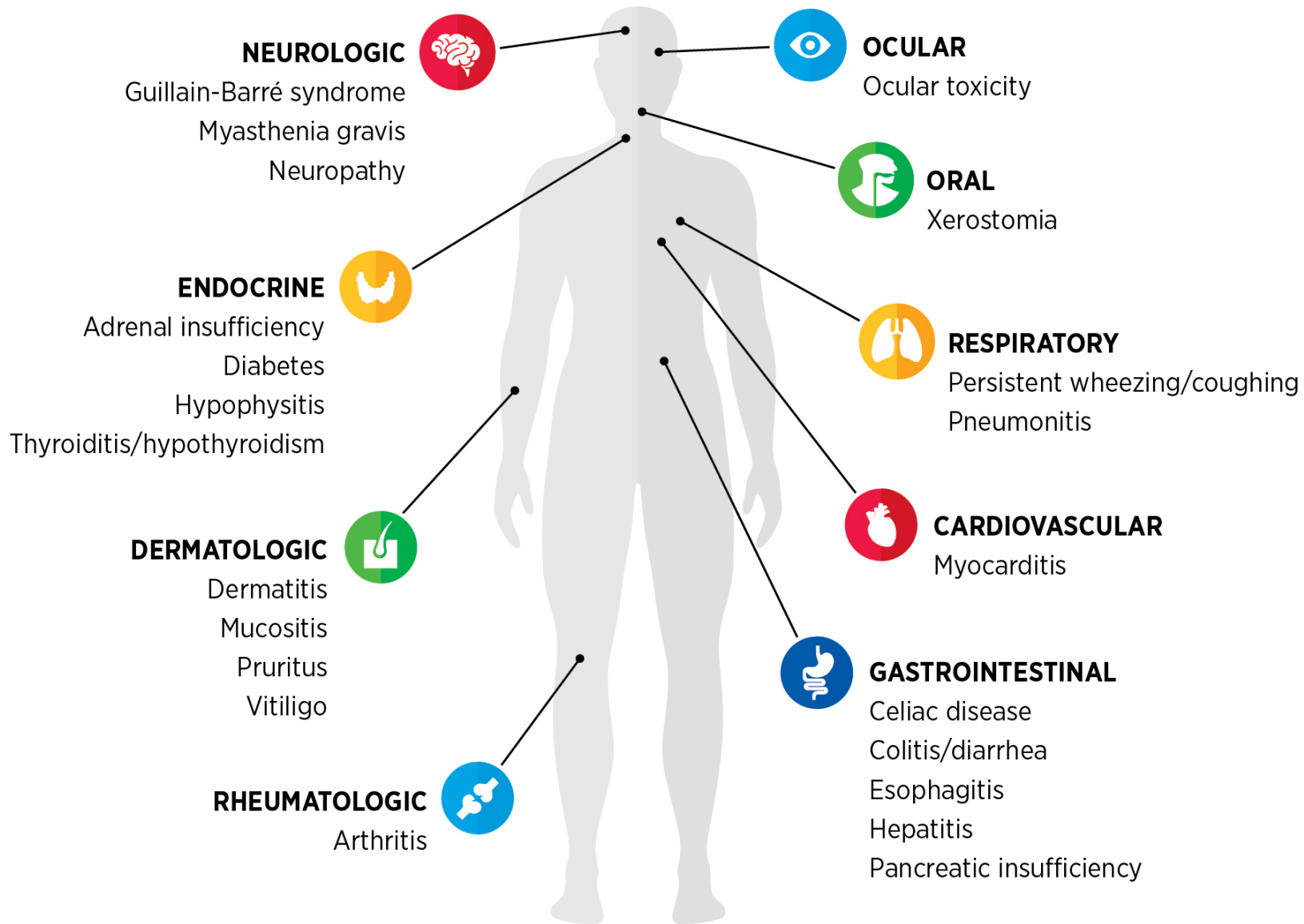


Going Deep with Immune Checkpoint Inhibitors

FDA-APPROVED AS OF 2023



Common Side Effects of Immune Checkpoint Inhibitors



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
 - Minorities
 - Under/uninsured
 - 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
 - Every patient is unique
 - 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**

Every cancer is unique

