

# Cancer in Primary Care

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## Disclosure

I have no financial interests or relationships to disclose.

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## CANCER IN PRIMARY CARE

- A. The war on cancer
- B. Cancer screening
- C. Cancer prevention
- D. Cancer survivorship

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## WAR ON CANCER

President Richard Nixon signs the National Cancer Act on December 23, 1971



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## WAR ON CANCER

President Joe Biden announces Cancer Moonshot on February 3, 2022



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## BURDEN OF DISEASE: PRE-COVID19

Morbidity and mortality

<i>Disease</i>	<i>World</i>	<i>High-income</i>
Circulatory	1	1
Infections	2	6
Mental, behavioral	3	3
Neonatal	4	7
<b>Cancers</b>	<b>5</b>	<b>2</b>
Musculoskeletal	6	4
Injuries	7	5

IMHE, Seattle, 10/20

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## PEOPLE WITH CANCER, 2024

*US: excluding non-melanoma skin cancer*

2,001,140 people newly diagnosed (2024 est.)

35% diagnosed less than 5 years ago

17,113,494 people living with cancer (2023 est.)

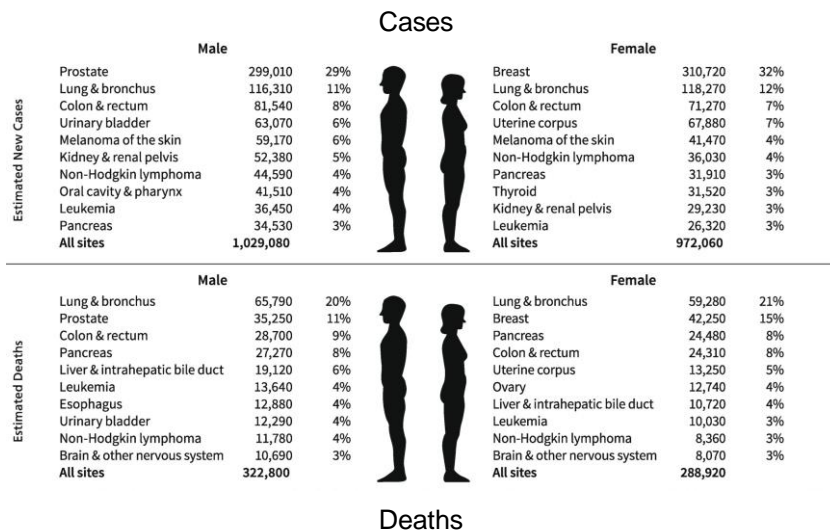
5-year survival: **70%** (was **50%** in 1975)

611,720 people die from cancer (2024 est.)

ACS, SEER

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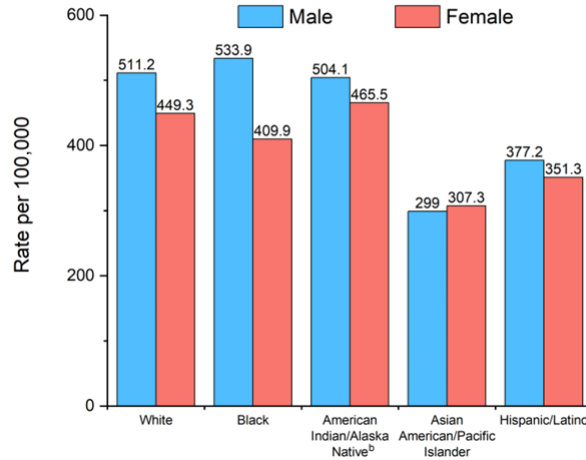
## CANCER, DIAGNOSES AND DEATHS, 2024



ACS

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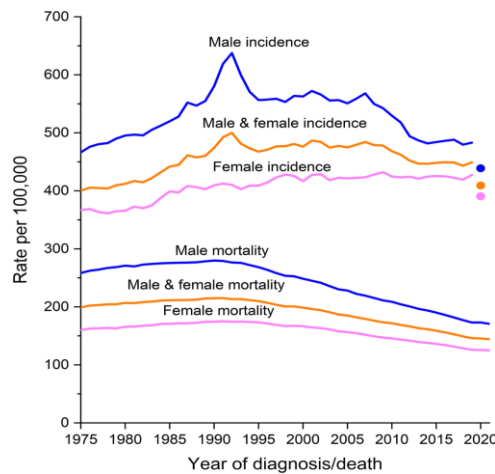
## CANCER INCIDENCE IN DIFFERENT GROUPS



ACS, SEER

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## CANCER INCIDENCE SINCE 1975



CA Journal, 1/2024

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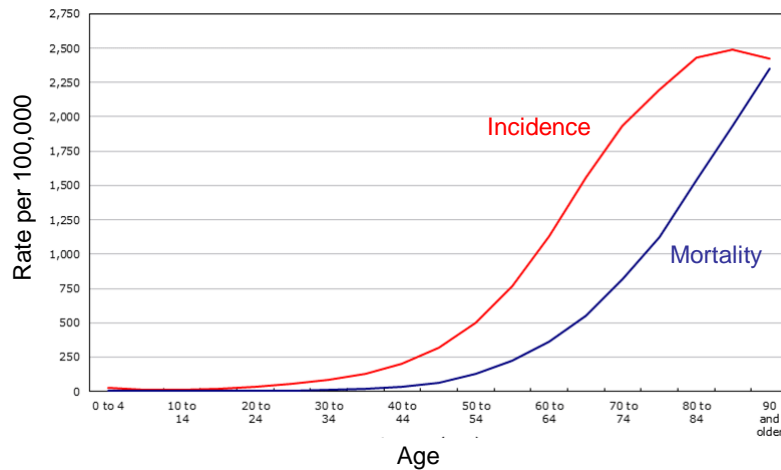
## CANCER 5-YEAR SURVIVAL SINCE 1975

Site	1975-77	1995-97	2013-2019
All sites	49	63	69
Breast (female)	75	87	91
Colon & rectum	50	61	64
Leukemia	34	48	67
Liver & intrahepatic bile duct	3	7	22
Lung & bronchus	12	15	25
Melanoma of the skin	82	91	94
Non-Hodgkin lymphoma	47	56	74
Ovary	36	43	51
Pancreas	3	4	13
Prostate	68	97	97
Uterine cervix	69	73	67
Uterine corpus	87	84	81

ACS/SEER

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## AGE AND CANCER



***Cancer Is a Disease of Older People***

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## LIFETIME PROBABILITY FOR CANCER

(Excluding non-melanoma skin cancer)

### Males

Site	Risk
All sites*	1 in 3
Prostate	1 in 9
Lung & bronchus	1 in 15
Colon & rectum	1 in 23
Urinary bladder†	1 in 27
Melanoma of the skin‡	1 in 27
Non-Hodgkin lymphoma	1 in 42
Kidney & renal pelvis	1 in 47
Leukemia	1 in 56
Oral cavity & pharynx	1 in 61
Pancreas	1 in 62

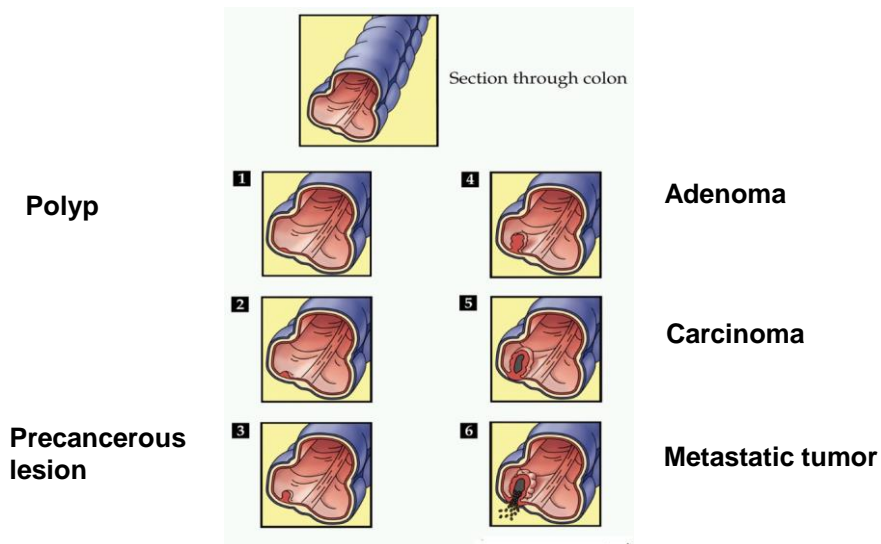
### Females

Site	Risk
All sites*	1 in 3
Breast	1 in 8
Lung & bronchus	1 in 17
Colon & rectum	1 in 25
Uterine corpus	1 in 35
Melanoma of the skin‡	1 in 40
Non-Hodgkin lymphoma	1 in 54
Thyroid	1 in 55
Pancreas	1 in 65
Ovary	1 in 79
Leukemia	1 in 80

- Incidence about **40%**
- Risk of dying from cancer: **25%**

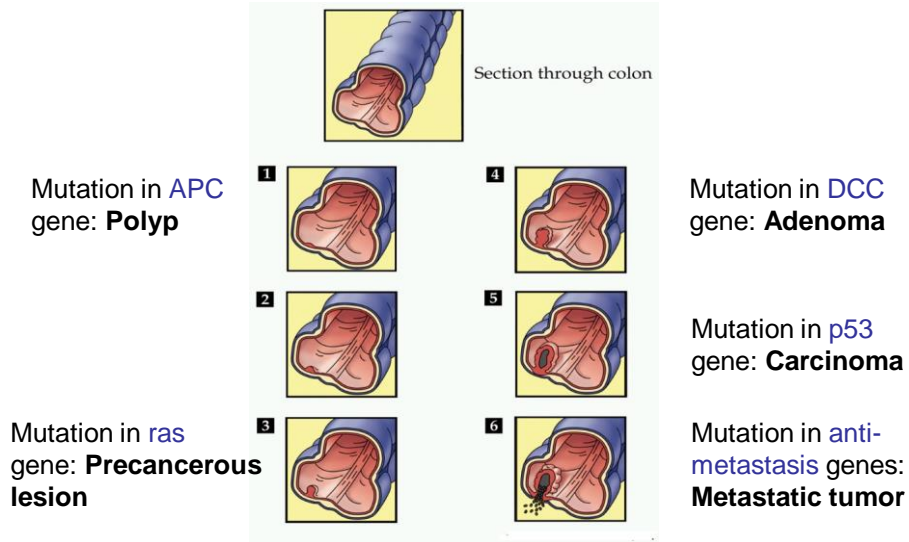
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## AGE AND CANCER: MOLEC. BIOGRAPHY



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## AGE AND CANCER: MOLEC. BIOGRAPHY

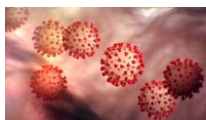


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## IMPACT OF COVID19 PANDEMIC ON CANCER

COVID19 Pandemic	Early Detection	Diagnosis	Treatment
<i>Reduced access to care</i>	<i>Delayed screening</i>	<i>Later stage diagnosis</i>	<i>Delayed treatment</i>

2020: 17% fewer breast cancer patients diagnosed



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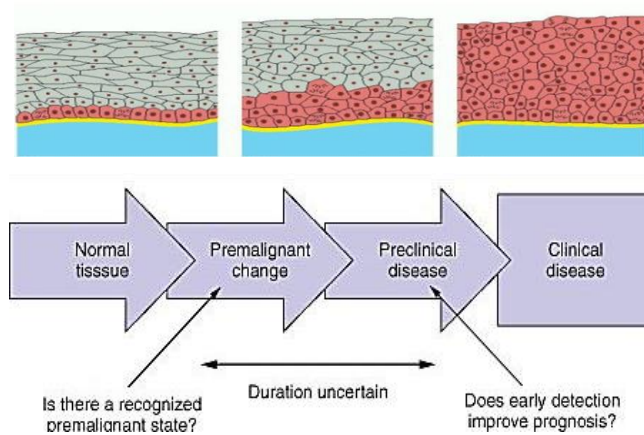


## CANCER IN PRIMARY CARE

- A. The war on cancer
- B. Cancer screening**
- C. Cancer prevention
- D. Cancer survivorship

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## THE LOGIC OF SCREENING



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## THE LOGIC OF SCREENING

**Benefit:** Reduced mortality

**Costs:** Expense  
Morbidity  
Acceptability

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## HOW GOOD IS A SCREENING TEST?

**Reliability:** Repeatable with same result.

**Validity:** Is the test an indicator of disease?

**Sensitivity:** Proportion of people *with* the disease who test positive

*False negative: burden on patient*

**Specificity:** Proportion of people *without* the disease who test negative

*False positive: burden on providers*

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## CANCER SCREENING IN PRIMARY CARE

*Screening tests detect disease before it is harmful:*

*Success: A good test widely applied*

- Cervical cancer screening is **very successful**
- Breast cancer screening is **successful**
- Colon cancer screening is **successful**
- Prostate cancer screening is **partially successful**
- Lung cancer screening is **partially successful**

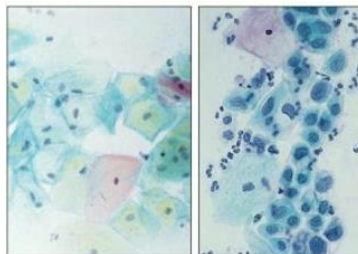
**Endpoint issue: Does detection result in improved survival?**

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## CERVICAL CANCER SCREENING: PAP SMEAR



G. Papanicolaou  
1928-1943



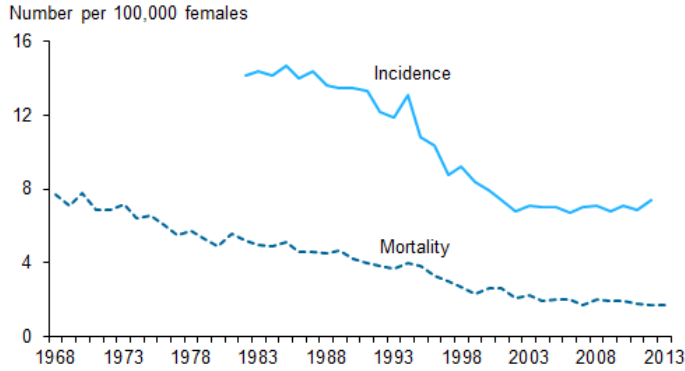
Normal

Precancerous

*This test is being replaced with HPV DNA testing of the cervical sample*

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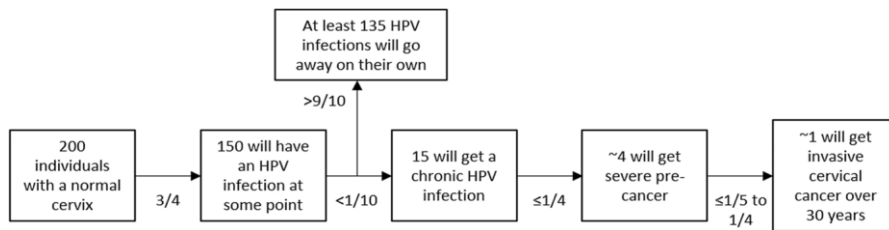
## CERVICAL CANCER USA



Over lifetime, with no screening incidence is **5%**  
with screening, incidence is **0.5%**

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## CERVICAL CANCER AND HPV



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## USPSTF:US PREVENTIVE SERVICES TASK FORCE, 2024

Michael Barry, MD (outcomes) Chair

Wanda Nicholson, MD (perinatal)  
 Esa Davis, MD, MPH (perinatal)  
 Tumaini Coker, MD (pediatrics)  
 Gbenga Obedegbe, MD (health disp.)  
 Gotham Rao, MD (cardiovascular)  
 Carlos Jaen, MD, MPH (family med)  
 Joel Tsevat, MD, MPH (quality of life)  
 John Wong, MD, MPH (primary care)

David Chelmow, MD (obgyn)  
 Katrina Donohue, MD (family med)  
 Li Li, MD, MPH (population health)  
 Lori Pbert, PhD (prevention)  
 Michael Silverstein (pediatrics)  
 James Stevermer, MD, MPH (prev)  
 Sandra Underwood, RN, PhD (health disp)  
 John Ruiz, PhD (psychology)

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## CERVICAL CANCER SCREENING: USPSTF 2018

Population	Recommendation	Evidence for screening
< 21 years	No screening	D
21-29 years	Cyt. every 3 years	A
30-65 years	Cyt. every 5 years or HPV every 5 years	A
>65 years	No screening	D
Hysterectomy with no prior lesion	No screening	D

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## CERVICAL CANCER SCREENING: PRIMARY CARE ISSUES

<b>&lt; 21 years</b>	<b>No screening</b>
----------------------	---------------------

*Primary care surveys: 19 % (2 million) females age 15-20 annual Pap smear  
Mostly unnecessary*

<b>30-65 years</b>	<b>Cyt. every 5 years or HPV every 5 years</b>
--------------------	--

*Cohort study of cyt .vs. HPV: HPV testing is 2x more sensitive in detecting neoplasia (2018)*

**>65 years      No screening**

*California study (2023): 17% of cervical cancer diagnoses were in women >65; generally advanced disease with poor outcome.  
Why stop screening?*

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## CERVICAL CANCER SCREENING: ACS 2023

Population	Recommendation	Evidence for screening
< 25 years	No screening	D
25-65 years	HPV every 5 years	A
25-65 years	Cyt. every 3 years with HPV every 5 years	A
>65 years	No screening	D
Hysterectomy with no prior lesion	No screening	D

Transition from cytology to HPV  
Issue: Local availability of HPV testing vs cytology

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## BREAST CANCER SCREENING

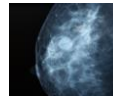
- Breast self-examination



- Clinical breast exam

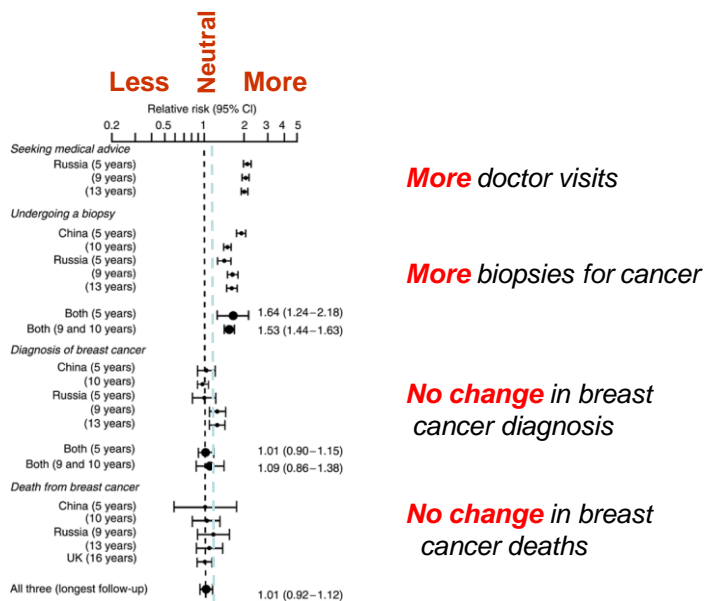


- Mammogram



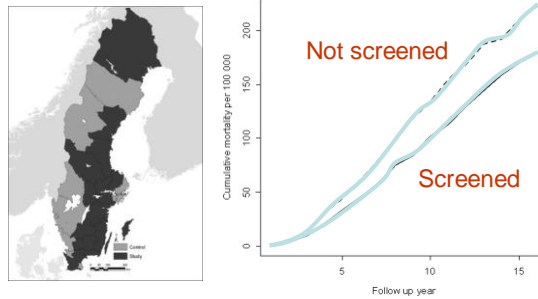
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## BREAST CANCER SCREENING: SELF EXAM



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## MAMMOGRAPHY SCREENING SWEDEN: 1986-2005



Reduction in deaths in screened group

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## BREAST CANCER SCREENING RECOMMENDATION 2024 USPSTF

<i>Population</i>	<i>Recommendation for mammography</i>	<i>Evidence for screening</i>
< 40 years	No screening unless genetic risk	D
40-74 years	Biennial	B
>75 years	No screening	I: insufficient evidence for benefit

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## BREAST CANCER SCREENING ARTIFICIAL INTELLIGENCE

*Can AI improve radiology screening?*

40,000 women screened med. age 54 mammo. in Sweden

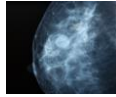
20,000 mammo. read by two radiologists

20,000 mammo. read by two radiologists **plus AI**

Results: Screening only: 203 breast cancer

Screening **plus AI**: 244 breast cancer (20% increase)

Lancet Oncol. 8/1/23



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## SCREENING FOR BREAST CANCER SUSCEPTIBILITY: MUTATIONS

*Clinical case:*

22-year-old female

Mother: breast cancer age 35

Grandmother: breast cancer age 38

*Analysis:*

DNA sequencing for 23 genes implicated in breast cancer: *ATM, BARD1, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, DICER, EPCAM, MLH1, MSH2, MSH6, NBN, NF1, PALB2, PMS2, PTEN, RAD51C, RAD51D, RECQL, SMARCA4, STK11, TP53*

- Patient: Change behavior to lower risk factors
- Physician: Advise preventive care, increase screening

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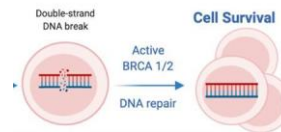
## SCREENING FOR BREAST CANCER SUSCEPTIBILITY: MUTATIONS

*Clinical case: DNA sequencing:*

Mutation in BRCA1: c211 A to G (very rare variant)

Result: aberrant splicing of pre-mRNA leading to premature stop codon and truncated, non-functional protein

BRCA1 normal role: DNA damage repair; tumor suppressor



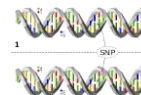
*Risk for breast cancer by age 70: 60% (normally 12%)*

*Patient may choose prophylactic mastectomy*

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## SCREENING FOR BREAST CANCER SUSCEPTIBILITY: POLYGENIC SCORE

**Polygenic risk score:** 377 SNP's in DNA



- Tested on 94K breast cancer patients and 75K controls

**Polygenic risk score**      **Breast cancer risk by age 80**

1-5%	0.05
40-60%	0.10
>99%	0.33

*For an individual with a high risk score:*

- Patient: Change behavior to lower risk factors
- Physician: Advise preventive care, increase screening

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## COLON CANCER SCREENING

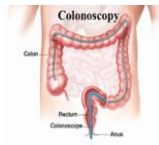
- **Fecal tests:**  
 FOBT: blood in stool  
 FIT: immuno. blood in stool  
 FIT-DNA: Tumor DNA



- **Sigmoidoscopy**  
 (distal colon)



- **Colonoscopy**



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## COLON CANCER LIVES SAVED BY SCREENING

	Screening interval age 45-75	CRC lives saved / 1000 screened
<b>FOBT</b>	Annual	26
<b>FIT</b>	Annual	26
<b>FIT-DNA</b>	Annual	26
<b>Sigmoid.</b>	5 yr	26
<b>Colonoscopy</b>	10 yr	27

USPSTF

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## COLON CANCER SCREENING

*Clinical case:* 65-year-old man

No history of bowel abnormalities

Mother died of colon cancer age 85

Declined primary care practitioner's recommendation for colonoscopy

*Test:* FIT home test positive



*Follow-up:* colonoscopy revealed multiple adenomatous polyps: removed; then chemotherapy  
DNA analysis: No germline mutations (not inherited)

*Treated* with surgery, chemotherapy

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## COLON CANCER SCREENING RECOMMENDATION 2021 USPSTF

<b><i>Population</i></b>	<b><i>Recommendation for screening</i></b>	<b><i>Evidence for screening</i></b>
45-49 years	Screening as below	B
45-75 years	<i>Stool:</i> FOBT: annual FIT: annual FIT-DNA: 1-3 yr	A
45-75 years	<i>Direct visualization:</i> Sigmoid: every 5 yr Colonoscopy: every 10 yr	A
>75 years	Selectively offer screening	C: low evidence of benefit

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## COLON CANCER SCREENING: NEW MOLECULAR TESTS

### **Multitarget stool DNA / RNA**

- Detects abnormal DNA markers in advanced colon cancer: e.g., *BMP4*, *NDRG4* methyl., *KRAS* mutation
- Sensitivity 92% for advanced, but 42% precancerous
- Specificity 80%: many false positives – follow up colonoscopy

### **Blood test circulating DNA: “liquid biopsy”**

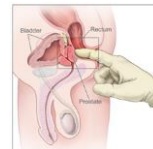
- Detects abnormal DNA methylation - 50 cancers
- Sensitivity for colon cancer: 40%, specificity >95%
- Large clinical trials underway
- Over 15 other tests underway, including sequencing

**So far, data on cancer detection but not yet on mortality**

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## PROSTATE CANCER SCREENING

- *Digital exam*: Sensitivity 51%  
Specificity 59%
- *Prostate specific antigen blood test (PSA)*  
Sensitivity 21%  
Specificity 91%  
(at 4 ng/ml)



*SEER*: 45% of prostate cancers “over-diagnosed”: would not decrease morbidity or mortality after treatment

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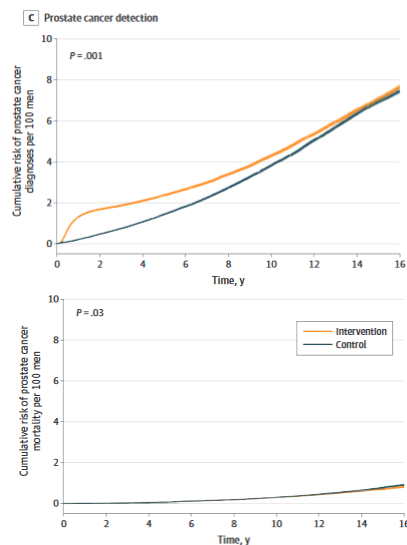
## PROSTATE CANCER SCREENING: PSA

### *The Great Prostate Mistake* RICHARD J. ABLIN

EACH year some 30 million American men undergo testing for prostate-specific antigen, an enzyme made by the prostate. Approved by the Food and Drug Administration in 1994, the P.S.A. test is the most commonly used tool for detecting prostate cancer. The test's popularity has led to a hugely expensive public health disaster. It's an issue I am painfully familiar with — I discovered P.S.A. in 1970.

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## PSA SCREENING AND PROSTATE CANCER: UK



JAMA 4/6/24

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## PROSTATE CANCER SCREENING RECOMMENDATION 2018 USPSTF

<i>Population</i>	<i>Recommendation for PSA screening</i>	<i>Evidence for screening</i>
< 55 years	No screening	D
55-69 years	Discuss: small benefit vs. harm by additional testing, over-diagnosis, treatment side effects	C
>70 years	No screening	D

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## OTHER WAYS TO SCREEN FOR PROSTATE CANCER?

- *Prostate Health Index (PHI)*: free PSA, total PSA, 2pro-PSA variant
- *MRI*: After a positive PSA screen or symptoms, MRI can detect whether prostate cancer is present: reduce need for biopsy or guide for biopsy
- *Exosomes*: Membrane-bound vesicles released from cancer cells to urine; levels of mRNA for PCA3 and two other genes correlate with aggressive PCa: reduce need for biopsy
- *MyProstateScore*: mRNA transcripts of 18 genes in urine indicate probability of aggressive tumor (Gleason >7)

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## LUNG CANCER SCREENING

5-year survival for breast cancer >90%

“ colorectal 65%

“ prostate >95%

*Screening detects cancers when localized*

“ **lung** **23%**

5-year survival for lung cancer after diagnosis:

Localized: 60% (25% of patients)

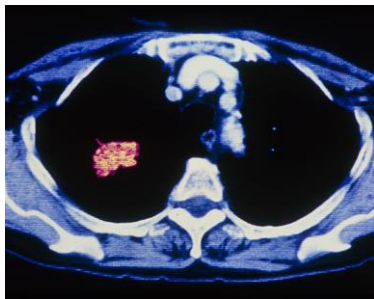
Regional: 30% (20% of patients)

Distant spread: 10% (55% of patients)

***Need test to detect localized disease***

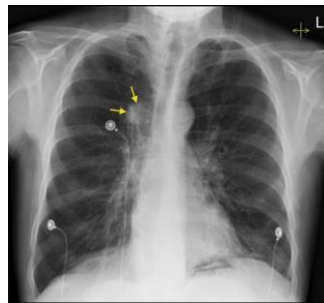
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## LUNG CANCER SCREENING



**Low-dose CT scan:**

Sensitivity 94%  
Specificity 95%



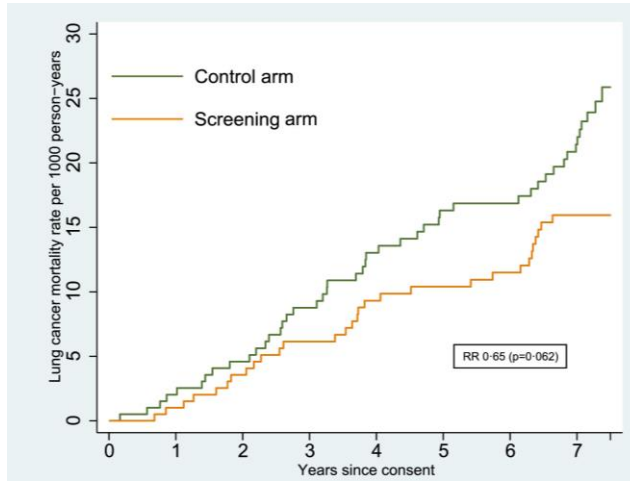
**X-ray:**

Sensitivity 73%  
Specificity 91%

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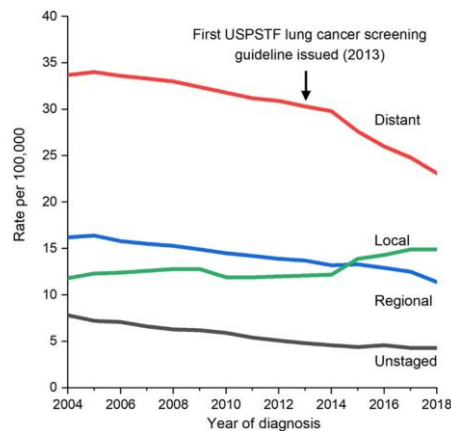
## LUNG CANCER SCREENING: MORTALITY



Lancet Regional Health Europe, 2021

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## LUNG CANCER SCREENING USA



**Only 10% participation by those eligible:  
14.5 million**

ACS, 2024

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## LUNG CANCER SCREENING RECOMMENDATION 2023 USPSTF

<i>Population</i>	<i>Recommendation for low-dose CT screening</i>	<i>Evidence for screening</i>
50-80 years	Current smokers and past smokers; annual screen	B

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## CANCER IN PRIMARY CARE

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## CAUSES OF CANCER



Nevada test site: 100 explosions, 1951-62



Filming site: St. George, Utah, downwind from Nevada test site

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## CAUSES OF CANCER



Dick Powell, dir.  
Lung cancer



Pedro Armendariz  
Kidney cancer



Susan Hayward  
Brain cancer



Agnes Moorhead  
Uterine cancer



John Hoyt  
Lung cancer

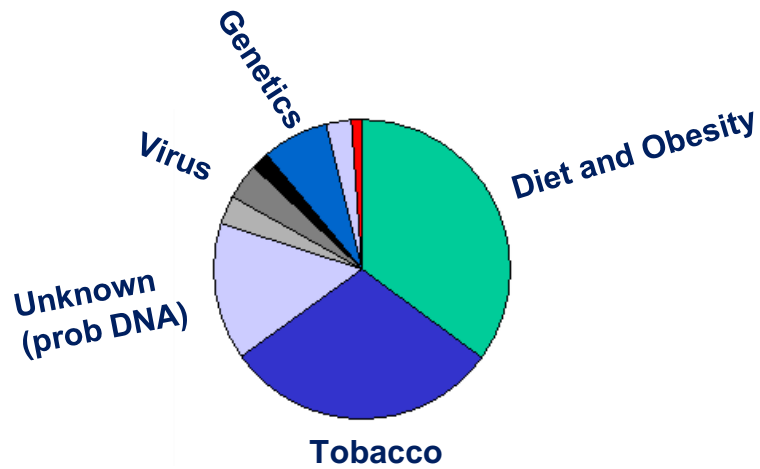


John Wayne  
Stomach cancer

Radiation cause? But they were smokers.

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## CAUSES OF CANCER



How do we know this?  
• *Epidemiology*

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## RISK ANALYSIS

***Hazard identification:*** Does it cause cancer?

***Dose response:*** How much cancer can it cause at what dose?

***Exposure assessment:*** How much of it gets into people?

***Risk characterization:*** Is the exposure worth the benefits?

*Discussions in the primary care setting*

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## CANCER PREVENTION: AVOIDING CARCINOGENS



Tobacco smoking causes 180K cancer deaths US/ yr (+ 300K from stroke, cardiovascular, lung diseases)

Tobacco smoke has over 7000 identifiable chemicals, of which 70 are known carcinogens: *not nicotine*

e.g., Benzpyrene binds to DNA, causes mutations in G bases

US Adults: 2022: 11% smokers US (2005: 21% and 1965: 42%)

- more smokers among those with less education, less income

Role of primary care physicians: **prevent** (adolescents); **stop** (adults)

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## CANCER PREVENTION: SMOKING: ADULTS



Method	Effectiveness: reduction after 1 year
None (self)	0.1%
Physician counseling	5%
Nicotine patch, gum, inhaler	10-16%
Bupropion (Wellbutrin)	15-23%
Varenicline (Chantix)	23-30%

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## CANCER PREVENTION: TOBACCO SMOKING: ADOLESCENTS



90% of smokers began before age 21

2% of middle school students smoke tobacco non-electronic  
*down from 4% 10 years ago*

5% of high school students smoke tobacco non-electronic  
*down from 16% 10 years ago*

USPSTF: recommend **counseling by primary care physicians for adolescents who have not begun smoking** (B evidence)

Public health: *ads: what works: conspiracies*  
*laws to make smoking an "outlaw activity"*

CDC

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## CANCER PREVENTION: VAPING



Many flavors: pods; online purchase

2023: 18% age 18-24 vaping

Most flavored vapes no longer sold

Must be 18 to purchase and possess

Low but significant levels of some carcinogens; irritants; bronchitis

CDC cautions against vaping in adolescents and non-smokers

*Does vaping lead to cigarette smoking in nonsmokers?*  
*Does vaping reduce cancer in smokers?*

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## CANCER PREVENTION: VAPING

*Does vaping reduce cancer in smokers?*

Surrogate end point: Does vaping reduce tobacco smoking in smokers?

China: 1060 smokers (10/day)

	Quit after 6 months
Electronic cigarettes	16%
Varenicline	14%
Nicotine gum	8%

Switzerland 1246 smokers (5/day)

	Quit after 6 months
Electronic cigarettes + counseling	29%
Counseling only control	16%

JAMA Int Med. 184: 291 (2024)  
NEJM 390: 601 (2024)

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## TOBACCO SMOKING CESSATION ADULTS: RECOMMENDATIONS 2021 USPSTF

Population	Recommendation	Evidence
Non-pregnant	Clinician counseling; FDA approved drugs	A
Pregnant	Clinician counseling; no drugs	A
All	E-cigarettes	I: insufficient evidence for benefit

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## HUMAN TUMOR VIRUSES

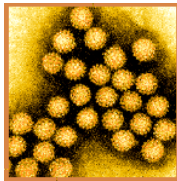
### *Virus*

### *Cancer*

Epstein-Barr virus	Lymphoma
Papilloma virus	Cervical cancer
Hepatitis B virus	Liver cancer
Human T-cell leukemia	T-cell leukemia virus
Herpes virus 8	Kaposi sarcoma
Polyoma virus	Merkel carcinoma

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## HPV AND CERVICAL CANCER



Harald zur Hausen, MD  
Nobel Prize, 12/2008



*HPV vaccine ages 15-26:*

- lowers HPV by >85%
- lowers CIN by 99% at 5 yr follow-up

**Issue: participation two doses**

By age 26: Australia 80%; USA 60%

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## CANCER AND NUTRITION

### EPIC: European Prospective Investigation into Cancer and Nutrition



**520,000** people enrolled 1992-2009

***Baseline:***

Diet, nutrition, lifestyle environment

***Follow-up:***

Medical history annually

9 million blood samples stored

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## EPIC: European Prospective Investigation into Cancer and Nutrition

- **Obesity:** Increased breast, colon cancer
- **Mediterranean diet:** No effect on cancer
- **Vitamin supplements:** No effect on cancer
- **Alcohol:** Slight increase in liver and breast cancer
- **Dietary fiber:** Less colon cancer
- **Cured meats:** More colon cancer

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## CANCER CHEMOPREVENTION CLINICAL TRIALS

### Natural substances

*Vitamins A, E*: Colon cancer in post-menopausal women

Result: *No change*

*Beta-carotene and vitamin A*: Lung cancer in smokers

Result: *Increased cancer*

### Drugs

*Finasteride*: Prostate cancer in men over 55 **at risk**

Result: *25% reduction*

*Tamoxifen, raloxifene*: Breast cancer in women **at risk**

Result: *50% reduction*

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## CANCER IN PRIMARY CARE

- A. The war on cancer
- B. Cancer screening
- C. Cancer prevention
- D. **Cancer survivorship**

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## CANCER SURVIVORSHIP

*Clinical vignette:*

- Primary care clinic: 62-year-old man has episodic abdominal pain and diarrhea
- Loss of appetite and weight loss
- Rapid fecal occult blood test is positive for hemoglobin
- Referred for colonoscopy: polyps, biopsy shows adenocarcinoma
- Referred for oncology; treated with surgery, chemotherapy
- **Six months later, patient is back in the primary care clinic**

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## CANCER SURVIVORSHIP

**Survivorship:** *Interval after treatment up to cure, recurrence, or death*

There are 18.1 million cancer survivors in the US

By 2030, there will be a 25% increase in cancer survivors

In 2024: 70% of people live 5 years after diagnosis

50% “ “ “ 10 “ “ “

20% “ “ “ 20 “ “ “

70% of survivors have functional limitations

***This is a significant issue for primary care practitioners***

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## CANCER SURVIVORSHIP

*Primary care practitioners:* Screening

*Oncologists, etc.:* Diagnosis, treatment

*Primary care practitioners:* Survivorship

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## CANCER TREATMENT

*The primary care practitioner is a gatekeeper for where a cancer patient is treated*

*National Cancer Inst. Cancer Centers: 71 in 36 states*

- Typically, academic centers, research, clin. trials
- Treat about 25% of all cancer patients
- 75% treated in local cancer centers

*Two major trends re primary care referral:*

- NCI centers buying out local cancer centers
- NCI centers PR campaign



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## CANCER SURVIVORSHIP

From a patient:

“The lack of guidelines and providers who understand the long-term needs of cancer survivors is an unmet need. My cancer was diagnosed 30 years ago, when I was 13. I have not found a provider who understands both sides of my current needs. (Primary care practitioners) do not understand my cancer and oncologists do not understand my non-cancer health maintenance needs, such as monitoring cholesterol and blood pressure.”

JNCI monographs, 40

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## CANCER SURVIVORSHIP CARE

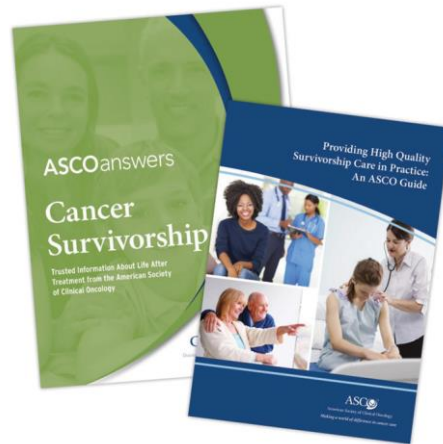
*A typical cancer survivorship plan for the primary care practitioner:*

- **Surveillance:** recurrence of primary; secondary cancers (8% of survivors)
- **Management** of late effects of treatment: fatigue, neuropathy, etc. (up to 80% have some disability); chronic pain (35%)
- **Psycho-social** implications of survivorship: mood disorders (20%), family, etc.
- **Coordination of care:** PCP and oncology team
- **Treatment plan:** Adapted to EHR

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## CANCER SURVIVORSHIP CARE

Patients



Practitioners

American Society of Clinical Oncology

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## CANCER IN PRIMARY CARE

- A. The war on cancer
- B. Cancer screening
- C. Cancer prevention
- D. Cancer survivorship

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