

Issues of Cancer in Primary Care: Screening, Prevention and Survivorship

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Disclosure

I have no financial interests or relationships
to disclose.



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ISSUES OF 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



President Joe Biden announces
The 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
Cancers	5	2
Musculoskeletal	6	4
Injuries	7	5

IMHE, Seattle, 10/20

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PEOPLE WITH CANCER, 2025

US: excluding non-melanoma skin cancer

2,041,910 people newly diagnosed (2025 est.)

35% diagnosed less than 5 years ago

18.5 million people living with cancer (2025 est.)

5-year survival: **69%** (was **49%** in 1975)

618,120 people die from cancer (2025 est.)

ACS, SEER

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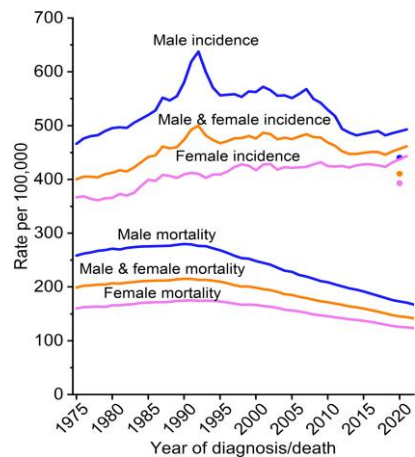
CANCER, DIAGNOSES AND DEATHS, 2025



ACS

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CANCER INCIDENCE AND MORTALITY SINCE 1975



ACS, CA Journal, 1/2025

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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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CANCER DEATHS AVERTED SINCE 1975

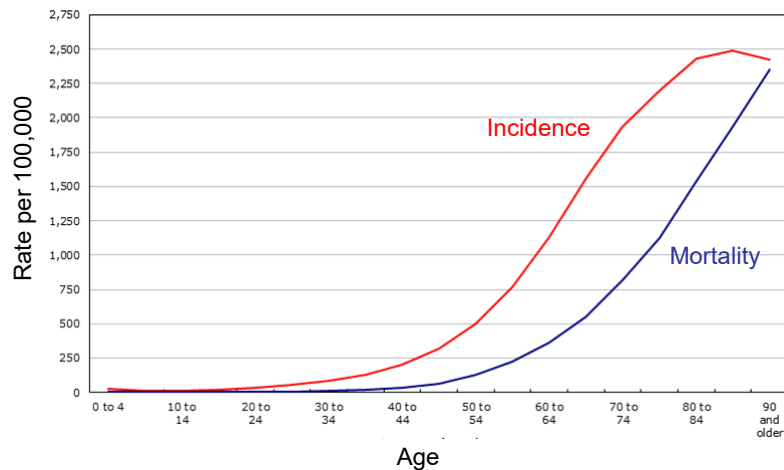
**6 million deaths due to cancer averted
since 1975 in US:**

- 50% due to decline in smoking
- 23% due to better screening
- 20% due to better treatment
- 7% due to better hygiene (e.g., *H. pylori*)

ACS/SEER

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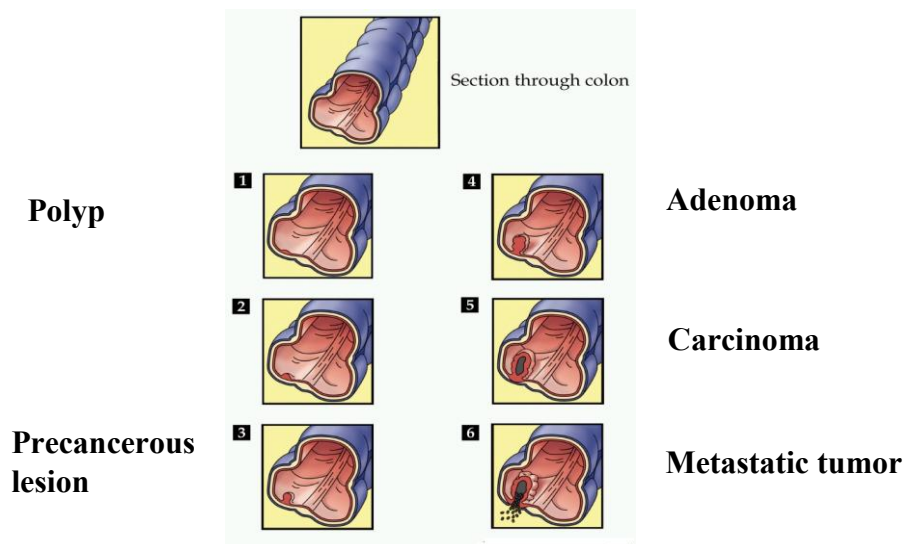
AGE AND CANCER



Cancer Is a Disease of Older People

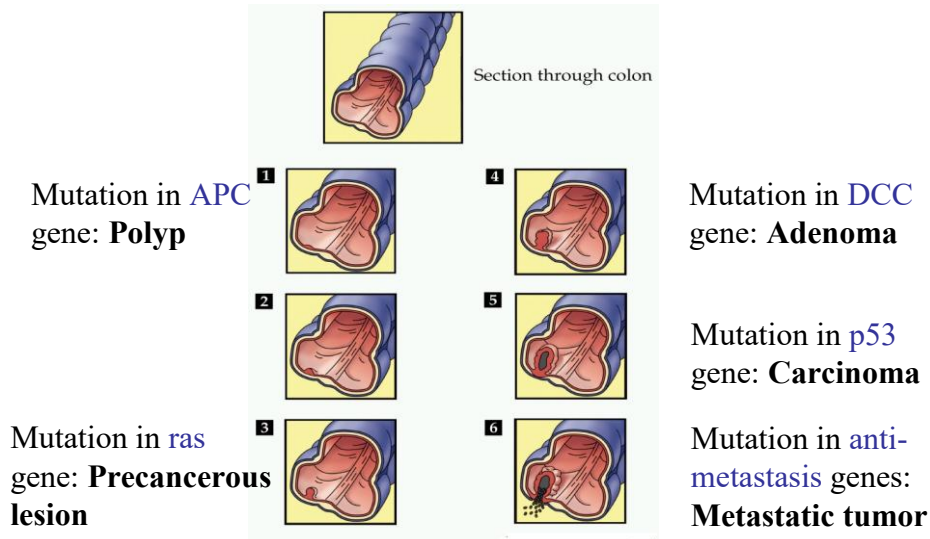
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AGE AND CANCER: MOLEC. BIOGRAPHY



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AGE AND CANCER: MOLEC. BIOGRAPHY



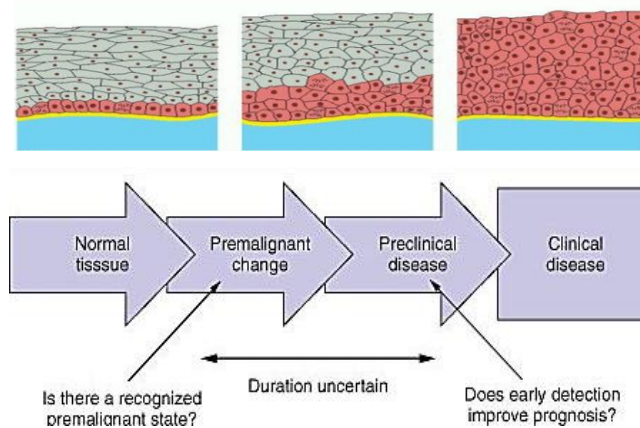
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ISSUES OF CANCER IN PRIMARY CARE

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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**

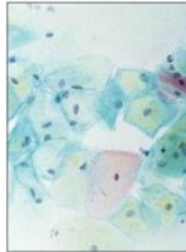
Endpoint Issue: Does Detection Result in Improved Survival?

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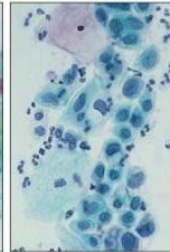
CERVICAL CANCER SCREENING: PAP SMEAR



G. Papanicolaou
1928-1943



Normal

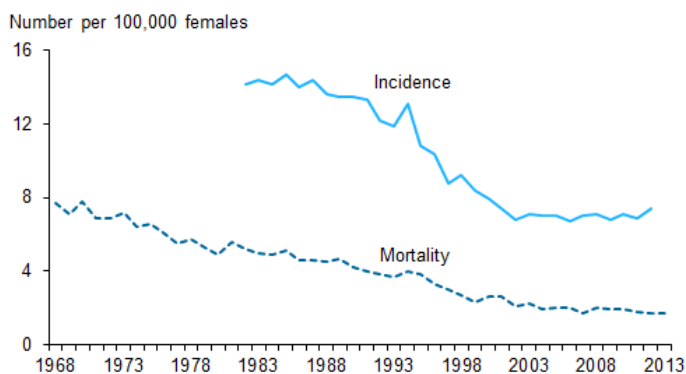


Precancerous

This Test Is Being Replaced with HPV DNA Testing of the Cervical Sample

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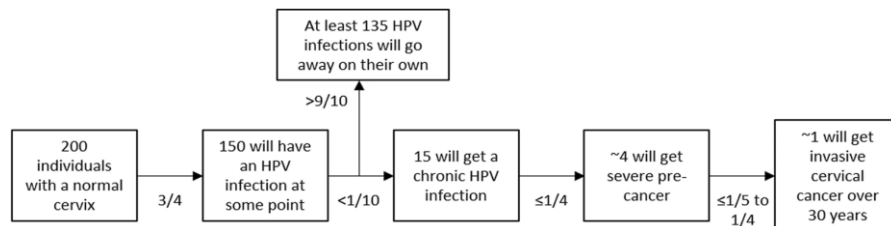
CERVICAL CANCER USA



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, 2025

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)

...Being Reconstituted with Fewer Physicians, 9/25...

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CERVICAL CANCER SCREENING: USPSTF 2025

Population	Recommendation	Evidence for screening
< 21 years	No screening	D
21-29 years	Cyt. every 3 years	A
30-65 years	HPV every 5 years or cyt. every 3 years or HPV & cyt. 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

< 21 years	No screening
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*Primary care surveys: 19 % (2 million) females age 15-20 annual Pap smear
Mostly unnecessary*

30-65 years	Cyt. every 3 years or HPV every 5 years
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*Cohort study of cyt .vs. HPV: HPV testing is 2x more sensitive in detecting neoplasia (2018)
HPV now preferable to cyt from USPSTF (2025)*

>65 years	No screening
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*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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BREAST CANCER SCREENING

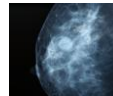
- Breast self-examination



- Clinical breast exam

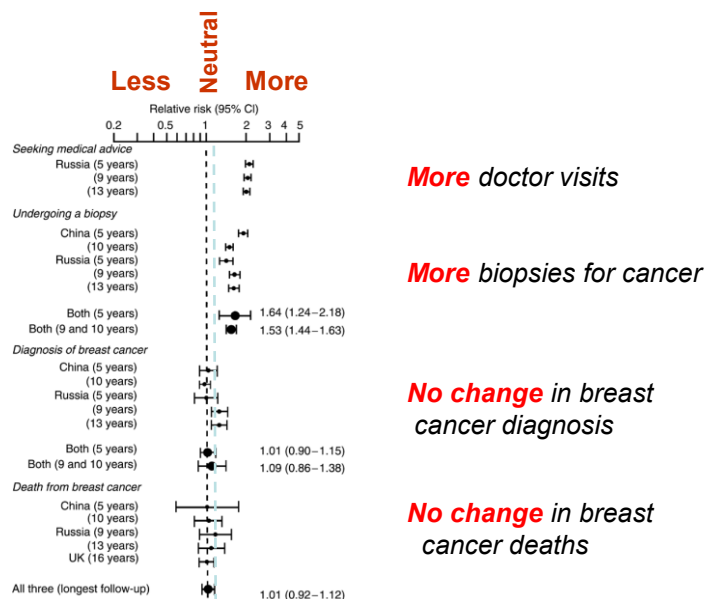


- Mammogram



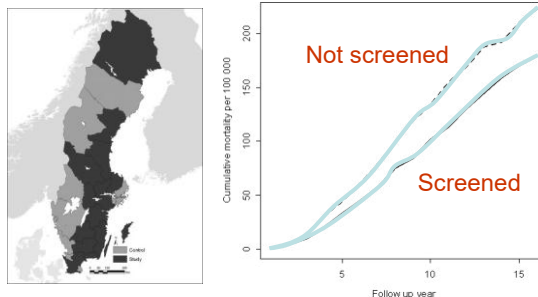
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BREAST CANCER SCREENING: SELF EXAM



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MAMMOGRAPHY SCREENING SWEDEN 1986-2005



***30% Reduction in Deaths in Screened Group Followed 20 yr
Greatest Mortality Benefit in Women Over Age 50***

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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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MAMMOGRAPHY SCREENING CLINICAL VIGNETTE

A 40 y.o. woman with no family background of breast cancer asks her primary care practitioner when to begin mammography

- For 1000 women of average risk ages 40-49, breast cancer incidence 1999-2018 rose from 1.54 to 1.60 cases
-
- Screening 1000 women ages 40-49 will result in 1 less death (compared to 7 less deaths for screening ages 50-74)
- Screening 1000 women ages 40-49: 500 more false positives, 65 more biopsies (adverse side effects), overdiagnosis

Discussions with Practitioner About Benefits vs Harms

Ann Int Med doi: 10.7326/M23-3325

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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 one radiologist **plus AI**

Results: Screening only: 203 breast cancer

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

If two radiologists flagged the case as malignant, 60% of patients were called back by medical team.

For one radiologist plus AI, 39% were called back.

Problem: Lack of Trust in AI by Medical Team.

Lancet Oncol. 8/1/23

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BREAST CANCER SCREENING: DNA

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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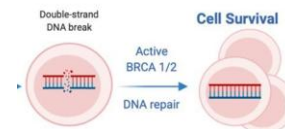
BREAST CANCER SCREENING: DNA

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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COLON CANCER SCREENING

- Fecal tests:**

FOBT: blood in stool

FIT: immuno. blood in stool

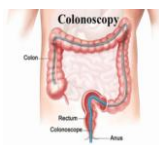
FIT-DNA: Tumor DNA



- Sigmoidoscopy**
(distal colon)



- Colonoscopy**



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COLON CANCER LIVES SAVED BY SCREENING: ESTIMATE

Based on Incidence /Detection Data – Not Mortality

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

USPSTF

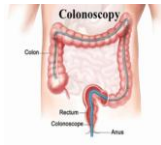
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COLON CANCER SCREENING: FIT VS COLONOSCOPY



The first **randomized trial** comparing two screening tests on colorectal cancer incidence and mortality

- 57,000 people in Spain, ages 5-69 years
- Randomly assigned to one time colonoscopy or FIT every 2 years
- After 10 years:
Colonoscopy: incidence 1.13%, mortality 0.22%
FIT: incidence 1.22%, mortality 0.24%



No significant differences

Lancet 405:1231-1239 (2025)

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COLON CANCER SCREENING: CLINICAL VIGNETTE

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



Treated with surgery, chemotherapy

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COLON CANCER SCREENING RECOMMENDATION 2021 USPSTF

Population	Recommendation for screening	Evidence for screening
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: DNA

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”

- Sensitivity for colon cancer: 87%, specificity >95%
- Precancerous lesions: sensitivity 13%
- Large clinical trials underway; expensive
- Over 15 other tests underway, including sequencing

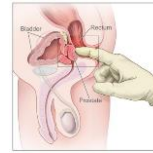
So Far, Data on Cancer Detection But Not Yet on Mortality

JAMA doi 10-1001/jama.2025.7515

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PROSTATE CANCER SCREENING

- *Digital exam*: Sensitivity 51%
Specificity 59%
- *Prostate specific antigen blood test (PSA)*
Sensitivity 93%
Specificity 30%
(at 4 ng/ml)



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

BMC Med. doi.org/10.1186/s12916-021-02230-y

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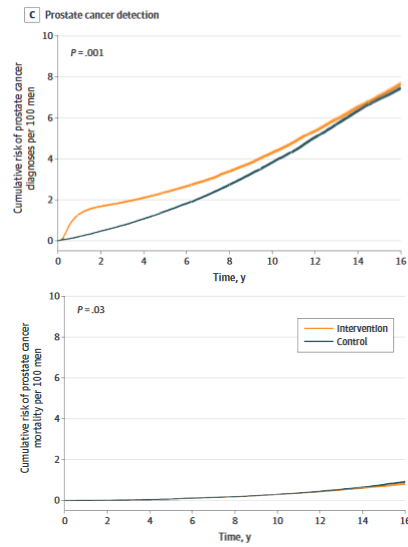
PROSTATE CANCER SCREENING: PSA

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

Population	Recommendation for PSA screening	Evidence for screening
< 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

Scheme for shared decision making for prostate cancer screening:

<https://pmc.ncbi.nlm.nih.gov/articles/PMC4412472/>

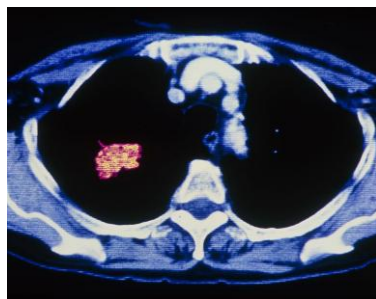
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OTHER WAYS TO SCREEN FOR PROSTATE CANCER?

- *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)
- *Polygenic risk score*: 130 SNPs linked to prostate cancer

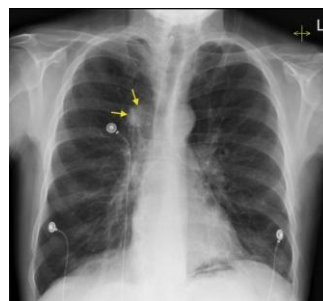
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LUNG CANCER SCREENING



Low-dose CT scan:

Sensitivity 94%
Specificity 95%

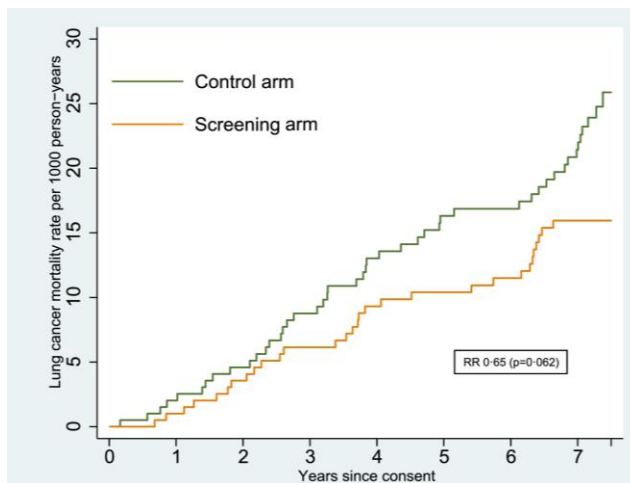


X-ray:

Sensitivity 73%
Specificity 91%

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LUNG CANCER SCREENING: MORTALITY



Lancet Regional Health Europe, 2021

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LUNG CANCER SCREENING RECOMMENDATION 2023 USPSTF

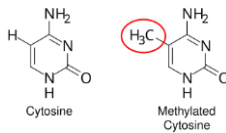
<i>Population</i>	<i>Recommendation for low-dose CT screening</i>	<i>Evidence for screening</i>
50-80 years	Current smokers and past smokers (20 pack-years); up to 15 years after quit; annual screen	B

Only 10% of eligible people are screened



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MULTICANCER EARLY DETECTION TESTS (MCED)



Basis:

- Dead cells release DNA fragments to blood
- Some DNA seq. are methylated (e.g., C)
- Methylation patterns are cell type specific
- 50 types of tumors: each with unique Me pattern that can be detected
- Detection in blood can be before clinical

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MULTICANCER EARLY DETECTION TESTS (MCED)

Evidence:

- For asymptomatic people, sens. = 50-70%
specificity = 98% - improving
- Detection best for early-stage cancers
- No evidence for reduced mortality (yet: UK-NHS study underway with 140,000 people)



Current:

- Not FDA approved; cost to patient \$650-\$950
- Use: as adjunct to conventional screening

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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 PREVENTION: CAUSES



Nevada test site: 100 explosions, 1951-62



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

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CANCER CAUSES: RADIATION?



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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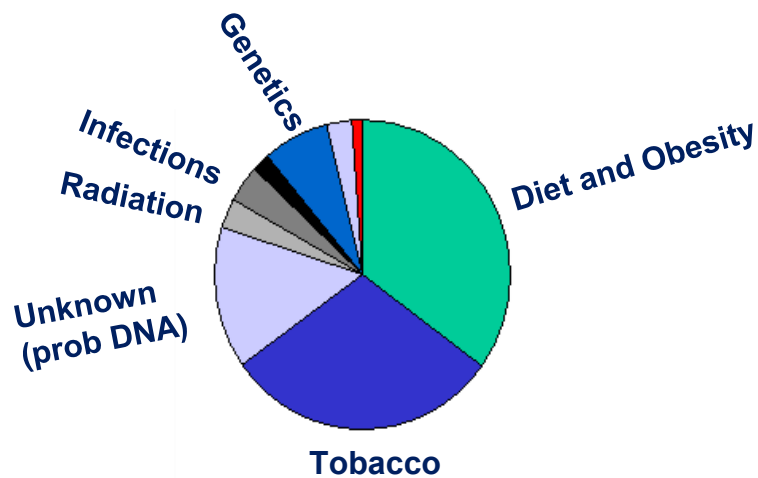
CANCER CAUSES: RADIATION



Radium Dial Painters

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CANCER PREVENTION: CAUSES



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: TOBACCO 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*

US adults: 2025: 11% smokers US (2005: 21% and 1965: 42%)
smokers among those with less education, less income

UK study over 5 decades: one cigarette results in 20 min less life

Primary Care Practitioners:) **Stop** (Adults); **Prevent** (Adolescents)

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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

2025: 10% age 18-24 vaping
4% over 24

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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SMOKING CESSATION ADULTS: RECOMMENDATIONS 2021 USPSTF

<i>Population</i>	<i>Recommendation</i>	<i>Evidence</i>
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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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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CANCER AND NUTRITION

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
- **Dietary fiber:** Less colon cancer
- **Cured meats:** More colon cancer

Dietary Interventions Reduce Cancer Incidence
e.g., Bariatric Surgery Reduces Breast Cancer by 50%

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CANCER AND NUTRITION: ALCOHOL

2020: 72% of US adults consume 1+ drink / wk



- Adverse physical, psychological and social effects of over-consumption
- Ethanol metabolite, acetaldehyde, causes DNA damage, blocks DNA methylation
- Apparently, no lower limit in dose-response
- 2025: US surgeon General: alcohol follows tobacco and obesity as preventable cause of cancer:
100,000 cases and 20,000 deaths/yr



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CANCER AND NUTRITION: ALCOHOL

UK study of 135,000 person-records over 12 years:
alcohol consumption and cancer-related mortality

<i>Group</i>	<i>G/day alcohol</i>	<i>Hazard ratio cancer death</i>
Occasional	3	1.00 (ref. group)
Low	3-20	1.11
Medium	20-40	1.15
High	>40	1.39

***12 oz Beer, 5 oz Wine, 1.5 oz Drink Has 14 g Alcohol
Even Low Consumption Increases Risk***

JAMA Network Open(2025) doi: 7(8) e2424495

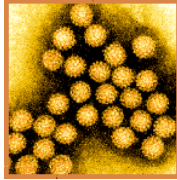
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HUMAN TUMOR VIRUSES

<i>Virus</i>	<i>Cancer</i>
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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PREVENTION OF HPV-CAUSED CERVICAL CANCER



Harald zur Hausen, MD
Nobel Prize, 12/2008



HPV vaccine ages 9-26:

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

Issue: participation two doses

By age 26: Australia 80%; USA 61%

Soon: Home HPV testing (now by prescription)

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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 2025: 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 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

From a primary care practitioner:

“Previously, I strove to reassure patients, trying to “fix it”, but I learned that it is more important to hold space for pain and validate suffering. Although initially awkward, this approach leads to a deeper understanding of patients and what they are experiencing...The time following treatment is especially fraught with uncertainty. Patients often feel anxiety regarding recurrence, apprehension about returning to typical responsibilities and a sense of loss from the decreased physician visits. Educate patients to anticipate this transition and explain the next steps for surveillance.”

Am. Fam. Phys. 108:17 (2023)

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CANCER SURVIVORSHIP CARE

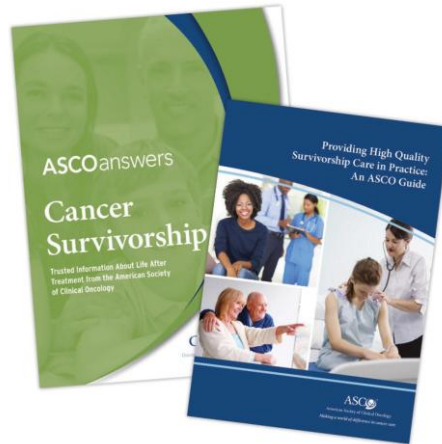
A typical cancer survivorship plan for the primary care practitioner:

- **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%); nutrition
- **Psycho-social** implications of survivorship: mood disorders (20%), family, etc.: Mindfulness, Tai-chi, psych consult
- **Financial toxicity:** discrimination in financial services
- **Coordination of care:** PCP and oncology team
- **Treatment plan:** Adapted to HER

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CANCER SURVIVORSHIP CARE

Patients



Practitioners

American Society of Clinical Oncology

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ISSUES OF CANCER IN PRIMARY CARE

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

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