Cancer Screening and Prevention Saving Women's Lives

Joan L. Walker, M.D. Gynecologic Oncology Stephenson Cancer Center



Site	Risk
All sites ^a	1 in 3 (39.0%)
Breast	1 in 8 (13.1%)
Lung & bronchus	1 in 18 (5.6%)
Colon & rectum	1 in 26 (3.8%)
Uterine corpus	1 in 32 (3.1%)
Melanoma of the skin ^b	1 in 40 (2.5%)

*Excludes basal cell and squamous cell skin cancers and in situ cancer except for urinary bladder. *Probabilities for non-Hispanic White individuals only. Data source: DevCan 6.9.0, National Cancer Institute, 2024.



Important News from the Data

- Cancer incidence is Increasing in Women
- Dramatically increasing in women under 50 yr
- Endometrial cancer is the only cancer increasing in incidence and mortality
- Endometrial cancer deaths > ovary
- Cancer prevention is feasible
 - cervix, endometrial, colon, ovary, HPV related CA
 - Disparities exist in mortality-Blacks and Native/AI

Estimated number of new cancer cases in the US in 2025



Male Prostate 313,780 30% Lung & bronchus 110,680 11% Colon & rectum 82,460 8% Urinary bladder 65,080 6% Melanoma of the skin 60,550 6% Kidney & renal pelvis 52,410 5% Non-Hodgkin lymphoma 45,140 4% Oral cavity & pharynx 42,500 4% Leukemia 38,720 4% Pancreas 34,950 3% All sites 1,053,250



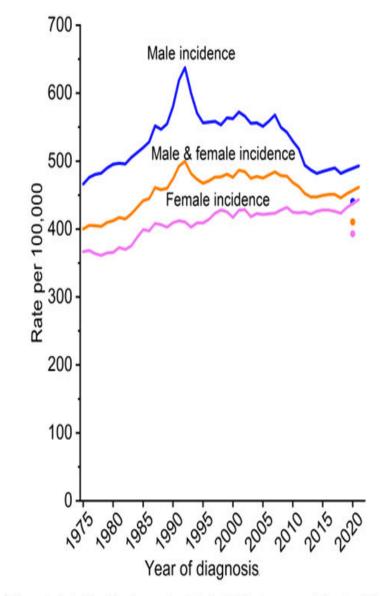
Female

Breast	316,950	32%
Lung & bronchus	115,970	12%
Colon & rectum	71,810	7%
Uterine corpus	69,120	7%
Melanoma of the skin	44,410	4%
Non-Hodgkin lymphoma	35,210	4%
Pancreas	32,490	3%
Thyroid	31,350	3%
Kidney & renal pelvis	28,570	3%
Leukemia	28,170	3%
All sites	988,660	

Excludes basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder. Source: Cancer Facts & Figures 2025. ©2025. American Cancer Society. Inc., Surveillance and Health Equity Science

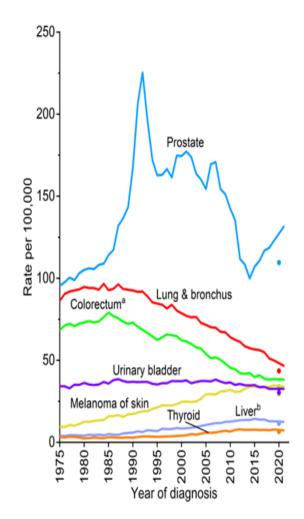
Society'

Trends in cancer incidence rates, US, 1975-2021



Rates are age adjusted to 2000 US standard population and adjusted for delays in reporting. Data for 2020 is shown separate from trend line. Data source: Surveillance, Epidemiology, and End Results program, National Cancer Institute 2024. ©2025, American Cancer Society, Inc., Surveillance and Health Equity Science

Trends in cancer incidence rates among males, US, 1975-2021



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^bIncludes intrahepatic bile duct.

Data source: Surveillance, Epidemiology, and End Results program, National Cancer Institute, 2024.





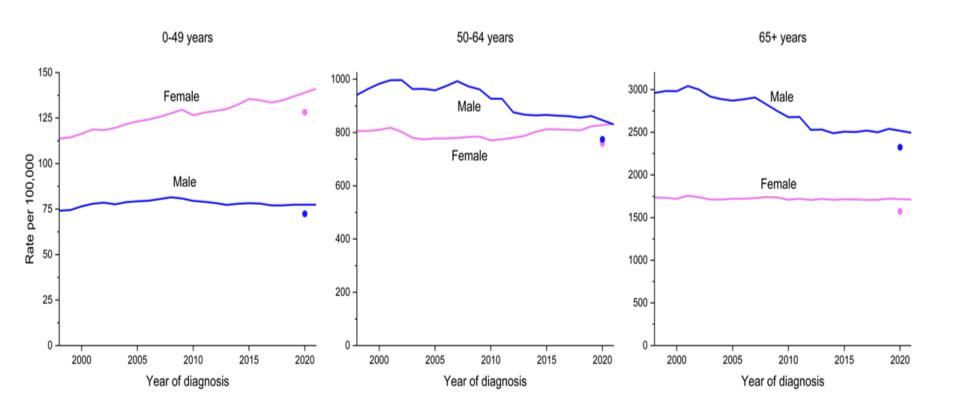
Lifetime probability of developing cancer for males, US, 2018-2019, 2021

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Colon & rectum	1 in 24 (4.1%)
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Kidney & renal pelvis	1 in 45 (2.2%)

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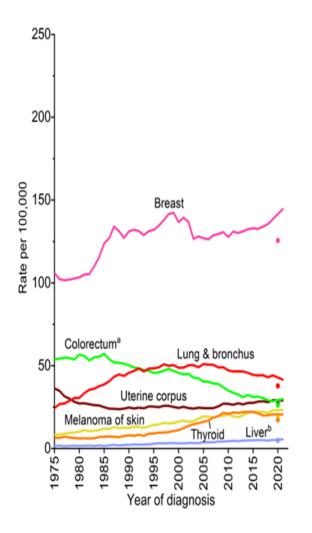
Trends in cancer incidence rates by sex and age, 1998-2021



Rates are age adjusted to the 2000 US standard population and adjusted for delays in case reporting. Data for 2020 are shown separate from trend lines. ©2025, American Cancer Society, Inc., Surveillance and Health Equity Science



Trends in cancer incidence rates among females, US, 1975-2021



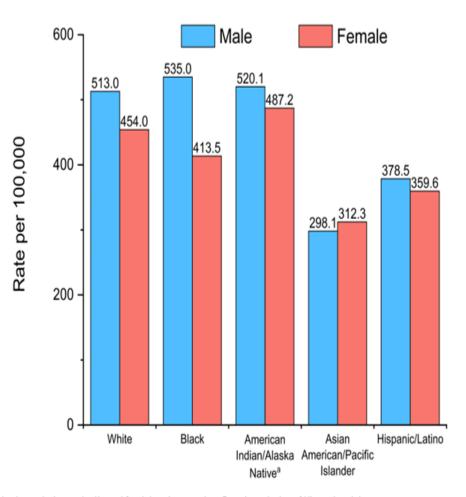
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Cancer incidence rates by race and ethnicity, US, 2017-2021





Rate is age adjusted to 2000 US standard population and adjusted for delays in reporting. Race is exclusive of Hispanic origin. •Rates for American Indian/Alaska Native people are restricted to Purchased/Referred Delivery Care Areas.

Data source: North American Association for Central Cancer Registries, 2024.



Trends in five-year relative survival (%), US, 1975-2020

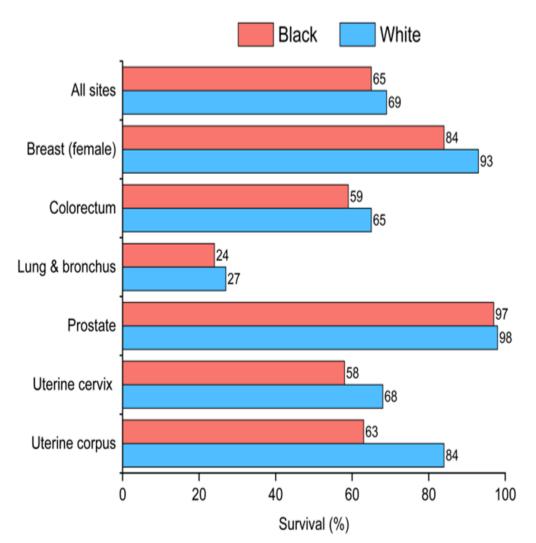
Site	1975-77	1995-97	2014-2020
All sites	49	63	69
Breast (female)	75	87	91
Colon & rectum	50	61	64
Leukemia	34	48	67
Liver & intrahepatic bile duct	3	7	22
Lung & bronchus	12	15	27
Melanoma of the skin	82	91	94
Non-Hodgkin lymphoma	47	56	74
Ovary	36	43	51
Pancreas	3	4	13
Prostate	68	97	97
Uterine cervix	69	73	67
Uterine corpus	87	84	81

Survival is age adjusted for normal life expectancy and are based on cases diagnosed in the Surveillance, Epidemiology, and End Results (SEER) 9

areas for 1975-1977 and 1995-1997 and in the SEER 22 areas for 2014-2020; cases followed through 2021.

Data source: Surveillance, Epidemiology, and End Results program, National Cancer Institute, 2025.

Five-year relative survival (%) by race, US, 2014-2020



Survival is age adjusted for normal life expectancy and are based on cases diagnosed in the Surveillance, Epidemiology, and End Results (SEER) 22 areas for 2014-2020 and cases were followed through 2021. Race is exclusive of Hispanic origin. Colorectum excludes appendiceal cancer. Source: Surveillance, Epidemiology, and End Results program, National Cancer Institute, 2024. ©2025, American Cancer Society, Inc., Surveillance and Health Equity Science



Estimated number of new cancer deaths in the US in 2025



Male			
Lung & bronchus	64,190	20%	
Prostate	35,770	11%	17
Colon & rectum	28,900	9%	
Pancreas	27,050	8%	
Liver & intrahepatic bile duct	19,250	6%	
Leukemia	13,500	4%	
Esophagus	12,940	4%	
Urinary bladder	12,640	4%	
Non-Hodgkin lymphoma	11,060	3%	
Brain & other nervous system	10,170	3%	
All sites	323,900		

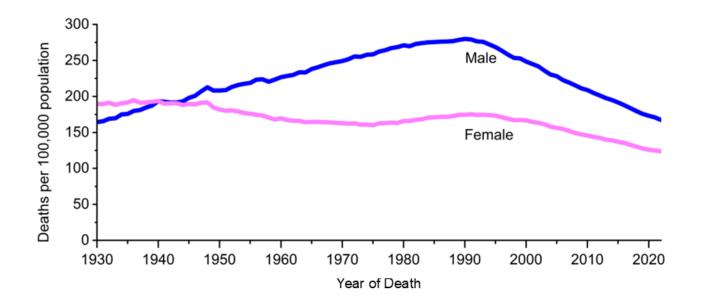
remate		
Lung & bronchus	60,540	21%
Breast	42,170	14%
Pancreas	24,930	8%
Colon & rectum	24,000	8%
Uterine corpus	13,860	5%
Ovary	12,730	4%
Liver & intrahepatic bile duct	10,840	4%
Leukemia	10,040	3%
Non-Hodgkin lymphoma	8,330	3%
Brain & other nervous system	8,160	3%
All sites	294,220	

Female

Excludes basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder. Source: Cancer Facts & Figures 2025. ©2025, American Cancer Society, Inc., Surveillance and Health Equity Science

Cancer Statistics 2025 Trends in cancer death rates, US, 1975–2022



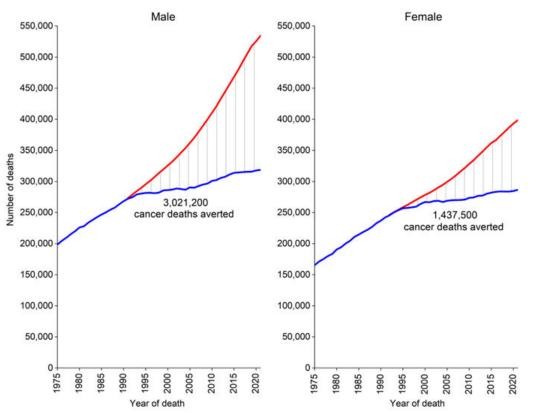


Rates are age adjusted to the 2000 US standard population.

Data source: National Center for Health Statistics, Centers for Disease Control and Prevention, 2024. ©2025, American Cancer Society, Inc., Surveillance and Health Equity Science

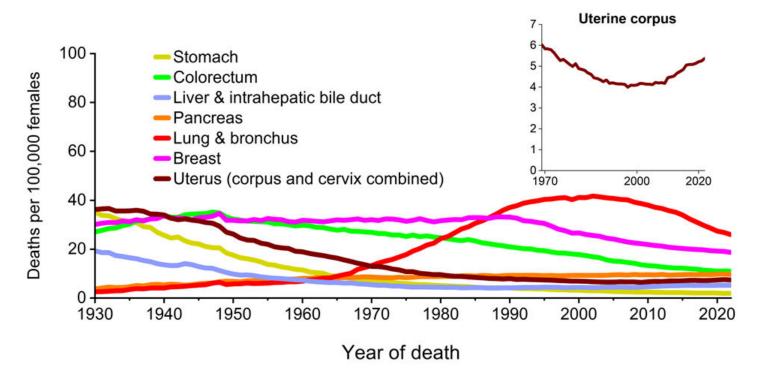
Cancer Statistics 2025 Total number of cancer deaths averted in men (1991 onward) and women (1992 onward), US





The blue line represents the actual number of cancer deaths recorded each year, and the red line represents the number of cancer deaths that would have been expected if cancer death rates had remained at their peak.

Trends in cancer death rates among females, US, 1930-2022

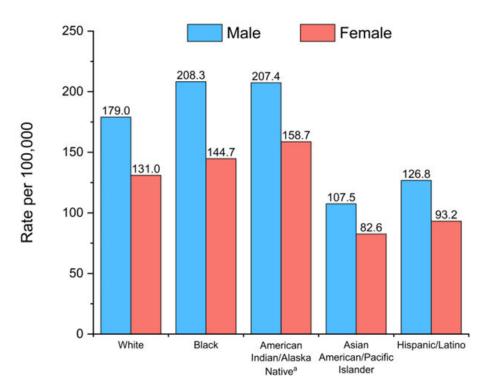


Rates are age adjusted to the 2000 US standard population and exclude deaths in Puerto Rico and other US territories. Due to improvements in classification, site-specific information differs from contemporary data for cancers of the liver, lung and bronchus, colon and rectum, and uterus.

Data source: National Center for Health Statistics, Center for Disease Control and Prevention, 2024.



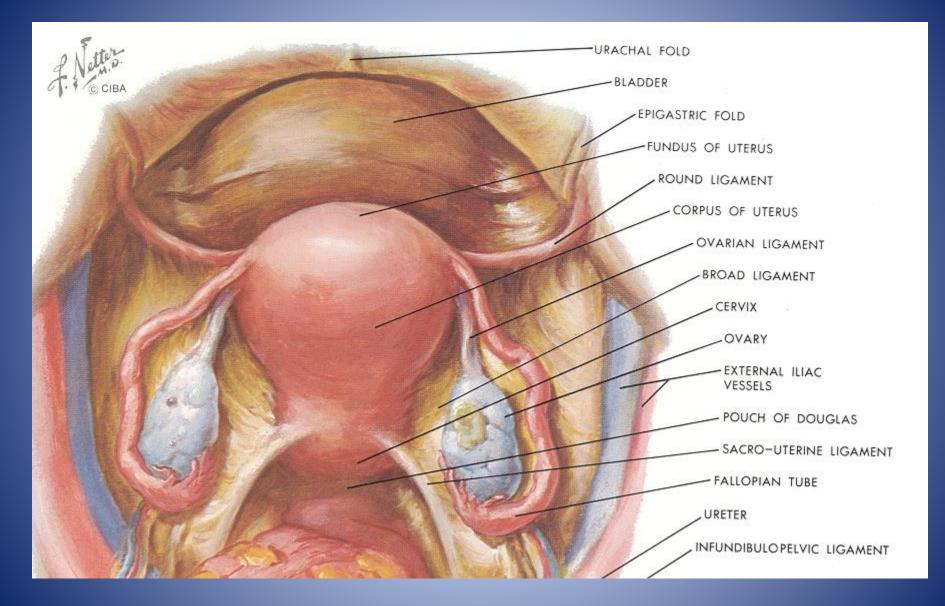
Cancer death rates by race and ethnicity, US, 2018-2022



Rate is age adjusted to 2000 US standard population and adjusted for delays in reporting. Race is exclusive of Hispanic origin. *Rates for American Indian/Alaska Native people are adjusted for racial misclassification on death certificates.

Source: National Centers for Health Statistics, Center for Disease Control and Prevention, 2024



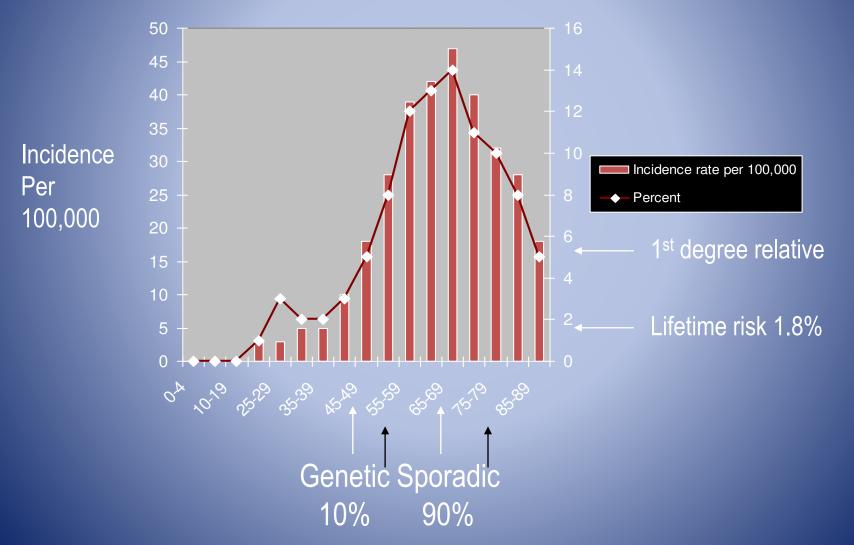


CANCER CASES AND DEATHS

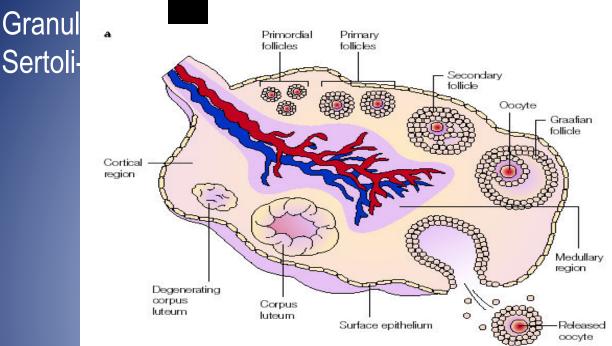
	CASES	OK CASES	DEATHS	LIFETIME RISK	RISK OF DEATH
ENDOMETRIAL	69,120	690	13,250	1:38	1:190
OVARY	19680	250	12,740	1:70	1:100
CERVIX	13,820	200	4,360	1:147	1:441
VULVA	6,900	100	950	1:300	
VAGINA	2,680	50	840		
other	8650		1870		
ALL GYN	118,179		29,910		

Incidence of Ovarian Cancer by Age

Percent

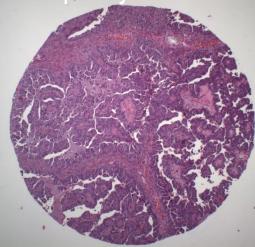


Stromal cell cancers (7%):

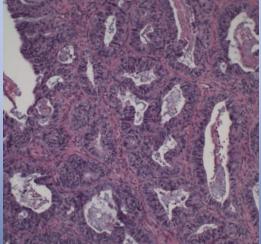


Germ cell cancers (2-3% Dysgerminoma Immature teratoma Embryonal carcinoma Choriocarcinoma Endodermal sinus tumor

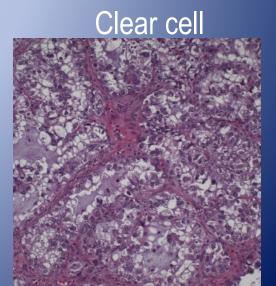
Epithelial cell cancers (90%) Papillary serous



Endometrioid



Naora H Nat Rev Cancer 2005



Latest Theories

- Low grade ovarian epithelial cancer-
 - Estrogen and endometriosis associated
 - Prevented by oral contraceptives
 - 20% of deaths
- High grade serous ovarian epithelial cancer
 - Starts in fallopian tube
 - Rarely stage I
 - Prevented by salpingectomy-RRSO
 - 80% of deaths

Risk Factors Epithelial Ovarian Cancer

- Age
- Family History RR=2.8 1FDR, 4.6 2FDR
- BRCA1 609
- BRCA2
- Lynch II Syndrome (HNPCC)
- Endometriosis
- Infertility/Nulliparity
- PCOS

1FDR, 4.6 2FDR 60% 30% 13% 3%

Protective Factors

- Prophylactic salpingectomy- OPPORTUNISTIC
- Oophorectomy
- Oral contraceptives
 - Risk reduction proportional to duration of use
 - Large cohort, n=103,551
 - Ever-users RR=0.6 (95% CI 0.5-0.7)
 - Long-term users (≥15 years) RR=0.1 (95% CI 0.01-0.6)
 - Lesser protection with progestin-only methods
- Tubal ligation
- Pregnancy

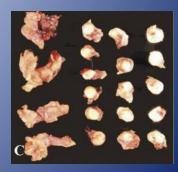
Kumle, Br J Cancer; 2004.

Occult RRSO malignancy is often tubal

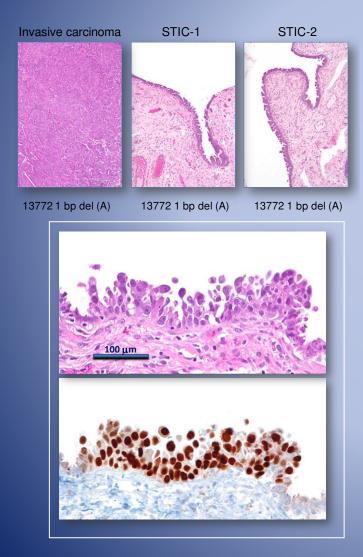
Table 1. Frequency of fallopian tube carcinoma in women with BRCA mutations.							
Authors Number Cancer (%) Fallopian t			Fallopian tube (%)	Comments			
Finch ⁴³	159	7 (4.4)	6 (84)				
Olopade ⁶	170	3	0	All classified as stage I ovary			
Kauff ³³	98	1	0	One classified as peritoneal			
Powell ⁴²	41	7	4 (56)	Three additional cases classified as ovary			
Medeiros ⁵⁰	13	5 (5)	5 (100)	Four cases involved fimbria			
Total	481	28	15				

Table 1. Involvement	of the FT in Patients	With Invasive Pelvic Carcinomas	and in High-Risk Popula
			and in right not ropula

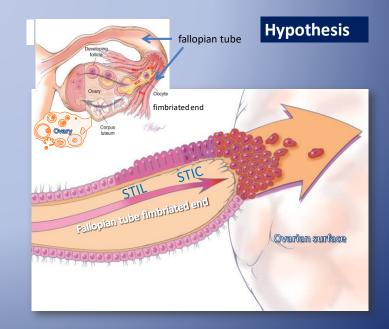
		No. of	BRCA Mutations Status		Pelvic Ca	arcinoma	Inv	olvement of FT	
	Study	Patients	No.	%	No.	%	N	0. %	_
1.7			онкнотн, т/	55					
	Lamb et al ⁸⁴	113	BRCA1, 40	35	7/113	6.2	5/7	71	
			BRCA2, 22	19					
			Not tested or no mutation, 51	45					
	Finch et al ⁸⁵	159	BRCA1, 94	59	7/159	4.4	6/7	85	
			BRCA2, 65	41					
	Callahan et al ⁸⁶	122	BRCA1, 60	49	7/122	5.7	7/7	100	
			BRCA2, 60	49					
			Not specified, 2	2					



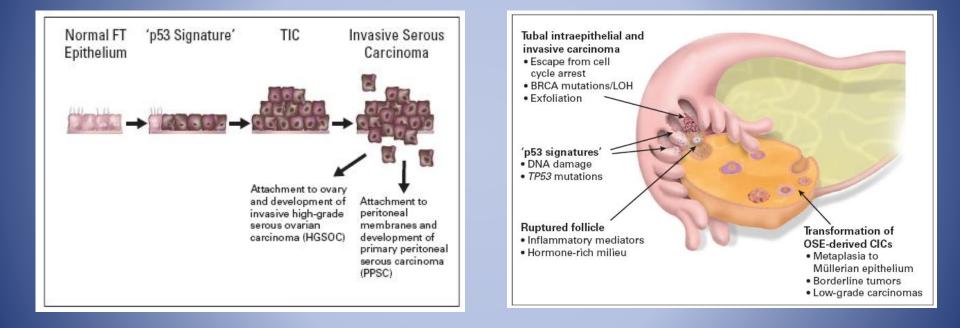
Serous Tubal Intra-epithelial Carcinoma (STIC) has same TP53 mutations as invasive tumors



Not circumstantialQuite convincingPrecursor lesion identified



Models of 'Ovarian' Tumorigenesis

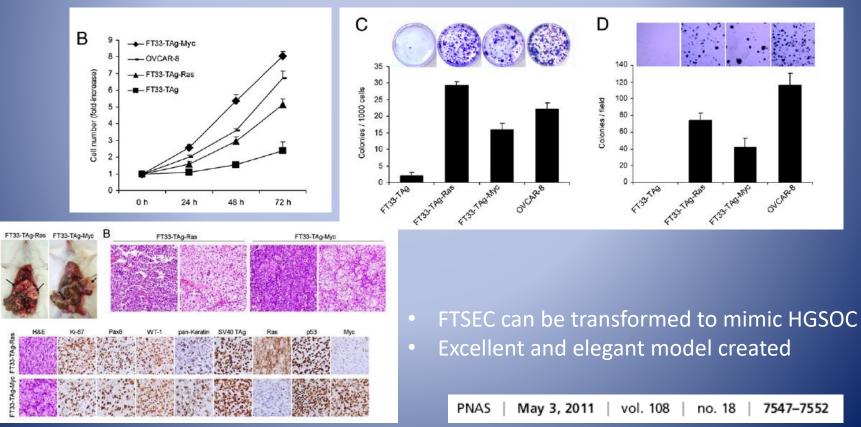


Modeling high-grade serous ovarian carcinogenesis from the fallopian tube

Alison M. Karst^a, Keren Levanon^{a,1}, and Ronny Drapkin^{a,b,2}

С

- FTSEC can be dissociated from fresh tissue and grown in culture
- Viral oncogenic transformation leads to increase proliferation, colony formation, and growth on soft agar
- Phenotype mimics HGSOC based on morphology and IHC



New Prevention Strategy

- Oral contraceptives when not pregnant
- Salpingectomy after last child
- Salpingectomy during any abdominal surgery
- Genetic testing
- Salpingo-Oophorectomy for genetic high-risk individuals near menopause
- Early detection with symptoms
 - Abd distension, early satiety, fatigue, abd pelvic pain

Estimated number of new cancer cases in the US in 2025



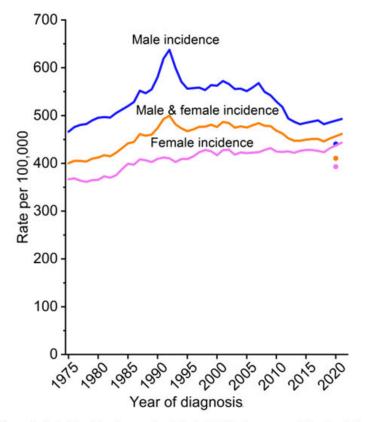
Male	9		
Prostate	313,780	30%	
Lung & bronchus	110,680	11%	
Colon & rectum	82,460	8%	
Urinary bladder	65,080	6%	
Melanoma of the skin	60,550	6%	
Kidney & renal pelvis	52,410	5%	
Non-Hodgkin lymphoma	45,140	4%	
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Excludes basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder. Source: Cancer Facts & Figures 2025. ©2025, American Cancer Society, Inc., Surveillance and Health Equity Science

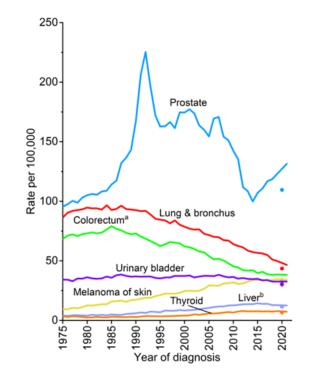
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Trends in cancer incidence rates among males, US, 1975-2021



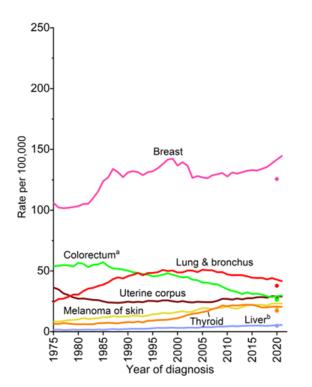
American

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^bIncludes intrahepatic bile duct.

Data source: Surveillance, Epidemiology, and End Results program, National Cancer Institute, 2024.

Trends in cancer incidence rates among females, US, 1975-2021



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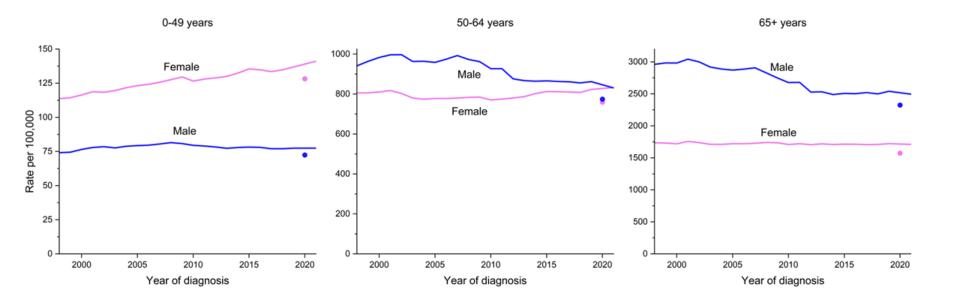
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American Cancer Society

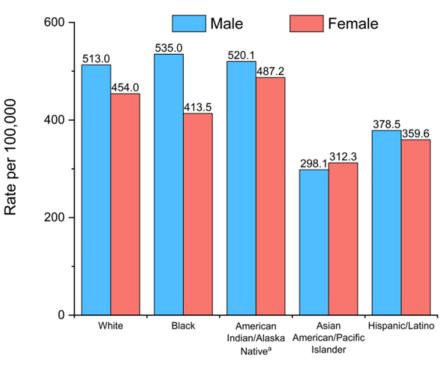
Trends in cancer incidence rates by sex and age, 1998-2021



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Cancer incidence rates by race and ethnicity, US, 2017-2021



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American Cancer Society



Lifetime probability of developing cancer for males, US, 2018-2019, 2021

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Lifetime probability of developing cancer for females, US, 2018-2019, 2021

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Trends in five-year relative survival (%), US, 1975-2020



Site	1975-77	1995-97	2014-2020
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
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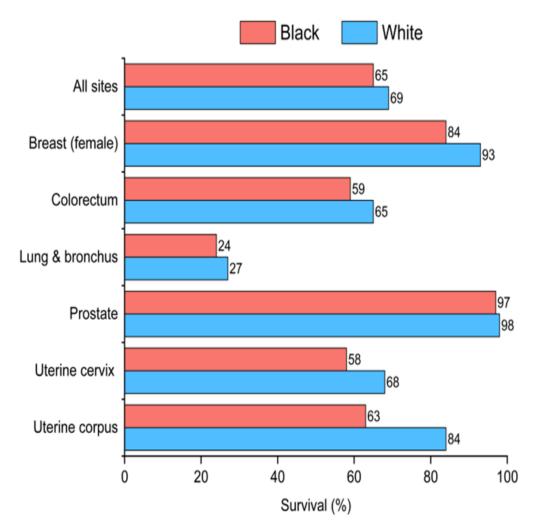
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Five-year relative survival (%) by race, US, 2014-2020



Survival is age adjusted for normal life expectancy and are based on cases diagnosed in the Surveillance, Epidemiology, and End Results (SEER) 22 areas for 2014-2020 and cases were followed through 2021. Race is exclusive of Hispanic origin. Colorectum excludes appendiceal cancer. Source: Surveillance, Epidemiology, and End Results program, National Cancer Institute, 2024. ©2025, American Cancer Society, Inc., Surveillance and Health Equity Science



Estimated number of new cancer deaths in the US in 2025



21% 14% 8% 5% 4% 4% 3% 3% 3%

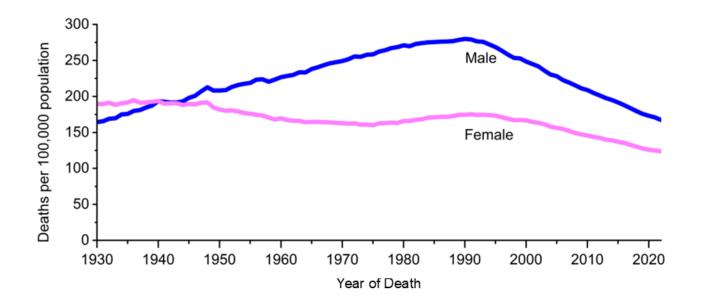
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Cancer Statistics 2025 Trends in cancer death rates, US, 1975–2022



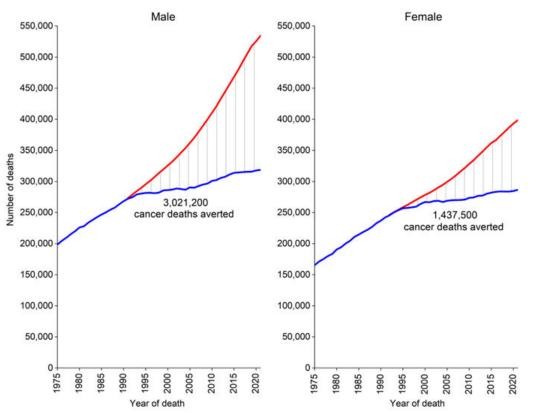


Rates are age adjusted to the 2000 US standard population.

Data source: National Center for Health Statistics, Centers for Disease Control and Prevention, 2024. ©2025, American Cancer Society, Inc., Surveillance and Health Equity Science

Cancer Statistics 2025 Total number of cancer deaths averted in men (1991 onward) and women (1992 onward), US

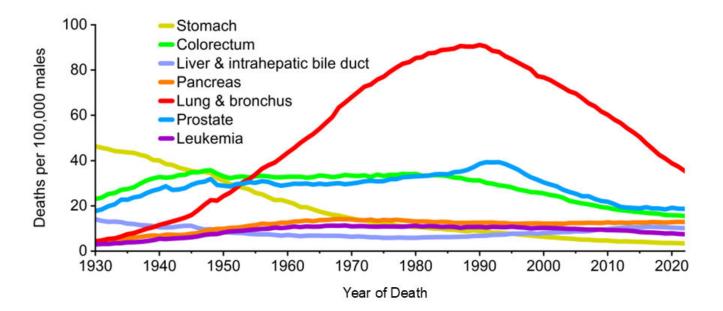




The blue line represents the actual number of cancer deaths recorded each year, and the red line represents the number of cancer deaths that would have been expected if cancer death rates had remained at their peak.

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Trends in cancer death rates among males, US, 1930-2022



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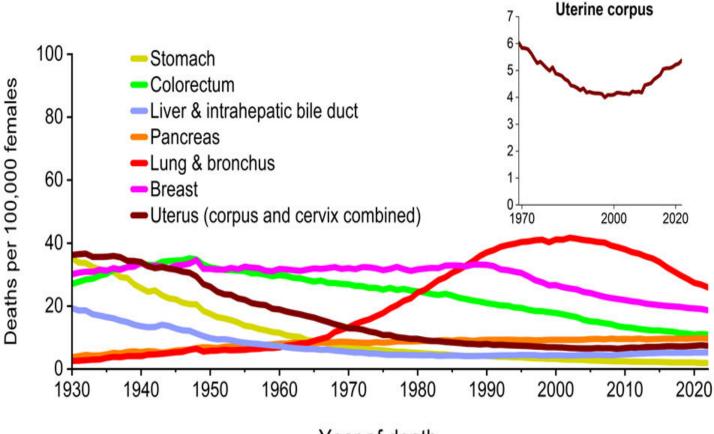
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Trends in cancer death rates among females, US, 1930-2022

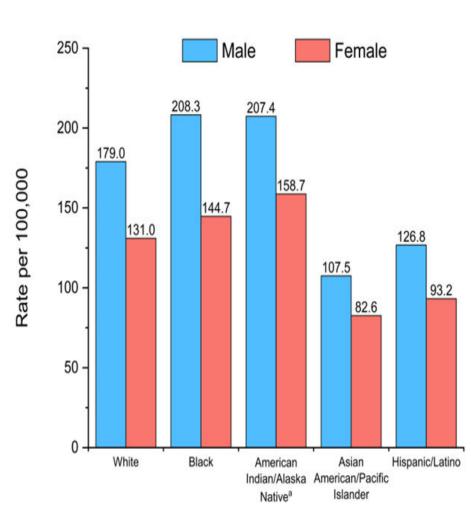




Year of death

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Cancer death rates by race and ethnicity, US, 2018-2022



Rate is age adjusted to 2000 US standard population and adjusted for delays in reporting. Race is exclusive of Hispanic origin. *Rates for American Indian/Alaska Native people are adjusted for racial misclassification on death certificates.

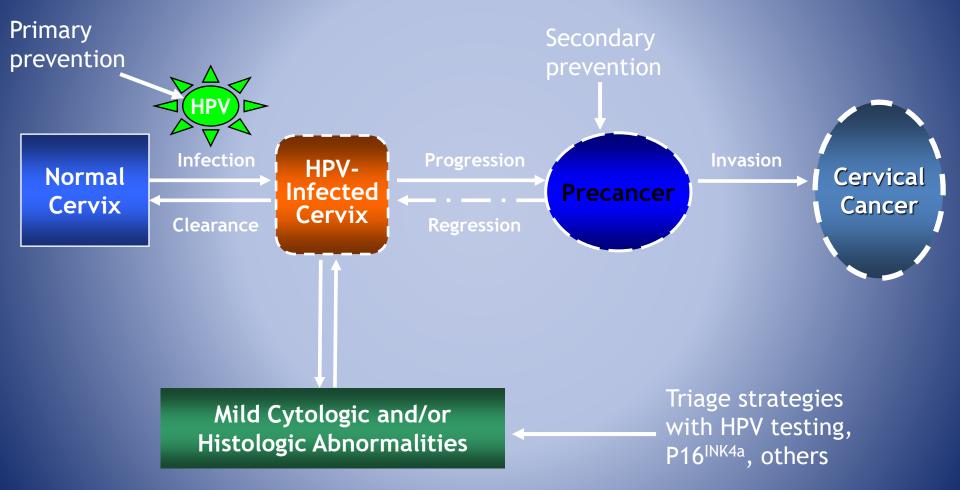
Source: National Centers for Health Statistics, Center for Disease Control and Prevention, 2024

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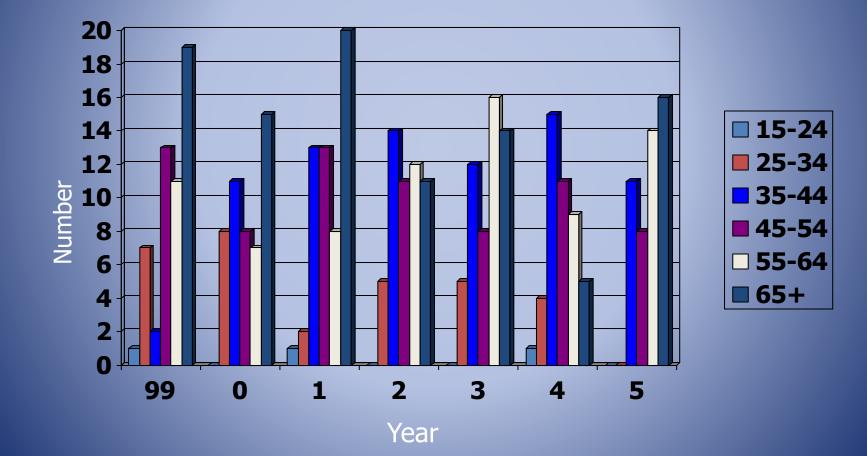


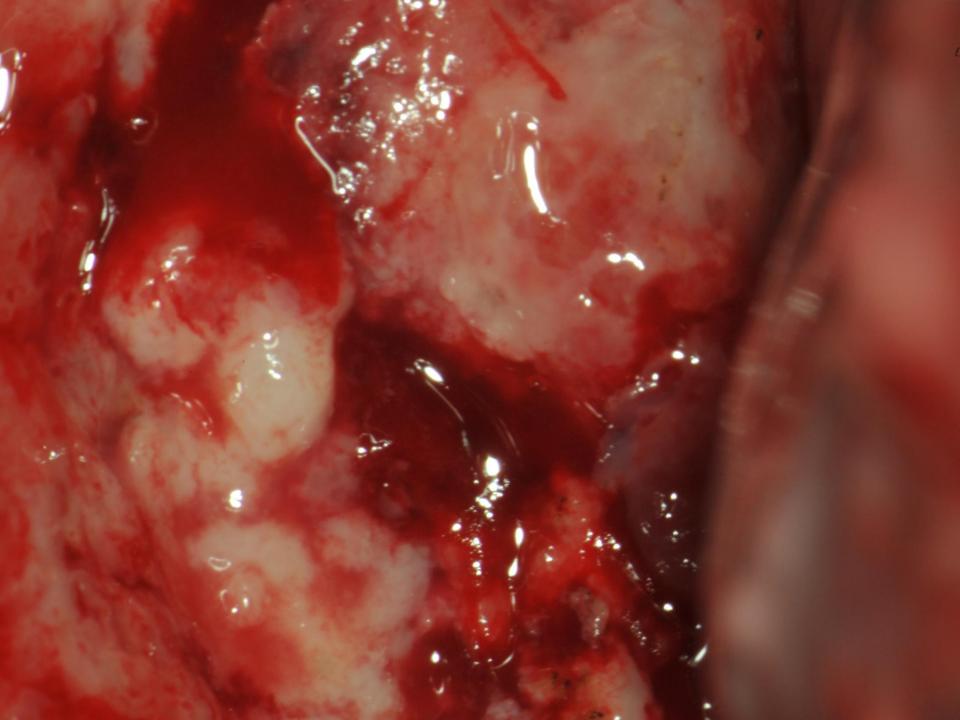
Natural History of Cervical Carcinogenesis



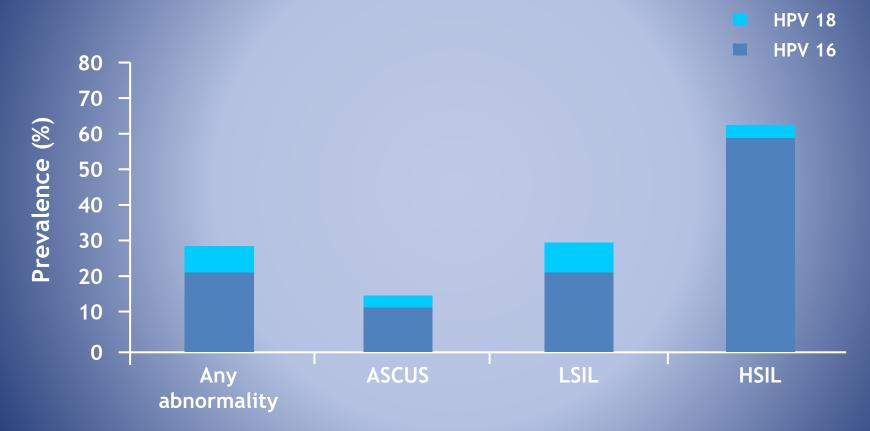
HPV=human papillomavirus. Schiffman M, Kjaer SK. *J Natl Cancer Inst Monogr.* 2003;(31):14-19.

Cervical Cancer Deaths Oklahoma





HPV 16 and 18 Prevalence by Cytology Sentinel Surveillance (2003-2004)



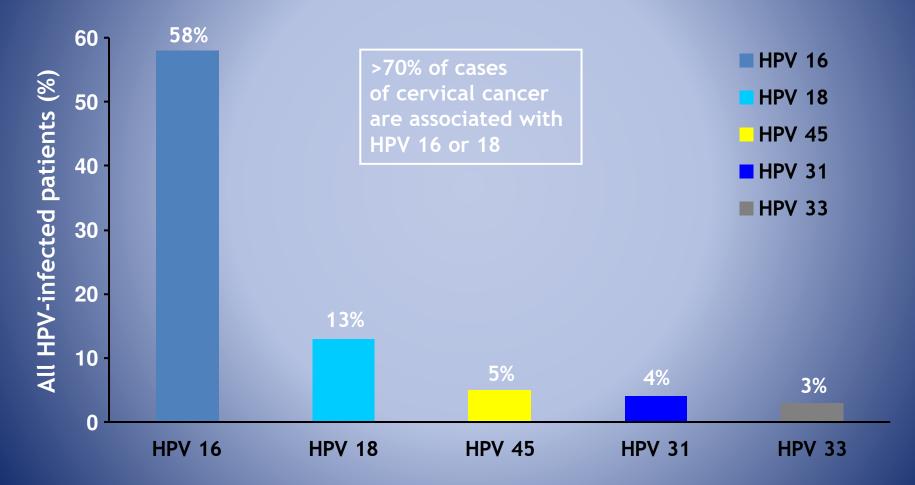
ACSUS=atypical squamous cells of undetermined significance; HSIL=high-grade squamous intraepithelial lesion; LSIL=low-grade squamous intraepithelial lesion.

Centers for Disease Control and Prevention, preliminary/unpublished data.

Modified from Advisory Committee on Immunization Practices. June 2006.

Available at http://www.cdc.gov/nip/ACIP/slides/mtg-slides-jun06.htm#hpv. Accessed on March 3, 2007.

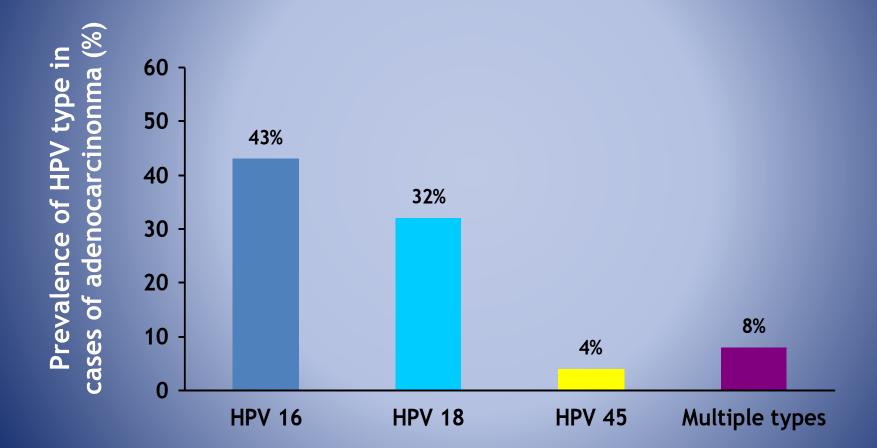
Most Prevalent HPV Types That Cause Cervical Squamous Cancer



N=1918 patients.

Munoz et al. N Engl J Med. 2003;348:518-527. Based on a worldwide survey.

Most Prevalent HPV Types That Cause Cervical Adenocarcinoma

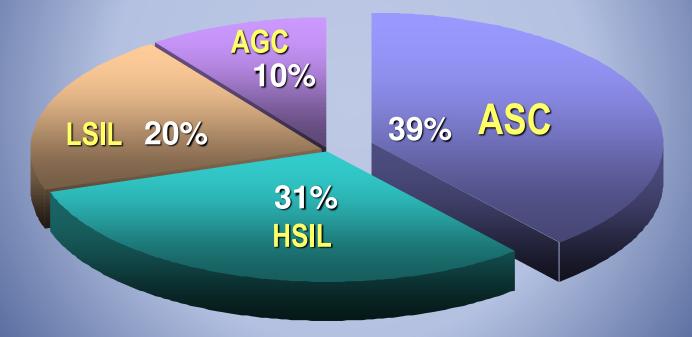


HPV DNA was detected in 93% of patients with cervical adenocarcinoma. Castellsague X et al. *J Natl Cancer Inst.* 2006;98:303-315.

Absolute Risk of CIN 2+

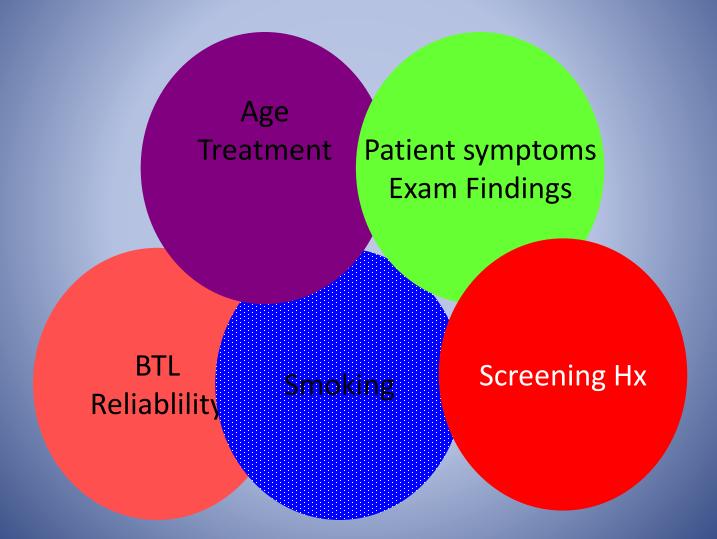
- CIN 1 post LSIL 12%
- ASC/HPV+ = LSIL = 25%
- ASC-H- 25-40%
- AGC 30-50%
- HSIL- 60-80%
- HSIL pap and Low Grade Colpo = 40%
- HSIL and High Grade colpo = 70-85%
- Post LEEP for CIN 3 = 5-15%
- Post Cone for AIS = 8%

Pap Diagnoses Preceding Histologic High-Grade Neoplasia



Modified from Kinney W, et al. Obstet Gynecol. 1998;91: 973-976.

Risk of Cervical Cancer



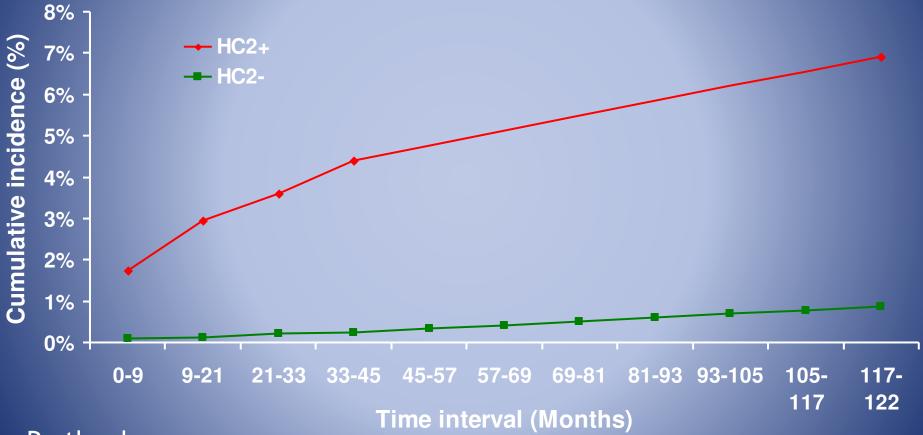
Limitations of Secondary Prevention

- Screening compliance
- Identifying true precursors from 3 million ASC and LSIL smears per year in the US
- Over treatment of patients with trivial lesions
- All of these problems are overcome if primary prevention with vaccines works

Risk of Genital HPV Infection From Time of First Sexual Intercourse



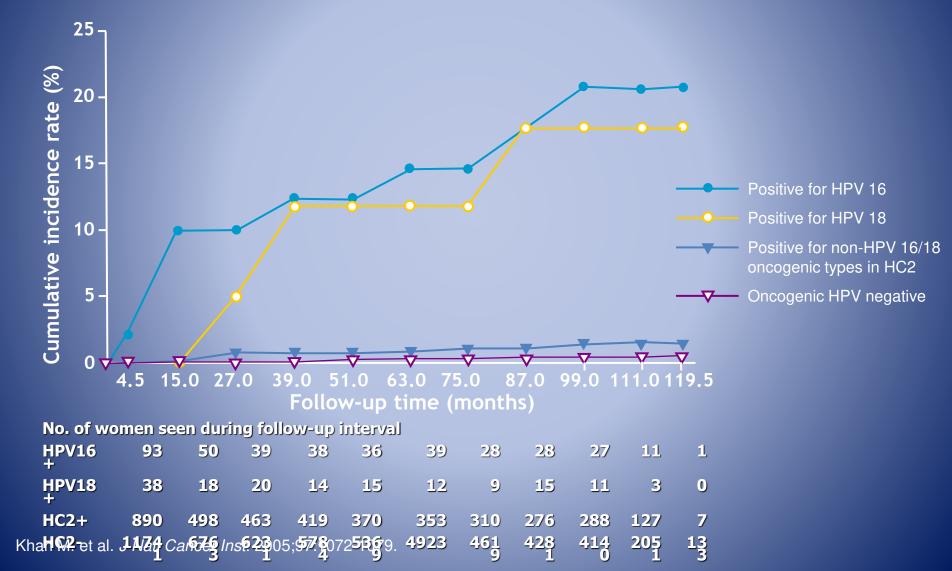
Cumulative Incidence of Cervical Precancer/Cancer After A Single HC2 Test



Portland

HC2=Hybrid Capture 2 HPV Test. Sherman ME et al. *J Natl Cancer Inst.* 2003;95:46-52.

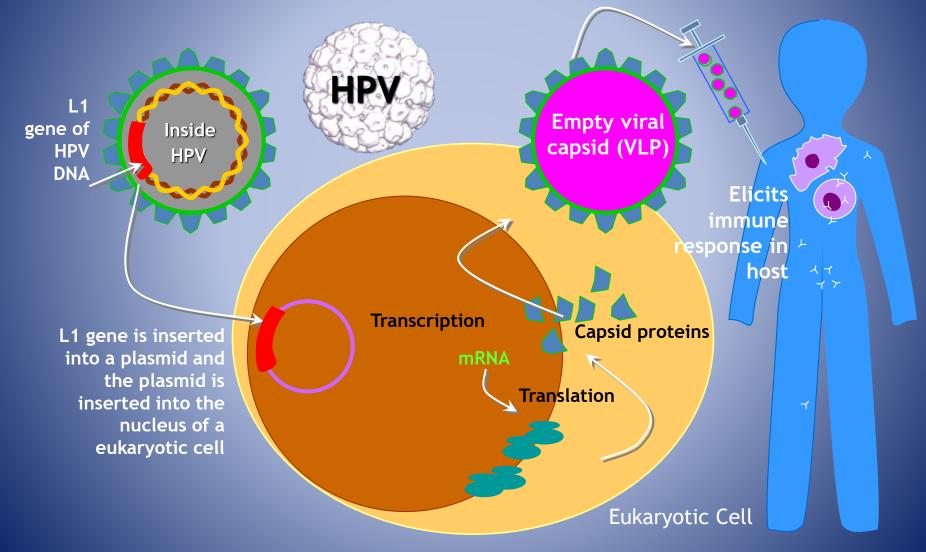
Cumulative Incidence of CIN 3+ in 12,976 Women Older Than 30 Years of Age



HPV Types in Cancer

•	16	54%
•	18	16%
•	33	4.4%
•	45	3.7%
•	31	3.5%
•	58	3.4%
•	35	1.8%
•	59	1.1%
•	56,51,39,73,68,82,	

HPV L1 Virus-Like Particle (VLP) Vaccine Synthesis



HPV=human papillomavirus; mRNA=messenger RNA; VLP=virus-like particles.

Gardasil – Merck HPV 6, 11, 16, 18 vaccine SKB HPV 16-18

- FDA approved- females and males
- 9-45 yrs
- Target age 9
- Health Dept+CDC make it free
- AGE <18 VFC

Clinical Impact of HPV Infection

Cervical cancer (CIN)

- 60 million Pap tests
- 3 million abnormal Paps
- 300,000 cases of high-grade dysplasia (CIN 2/3)
- 9710 cervical cancer cases (3700 deaths)
- Vulvar cancer (VIN) 3740 cases, 880 deaths
- Vaginal cancer (VaIN) 2420 cases, 820 deaths
- HEAD AND NECK IS FASTEST GROWING
- Anogenital warts & anal cancer in women and men
 - 1.4 million annual subject-visits for care
 - 4660 anal cancer cases

ValN=vaginal intraepithelial neoplasia; VIN=vulvar intraepithelial neoplasia. Source: National Cancer Institute and American Cancer Society.

Impact on Screening

- 75% reduction of cervical cancer in 25 years
 - HPV 16 50-60%
 - HPV 18 20-30%
- Decrease in CIN 3
- ASC/LSIL continue with less CIN 3
- Decrease in cost-effectiveness of cervical cytology and colpo

Endometrial Cancer

1/30 Lifetime RiskincreasingCases: 69,129Deaths: 13,250

White

- BMI 40- 10%
- MORE GRADE 1
- > 65 yrs 80.8% 5 yr survival

Blacks

- MORE SEROUS
- ADVANCED STAGE
- >65 yrs -53.3%
 - 5 yr survival

Etiology

• Type I- survival

- Low Grade
- Unopposed estrogen
- Obesity
- Diabetes
- Anovulation
- Colon cancer
- Type II- death
 - P53 Serous carcinoma
 - Associated with breast cancer
 - Age
 - tamoxifen

Prevention

- Lean body weight
- Mirena IUD- progestin
- Aromatase inhibitors instead of tamoxifen
- Lynch syndrome screening- prophylaxis

Early Detection- OBESE POPULATION

- PROGESTIN CHALLENGE TEST
- PROVERA 10 MG X 10 DAYS PO
- Biopsy for bleeding
- LEVONORGESTREL IUD- PROGESTIN FOR LIFE
- BMI 40= 10% LESION- CANCER OR AEH
- BMI 30 4% (AGE)
- Endometrial hyperplasia
- ATYPICAL ENDOMETRIAL HYPERPLASIA AEH
 - Hysterectomy
 - 40% of Atypical endometrial hyperplasia patients will have cancer