Cancer Screening and Prevention Saving Women's Lives

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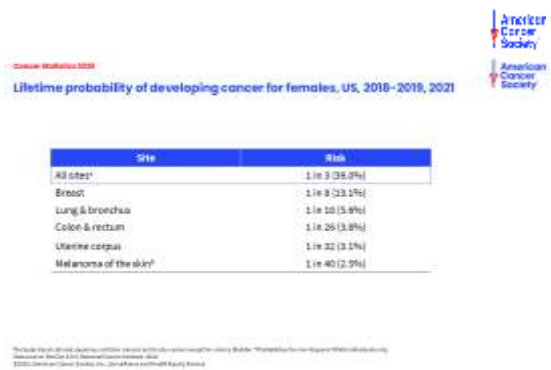
Gynecologic Oncology
Stephenson Cancer Center



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

Cancer Statistics 2025

Estimated number of new cancer cases in the US in 2025

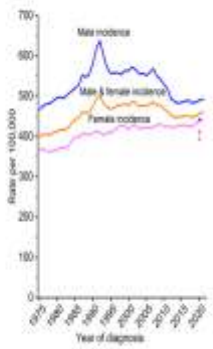
American Cancer Society

Male			Female		
Prostate	313,780	30%	Breast	316,950	32%
Lung & bronchus	130,180	13%	Lung & bronchus	115,920	12%
Colon & rectum	81,860	8%	Colon & rectum	71,830	7%
Urinary bladder	65,280	6%	Uterine corpus	69,120	7%
Melanoma of the skin	62,550	6%	Melanoma of the skin	44,410	4%
Kidney & renal pelvis	52,430	5%	Non-Hodgkin lymphoma	35,230	4%
Non-Hodgkin lymphoma	45,140	4%	Pancreas	32,490	3%
Oral cavity & pharynx	42,580	4%	Thyroid	31,200	3%
Leukemia	30,720	3%	Kidney & renal pelvis	28,530	3%
Pancreas	34,950	3%	Leukemia	28,130	3%
All sites	1,893,150		All sites	998,660	

Cancer Statistics 2025

Trends in cancer incidence rates, US, 1975–2021

American Cancer Society



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

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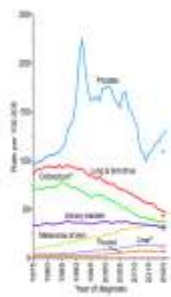

Cancer Statistics 2021

American Cancer Society

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

Site	Risk
All sites[1]	1 in 3 (38.9%)
Prostate	1 in 8 (12.8%)
Lung & bronchus	1 in 17 (5.8%)
Colon & rectum	1 in 24 (4.1%)
Melanoma of the skin[2]	1 in 29 (3.5%)
Kidney & renal pelvis	1 in 45 (2.2%)

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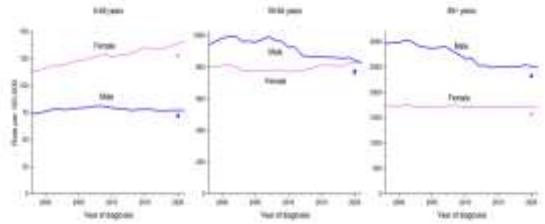
Trends in cancer incidence rates by sex and age, 1998-2021



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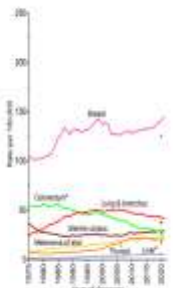
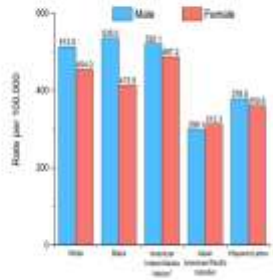
Trends in cancer incidence rates among females, US, 1975-2021



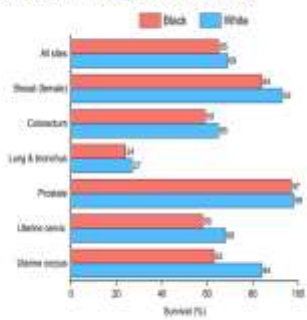
Cancer incidence rates by race and ethnicity, US, 2017–2021



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	38	43	51
Pancreas	3	4	13
Prostate	68	97	97
Uterine cervix	69	73	67
Uterine corpus	87	84	81

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



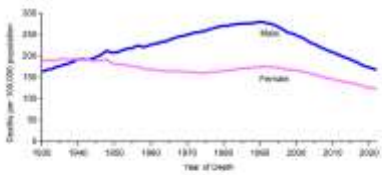
Estimated number of new cancer deaths in the US in 2025

American Cancer Society

Male			Female		
Lung & bronchus	64,370	28%	Lung & bronchus	46,590	21%
Prostate	35,770	11%	Breast	42,170	34%
Colon & rectum	28,900	9%	Pancreas	24,930	8%
Pancreas	27,970	8%	Colon & rectum	24,080	8%
Liver & intrahepatic bile duct	19,210	6%	Uterine corpus	13,860	5%
Leukemia	13,920	4%	Ovary	12,730	4%
Esophagus	12,940	4%	Liver & intrahepatic bile duct	10,660	4%
Urinary bladder	12,840	4%	Leukemia	10,040	3%
Non-Hodgkin lymphoma	11,050	3%	Non-Hodgkin lymphoma	8,230	3%
Brain & other nervous system	10,170	3%	Brain & other nervous system	8,160	3%
All sites	**323,900**		**All sites**	**294,220**	

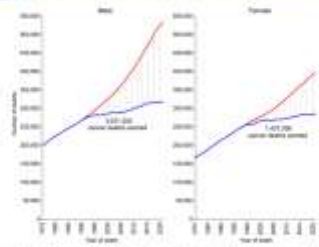
Trends in cancer death rates, US, 1975–2022

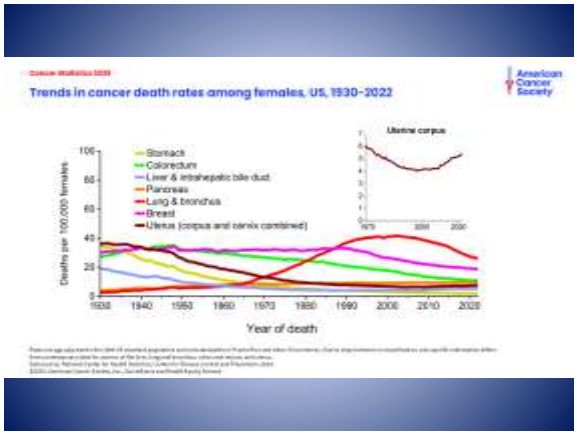
American Cancer Society

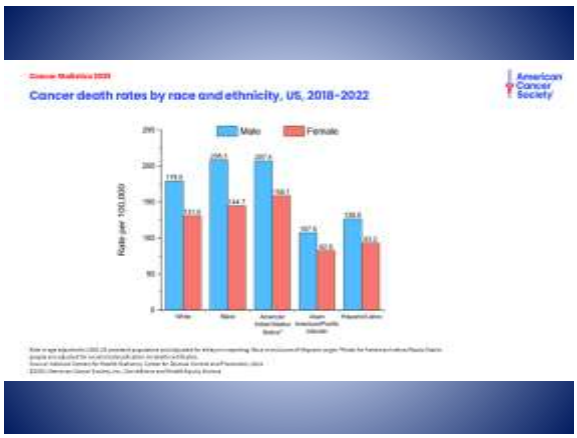


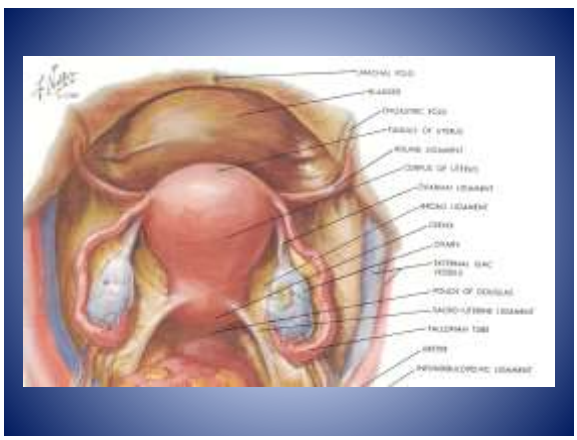
Total number of cancer deaths averted in men (1991 onward) and women (1992 onward), US

American Cancer Society




Trends in cancer death rates among females, US, 1930–2022
American Cancer Society
Stomach
Colorectum
Liver & intrahepatic bile duct
Pancreas
Lung & bronchus
Breast
Uterus (corpus and cervix combined)
Uterine corpus
Deaths per 100,000 females
Year of death

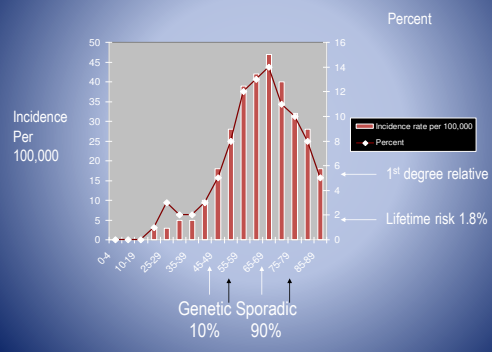

Cancer death rates by race and ethnicity, US, 2018–2022
American Cancer Society
Male
Female
Rate per 100,000



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



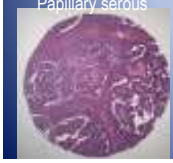
Stromal cell cancers (7%):
Granu
Sertoli

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

Naora H *Nat Rev Cancer* 2005

Epithelial cell cancers (90%)

Papillary serous



Endometrioid

Clear cell

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

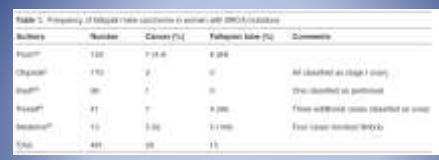
- Age
- Family History RR=2.8 1FDR, 4.6 2FDR
- BRCA1 60%
- BRCA2 30%
- Lynch II Syndrome (HNPCC) 13%
- Endometriosis 3%
- Infertility/Nulliparity
- PCOS

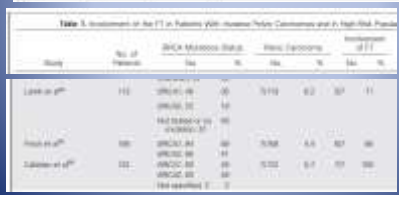
Protective Factors

- 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.

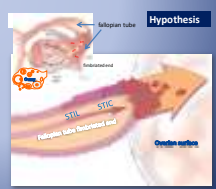
Occult RRSO malignancy is often tubal



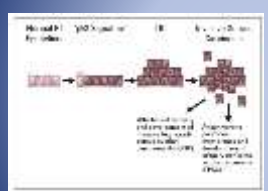


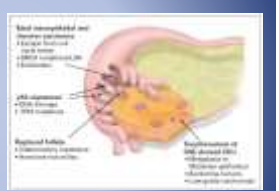
Serous Tubal Intra-epithelial Carcinoma (STIC) has same TP53 mutations as invasive tumors

- Not circumstantial
- Quite convincing
- Precursor lesion identified



Models of 'Ovarian' Tumorigenesis



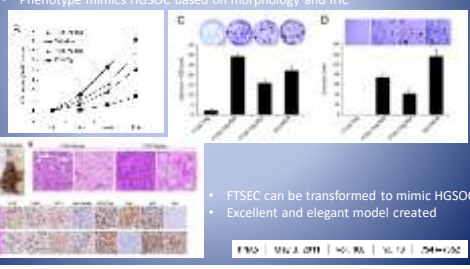


Levanon K et al JCO 2008

Modeling high-grade serous ovarian carcinogenesis from the fallopian tube

Alison M. Kurst[1], Karen Lounsbury[2,3], and Ronny Drapkin[2,3,4]

- 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



- FTSEC can be transformed to mimic HGSOC
- Excellent and elegant model created

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

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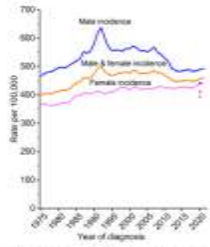

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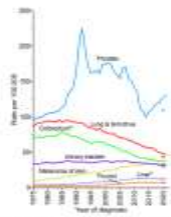

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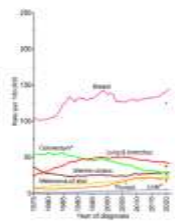

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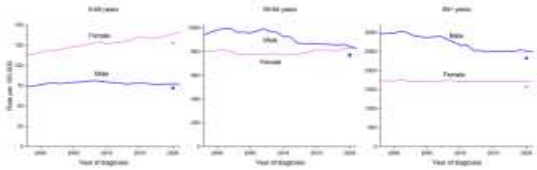
Trends in cancer incidence rates by sex and age, 1998–2021



Cancer Statistics 2025

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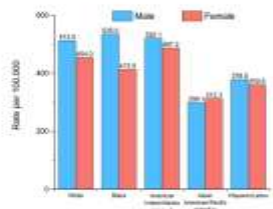
Cancer incidence rates by race and ethnicity, US, 2017–2021



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

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Cancer Statistics 2021

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

Site	Risk
All sites*	1 in 3 (38.9%)
Breast	1 in 8 (13.1%)
Lung & bronchus	1 in 16 (5.8%)
Colon & rectum	1 in 26 (3.8%)
Uterine corpus	1 in 32 (3.1%)
Melanoma of the skin†	1 in 40 (2.5%)

Cancer Statistics 2021

American Cancer Society

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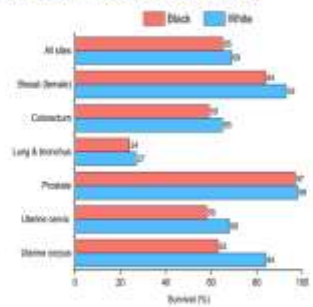
Cancer Statistics 2021

American Cancer Society

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



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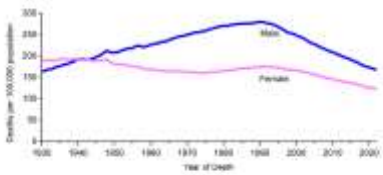
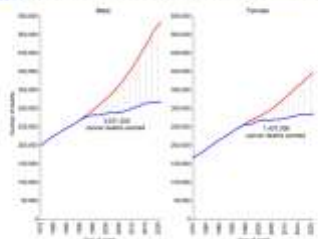


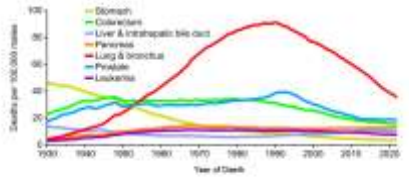
Cancer Statistics 2025

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

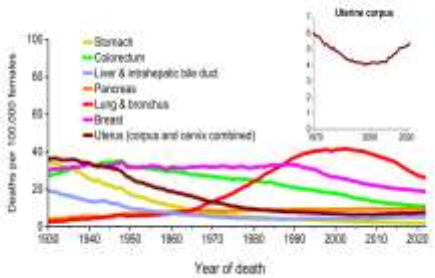
American Cancer Society



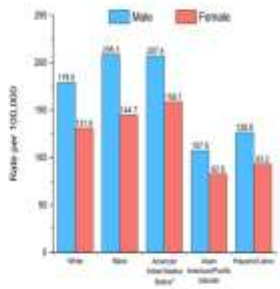
Trends in cancer death rates among males, US, 1930-2022

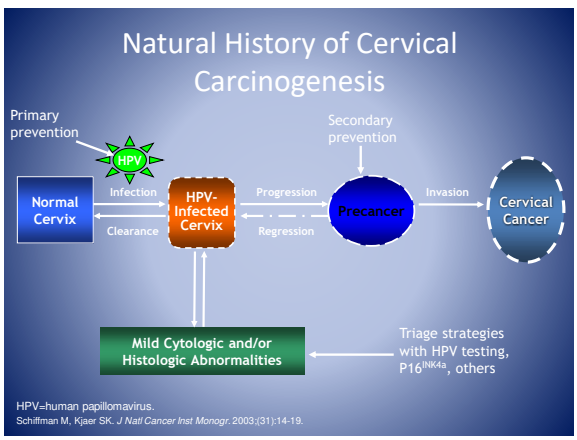


Trends in cancer death rates among females, US, 1930-2022

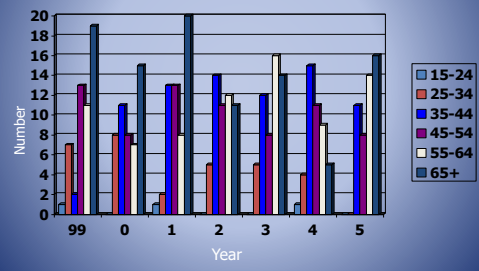


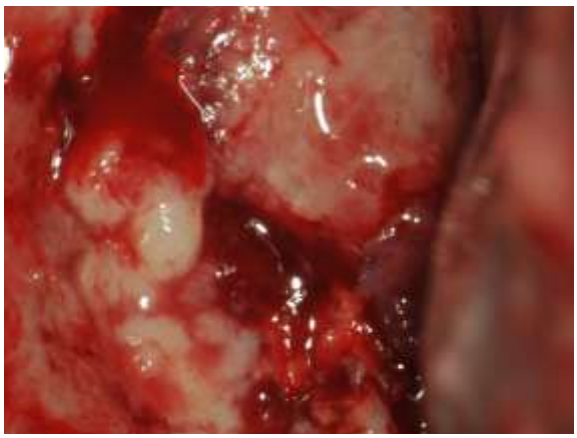
Cancer death rates by race and ethnicity, US, 2018-2022



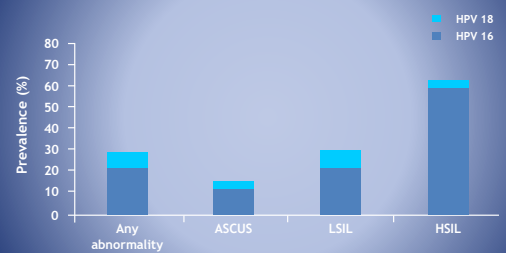

Natural History of Cervical Carcinogenesis
Primary prevention
HPV
Secondary prevention
Normal Cervix
Infection
Clearance
HPV-Infected Cervix
Progression
Regression
Precancer
Invasion
Cervical Cancer
Mild Cytologic and/or Histologic Abnormalities
Triage strategies with HPV testing, P16INK4a, others
HPV=human papillomavirus.
Schiffman M, Kjaer SK. J Natl Cancer Inst Monogr. 2003;(31):14-19.

Cervical Cancer Deaths Oklahoma





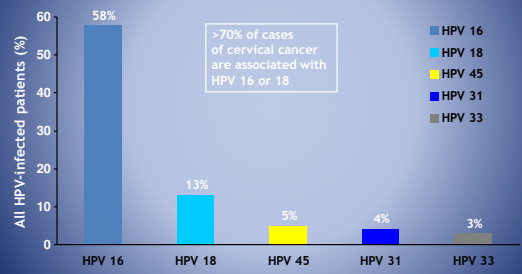
HPV 16 and 18 Prevalence by Cytology Sentinel Surveillance (2003-2004)



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.

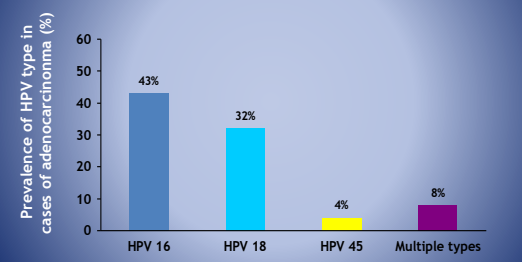
Most Prevalent HPV Types That Cause Cervical Squamous Cancer



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



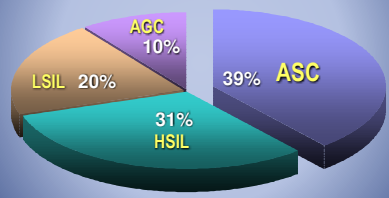
HPV DNA was detected in 93% of patients with cervical adenocarcinoma.

Castellsague X et al. *J Natl Cancer Inst.* 2006;98:303-315.

Absolute Risk of CIN 2+

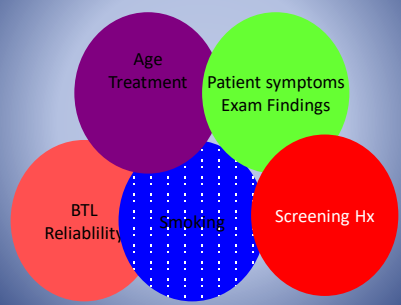
- CIN 1 post LSIL – 12%
- ASC/HPV+ = LSIL = 25%
- ASC-H- 25-40%
- AGC – 30-50%
- HSIL- 60-80%
- HSIL pap and Low Grade Colpo = 40%
- HSIL and High Grade colpo = 70-85%
- Post LEEP for CIN 3 = 5-15%
- Post Cone for AIS = 8%

Pap Diagnoses Preceding Histologic High-Grade Neoplasia



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

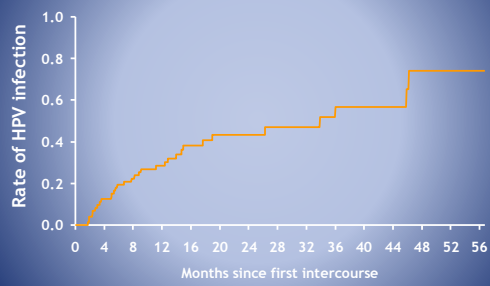
Risk of Cervical Cancer



Limitations of Secondary Prevention

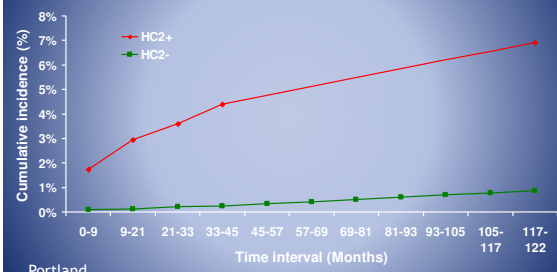
- Screening compliance
- Identifying true precursors from 3 million ASC and LSIL smears per year in the US
- Over treatment of patients with trivial lesions
- All of these problems are overcome if primary prevention with vaccines works

Risk of Genital HPV Infection From Time of First Sexual Intercourse



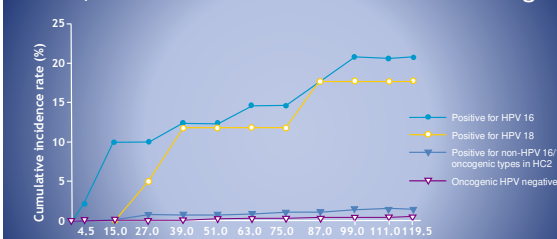
Winer RL et al. *Am J Epidemiol.* 2003;157:218-226.

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



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



No. of women seen during follow-up interval

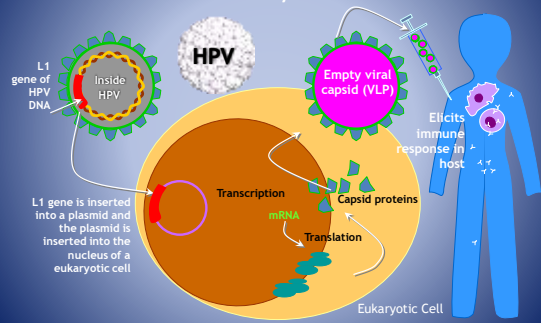
HPV16+	93	50	39	38	36	39	28	28	27	11	1
HPV18+	38	18	20	14	15	12	9	15	11	3	0
HC2+	890	498	463	419	370	353	310	276	288	127	7
HC2-	1174	676	622	578	536	4923	461	428	414	205	13
	1	3	1	4	9		9	1	0	1	3

Khan MJ et al. *J Natl Cancer Inst.* 2005;97:1072-1079.

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

VaIN=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

CA: A Cancer Journal for Clinicians. 53(1):27-43, 2003.

Endometrial Cancer

1/30 Lifetime Risk- increasing

Cases: 69,129

Deaths: 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