Cancer Screening Guidelines

Diablo Valley Oncology/Hematology Medial Group



Dr. Tiffany Svahn



Dr. Robert Robles



Dr. Gigi Chen



Dr. Jewel Johl



Estimated Cancer Deaths in the US in 2013

Lung & bronchus	28%
Prostate	10%
Colon & rectum	9%
Pancreas	6%
Liver & intrahepatic bile duct	5%
Leukemia	49
Esophagus	49
Urinary bladder	49
Non-Hodgkin	3%
lymphoma	
Kidney & renal pelvis	3%
All other sites	249



26%	Lung & bronchus
14%	Breast
9%	Colon & rectum
7%	Pancreas
5%	Ovary
4%	Leukemia
3%	Non-Hodgkin Iymphoma
3%	Uterine corpus
2%	Liver & intrahepatic bile duct
2%	Brain/other nervous system
25%	All other sites



Cancer Death Rates* Among Men, US, 1930-2009



*Age-adjusted to the 2000 US standard population. Source: US Mortality Data 1960-2009, US Mortality Volumes 1930-1959, National Center for Health Statistics, Centers for Disease Control and Prevention.

Cancer Death Rates* Among Women, US,1930-2009



*Age-adjusted to the 2000 US standard population. Source: US Mortality Data 1960-2009, US Mortality Volumes 1930-1959, National Center for Health Statistics, Centers for Disease Control and Prevention.

Cancer Death Rates* by Race and Ethnicity, US, 2005-2009



*Per 100,000, age-adjusted to the 2000 US standard population. *Persons of Hispanic origin may be of any race.



Estimated New Cancer Cases* in the US in 2013



*Excludes basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder.



The Lifetime Probability of Developing Cancer for Men, 2007-2009*

Site	Risk
All sites [†]	1 in 2
Prostate	1 in 6
Lung and bronchus	1 in 13
Colon and rectum	1 in 19
Urinary bladder [‡]	1 in 26
Melanoma [§]	1 in 35
Non-Hodgkin lymphoma	1 in 43
Kidney	1 in 49
Leukemia	1 in 63
Oral Cavity	1 in 66
Stomach	1 in 92

* For those free of cancer at beginning of age interval.

† All sites exclude basal and squamous cell skin cancers and in situ cancers except urinary bladder.

‡ Includes invasive and in situ cancer cases

§ Statistic for white men.

Source: DevCan: Probability of Developing or Dying of Cancer Software, Version 6.6.1 Statistical Possarab and Applications Branch, National Cancer Institute, 2012.

The Lifetime Probability of Developing Cancer for Women, 2007-2009*

Site	Risk
All sites [†]	1 in 3
Breast	1 in 8
Lung & bronchus	1 in 16
Colon & rectum	1 in 21
Uterine corpus	1 in 38
Non-Hodgkin lymphoma	1 in 52
Urinary bladder [‡]	1 in 87
Melanoma [§]	1 in 54
Ovary	1 in 72
Pancreas	1 in 69
Uterine cervix	1 in 147

* For those free of cancer at beginning of age interval. † All sites exclude basal and squamous cell skin cancers and in situ cancers except urinary bladder.

Includes invasive and in situ cancer cases

§ Statistic for white women.

Source: DevCan: Probability of Developing or Dying of Cancer Software, Version 6.6.1 Statistical Passarah and Applications Branch, National Cancer Institute, 2012.

Lung Cancer Screening



Trends in Cigarette Smoking, Adults 18 and Older, US, 1965-2011



Redesign of survey in 1997 may affect trends. Estimates are age adjusted to the 2000 US standard population. Source: National Health Interview Survey, National Center for Health Statistics, Centers for Disease Control and Prevention, 2012.



Trends in Tobacco Use and Lung Cancer Death Rates* in the US



*Age-adjusted to 2000 US standard population.

Source: Death rates: US Mortality Data, 1960-2009, US Mortality Volumes, 1930-1959, National Center for Health Statistics, Centers for Disease Control and Prevention. Cigarette consumption: US Department of Agriculture, 1900-2007.

Lung cancer screening

- Early trials of chest x-ray screening in males at high risk for lung cancer found no OS benefit for X-ray alone or x-ray +sputum cytology.
- Large randomized trial PLCO trial of single view chest x-ray did not find reduction in lung cancer incidence or mortality with screening.



Evidence for low dose CT screening

- NLST: large randomized trial of screening LDCT in high risk individuals, demonstrated a lung cancer mortality benefit of 20%. That is, screening would prevent 3.9 deaths over 6 years per 1000 persons. In US, 8.6 million people in US would meet criteria for screening, therefore, could potentially avert 12,000 deaths from lung cancer per year in the US.
- Issue is the cost effectiveness.



LDCT lung cancer screening

- Low-dose CT (LDCT): noncontrast CT study obtained during a single maximal inspiratory breath-hold with a scanning time under 25 seconds.
- Radiation dose exposure is less than a third of a standard-dose diagnostic chest CT examination



Lung Cancer Screening

- USPSTF 2013: recommend annual low dose CT scan screening for high risk individuals
- High Risk is defined as: ages 55 to 80 with 30 pack year history of smoking and current smoker or quit within past 15 years
- ACS 2013: recommend annual low dose CT scan screening for high risk individuals.
- Informed individual decision making before testing



Counseling for lung cancer screening

- Smoking cessation is a more proven and powerful intervention for preventing death and complications from lung cancer and other diseases than screening.
- Lung cancer screening requires an ongoing commitment; cancers are detected on initial and annual studies, and a single baseline study is insufficient.
- The most likely "positive" result of screening is detection of benign nodules requiring further evaluation, and this evaluation may require invasive studies, possibly even surgery.



Lung cancer screening

- Lung cancer screening program should involve a multidisciplinary team experienced in evaluation and management of early lung cancer.
- Smoking cessation program needs to be integrated in to the screening program.



Breast Cancer Screening



Overview

- Most common cancer in women
- Second most common cause of cancer death in women
- >240,000 new diagnoses in US in 2013
- >41,000 deaths in US in 2013
- Decreased mortality
- More than 2.5 million breast cancer survivors in US now



Breast Cancer Screening Guidelines

Annual mammograms beginning at age 40

Clinical breast exam:

- > Ages 20-39, as part of a periodic health exam at least every 3 years
- > Ages 40+, prior to mammogram as part of a periodic health exam annually.

Breast self-exam:

Optional; beginning in their early 20s, women should be told about the benefits and limitations of breast-self examination. Women should know how their breasts normally feel and report any breast changes promptly to their health care providers.



Multiple Guidelines

Table 4. Guidelines for Breast-Cancer Screening.*					
Organization	Year Guidelines Issued	d Mammography	Clinical Breast Examination	Breast Self- Examination	
USPSTF	2009	Age 50–74 yr, every 2 yr; age 40–49 yr and age ≥75 yr, individualize the decision (every 2 yr, if performed)	Insufficient evidence for recommendation	Not recommended	
American Cancer Society	2010	Age ≥40 yr, annually†	Age 20–39 yr, every 3 yr	Optional, ≥20 yr of age	
			Age ≥40 yr, annually		
National Comprehensive	2011	Age ≥40 yr, annually†	Age 20–39 yr, every 1–3 yr	Optional, \geq 20 yr of age	
Cancer Network			Age ≥40 yr, annually		
National Cancer Institute	2010	Age ≥40 yr, every 1–2 yr†	Age and frequency not stated	Optional	
American College of Physicians	2007	Age 50–74 yr, every 1–2 yr‡; age 40–49 yr, individualize the decision (every 1–2 yr, if performed)	Not stated	Not stated	
American College of Obstetricians and Gynecologists	2003	Age 40–49 yr, every 1–2 yr; age ≥50 yr, annually†	Age ≥20 yr, annually	Optional	
American College of Radiology	2008	Age ≥40 yr, annually†	Not stated	Not stated	
Canadian Task Force on Preventive Health Care	1998–2001 e	Age 50–69 yr, every 1–2 yr; age 40–49 yr, individualize the decision (every 1–2 yr, if performed)	Every 1–3 yr, with periodic health examinations, for ages <40 and >70 yr	Not recommended for women 40–69 yr of age Optional, ≥70 yr of age	
National Health Service, United Kingdom	2011	Age 47–73 yr, every 3 yr	Not stated	Not stated	

* USPSTF denotes U.S. Preventive Services Task Force.

† No upper age limit was specified.

⁺ These recommendations have not been updated since 1989.



Breast Exam

- SBE USPSTF recommends against teaching - ACS - SBE is an option for some women in order to know what is normal (Teach correctly if woman chooses SBE)
- CBE 5% of breast cancer identified by CBE alone
- Most important to be done in conjunction with mammography



Mammography

- Several large randomized trials have addressed effectiveness (0-25% reduction in risk of death)
- Cochrane Breast Cancer Group did metaanalysis of 7 trials - screening reduces breast cancer mortality
- Universal recommendation for screening 50-69 years
- Meta-analysis
 - 50's 14% reduction in Breast CA deaths
 - 60's 32% reduction in Breast CA deaths



Age Considerations

- Age 70 and older based on overall health, life expectancy, ability to tolerate treatment
- Age 40-49:
- No single randomized trial shows benefit
- Meta-analysis including 40's showed 15-20% risk reduction
- Breast density (decrease sensitivity)



Breast Density and Ultrasound

- Breast density: percent mammography density (PMD) on mammogram
- Impacts detection of breast cancer
- Independent risk factor for breast cancer (4.6x increased risk)
- No data showing survival benefit of screening with supplemental whole breast ultrasound screening (WB-US) in addition to mammography
- Not recommended by NCCN, ACS, or USPSTF
- Incremental cancer detection rate 3.6/1000



ACS Guidelines for MRI Screening

Recommend Annual MRI Screening (Based on Evidence*)

BRCA mutation

First-degree relative of BRCA carrier, but untested

Lifetime risk \sim 20–25% or greater, as defined by BRCAPRO or other models that are largely dependent on family history

Recommend Annual MRI Screening (Based on Expert Consensus Opinion⁺)

Radiation to chest between age 10 and 30 years

Li-Fraumeni syndrome and first-degree relatives

Cowden and Bannayan-Riley-Ruvalcaba syndromes and first-degree relatives

Insufficient Evidence to Recommend for or Against MRI Screening‡

Lifetime risk 15–20%, as defined by BRCAPRO or other models that are largely dependent on family history

Lobular carcinoma in situ (LCIS) or atypical lobular hyperplasia (ALH)

Atypical ductal hyperplasia (ADH)

Heterogeneously or extremely dense breast on mammography

Women with a personal history of breast cancer, including ductal carcinoma in situ (DCIS)

Recommend Against MRI Screening (Based on Expert Consensus Opinion)

Riable Valley ONCOLOGY/HEMATOLOGY

Women at <15% lifetime risk

3D Mammography

- JAMA paper published 6/25/2014 digital mammogram +/- tomosynthesis
- 1 additional cancer detected per 1000 scans done
 - 16% decrease in false positives
- no information on clinical outcomes/ survival



Prostate Cancer Screening



Magnitude of prostate cancer in U.S.

- In 2014, 233,000 new cases of prostate cancer.
- 29,480 deaths from prostate cancer.
- 1 in 7 American men will be diagnosed with prostate cancer.
- 1 in 30 will eventually die of prostate cancer.
- Over the past 20 years, mortality from prostate cancer has fallen by 45%
- Coinciding with the introduction of PSA testing



Screening modalities-DRE

- Digital Rectal Exam (DRE)
- Although PSA is more sensitive and specific than DRE, DRE is still helpful to detect cancers that could be missed by PSA cutpoint.



Screening modality-PSA

- PSA-a glycoprotein secreted by prostatic epithelial cells
- Commercially available tests for PSA appear to be equally good.
- PSA values from different assays cannot be directly compared.
- PSA an be elevated by trauma, infection, ejaculation, and surgery.



Available screening trials

- 5 recent randomized controlled screening trials for prostate cancer.
- Let's review the 2 largest and most influential trials.



What is the data?

- European Randomized Study of Screening for Prostate Cancer (ERSPC) Trial (*NEJM 2009;* 360: 1320-8)
- 182,000 men randomized to PSA screening (mean q 4 years) or observation.
- After median follow up of 11 years, HR for prostate-specific death was 0.79.
- 21% reduction in risk of death from prostate cancer.
- 20-25% of control patients had a PSA test.



ERSPC Trial continued

- As trial matured, results improved:
- Number of men needed to be screened to detect one prostate cancer: 200
- Number of men with a diagnosed prostate cancer that needed to be treated to prevent one prostate cancer death: 5
- Analyses of individual country screening from trial confirmed overall results.



PLCO (JNCI 2012; 104: 125-132)

- US trial randomizing 76,685 men ages 55-74 to annual PSA + DRE x 4 years versus "usual care".
- After 13 years of follow-up, no difference in prostate-specific death rates between arms.
- However, 74% of men in "usual care" arm received at least one PSA test.
- So not really a true screening study.



Recommendations-Pro screening

- American Urologic Association
- National Comprehensive Cancer Network (NCCN)
- American Cancer Society



Recommendations-Against Screening

- United States Preventive Services Task Force
- American Society of Clinical Oncology



More screening controversies

- When to start screening
- When to stop screening
- How frequently to screen with PSA
- When to biopsy



NCCN screening recommendations

- 45-49 years old
- NI DRE and PSA>1-repeat every 1-2 years
- NI DRE PSA<1-repeat at age 50 yrs.
- >50 years old: NI DRE and PSA<3, repeat testing every 1-2 years.



When to biopsy (NCCN)

- PSA >3
- Suspicious DRE
- Excess risk based on multiple factors (family history, ethnicity, risk calculators)



Potential Harms

- 4% hospitalization rate after prostate biopsy (75% due to infections).
- Harm from treating indolent cancers
- Rate of "overtreatment" unknown



Colon Cancer Screening



Colorectal Cancer Basics

- Third-leading cause of cancer deaths in the U.S.
- Men and women are at equal risk
- Early detection
- Easier treatments
- Higher survival rates.
- More than one-third of colorectal cancer deaths could be avoided if all eligible individuals participated in regular screening.
- Colorectal cancer screening is safe and effective

Colon Cancer Risk

- Average risk population: 5%
- High risk population (2-6 x)
 - Family history of colon cancer
 - Family history of colon polyp
 - Personal history of colon cancer or polyp
 - Longstanding ulcerative colitis



Who should be screened?

- Average risk patients: Age 50, every 10 years
- High risk patients:
 - Family history of colon cancer: age 40, every 5 yrs
 - Family history of colon polyp: age 40, every 5 yrs
 - Personal history of colon polyp: every 5 yrs
 - Ulcerative Colitis: every 1-2 yrs after 8-15 yrs
 - HNPCC: start in 20s, every 1-2 years
 - FAP: Colectomy



Screening Guidelines

Increased Risk: Typically Age 40, 10 years prior or variable

- Personal history
 - Colorectal cancer
 - Adenomatous or polyps
- Family history one or more parents, siblings, or children
 - Colorectal cancer or adenomatous polyps
- Family history of multiple cancers
 - Including colorectal cancer, uterus, ovary and other organs
- Inflammatory bowel disease
 - Ulcerative colitis or Crohn's disease
- Inherited syndromes
 - Familial Adenomatous Polyposis (FAP)
 - Characterized by >100 polyps
 - Develop cancer by age 30
 - Lynch Syndrome: Hereditary Non-Polyposis Colon Cancer (HNPCC)
 - Not characterized by a large number of polyps
 - Family history of colorectal cancer among multiple family members in multiple generations

Average risk: Age 50 years old

African-Americans are at a higher risk : Should begin their screening at age 45 years old

- Diagnosed at a younger average age than other people Therefore, some experts suggest that African-Americans.
- Incidence is higher than any other population group
- Death rates is higher than any other population group
- Less likely than Caucasians to get screening tests
 - Detect colorectal polyps detected at a time when they cannot easily be removed
 - More likely to be diagnosed in advanced stages when there are fewer treatment
 options available
- May be genetic factors that contribute to the higher incidence of CRC
- African-American women have the same chance of getting CRC as men
 - Higher mortality from CRC than are women of any other ethnic or racial group.
- African-American patients are more likely to have polyps deeper in the colon (on the right side of the colon
- Surveillance, Epidemiology, and End Results (SEER) Study, 2014
 - Under current trends between 2010 to 2030, CRC increase expected:
 - 20 -34 year olds by 90- 124%
 - 35-49 year olds by 28-46%
 - >50 year olds: Significant decrease
 - Due to Obesity (Diet, Inactivity)



CRC & Polyps

"All Colon Cancer comes from Polyps but very few Polyps will ever become Colon Cancer"

- Size & Type Important
- Hyperplastic
- Adenomas
- < 1 cm: 99.5% Benign
- > 2 cm: 30-50% Cancerous







How to screen Colon Cancer?

- Fecal occult blood test (FOBT)
- Barium enema
- CT Colonography ("Virtual colonoscopy")
- Flexible sigmoidoscopy
- Colonoscopy



How to screen Colon Cancer continued

Emerging Technology

- Immunochemical Fecal Occult Blood Tests
- Detection of altered human DNA in stool samples
- Video Capsule Endoscopy



Colorectal Cancer Screening Guidelines*

Beginning at age 50, men and women should follow one of the following examination schedules:

Test	Time interval
Fecal occult blood test	Annual
Flexible sigmoidoscopy	5 yrs
Double contrast barium enema	5 yrs
Colonoscopy	10 yrs
CT Colonography	5 yrs

*For people at average risk; individuals at higher risk should talk with a doctor about a different testing schedule.



Detection: Early Cancer with Stool Assays

- Fecal Occult Blood Test (FOBT)
- Recommended annually for persons beginning at age 50
- Stool is tested in a laboratory for the presence of occult or hidden blood
- Collect the stool samples at home.
- Easy and inexpensive
- Does not detect pre-cancerous polyps
- If the FOBT is abnormal, you will require a regular colonoscopy for further evaluation
- Test affected by: cabbage, radish, red meat, Vitamin C, etc
- Collection of all 3 samples is important because test sensitivity improves with each additional stool sample
- Controlled trials with FOBT
- Screened patients have cancers detected at an early and more curable stage than unscreened patients
- Over time (8–13 years), each of the trials demonstrated significant reductions in CRC mortality of 15% to 33%



Detection: Early Cancer with Stool Assays

Fecal Immunohistochemical Test (FIT)

- FIT is a test that can detect hidden blood in the stool with great accuracy
- Available in a kit with which you can collect the stool samples at home
- Easy to perform and inexpensive
- Can only detect early cancers, not pre-cancerous polyps
- No special diet required
- If the FIT test is abnormal, you will require a regular colonoscopy for further evaluation.
- Latest Meta-Anaysis Study (Kaiser, Oakland : Ann Int Med 2014)
- Sensitivity : 79%
- Specificity: 94%

Stool DNA (sDNA)

- sDNA assesses for genetic DNA mutations
- Colorectal cancer cells that contain genetic DNA mutations are shed into the large bowel and passed into the stool.
- Not currently available in the U.S.
- Must have access to a working freezer as the stool specimen will need to be submitted in aspecially designed ice pack.
- Does not require a restricted diet
- The screening interval for sDNA is unknown at this time
- Most insurance does not cover this test

Detection: Early Cancer & Polyps with Imaging

Double Contrast Barium Enema

- Accepted as screening modality in 1997 for average risk individuals every 5 years
- Evaluates the colon in its entirety
- Coats the mucosal surface with high-density barium
- Distention with air introduced through a flexible catheter that is inserted into the rectum
- Multiple radiographs are acquired while varying the patient position
- Colonic preparation, usually a



24-hour dietary and laxative regimen, is essential for an optimal examination

- Sedation is not utilized
- Duration of the procedure averages about 20 to 40 minutes
- Mild to moderate discomfort due to distention



Detection: Early Cancer & Polyps with Imaging

Computed Tomographic (CT) Colonography

- Recommended every 5 years for average risk individuals
- Examination of your colon and rectum using a CT scanner
- Computer reconstructs images creating both 2- and 3dimensional views that allow a specially trained physician to "fly through" images of your colon and rectum to look for polyps and cancer
- Does not require sedation
- May be somewhat uncomfortable because air is put in your colon during the exam
- Need to take a preparation to cleanse your colon similar to a colonoscopy



If a polyp or other abnormality is discovered during the CT colonography, you will require a regular colonoscopy to biopsy or remove the abnormality or polyp



Early Detection: Endoscopy

Flexible sigmoidoscopy



Indicated for Average Risk Individuals every 5 years

- Endoscopic assessment from the rectum to the descending colon
- Assess for left sided polyps and disease: direct biopsies obtained
- No sedation administered
- Bowel preparation with enemas after drinking only clear liquids for 12 to 24 hours
- Mild to Severe discomfort due to air and manipulation of scope
- Procedure time 10 to 20 minutes while patient lies on left-side
- A 2010 British study showed sigmoidoscopy reduced overall colorectal cancer incidence and mortality
- Overall colon-cancer mortality was reduced by 43% (1 cancer per 200 screenings)



Early Detection: Endoscopy

Colonoscopy

Indicated for Average and Increased Risk Individuals

- Examination of the colon by use of a long, flexible, lighted tube called the colonoscope
- View the entire colon and rectum for polyps or cancer and during the same exam remove pre-cancerous polyps
- Single best screening exam for colorectal cancer
- Only method that combines both screening and prevention (by removal of pre-cancerous polyps)
- Performed in an ambulatory surgical center or a hospital
- Bowel preparation (oral laxative) after 24 hours of a liquid diet
- Sedated procedure (typically no discomfort during procedure)



Cervical Cancer Screening



Trends in Pap Test Prevalence* by Health Insurance Status, US, 2000-2010



*A Pap test within the past three years among women age 21-65; estimates age-adjusted to the 2000 US standard population. Source: National Health Interview Survey, National Center for Health Statistics, Centers for Disease Control and Prevention.



Cervical Cancer Screening

- Starting age:
 - For women at average risk of cervical cancer, the US guidelines recommend screening be initiated at age 21
 - ACOG recommends initiating screening at the time of initial intercourse for women under 21 who have HIV infection or who are on chronic immunosuppressive therapy for systemic lupus erythematosus or post organ transplantation.



Cervical Cancer Screening Guidelines

- Cervical cancer screening should begin at age 21.
- Preferred screening test/s and frequency vary by age:

<u>Age</u>	Frequency	<u>Test</u>
21-29	Every 3 yrs	Pap test*
30-65+	Every 5 yrs	HPV & Pap tests

*Conventional or liquid-based test.

†Every 3 years with the Pap test alone is acceptable.

- Women should stop screening:
 - 1. At age 66 with adequate negative prior screening
 - > \geq 3 consecutive negative Pap tests within 10 yrs, most recent within 5 yrs **OR**
 - \geq 2 consecutive negative HPV and Pap tests within 10 yrs, most recent within 5 yrs
 - 2. After hysterectomy



Stopping age

- The USPSTF suggest stopping screening at age 65 for women who have had adequate recent screening.
- Adequate screening is defined as three consecutive negative cytology tests or two consecutive negative HPV/Pap co-tests in the 10 years prior to stopping, with the most recent test within five years.
- Women should continue testing for 20 years after management of a high-grade precancerous lesion.



Screening Modality

- No difference between liquid-based and conventional smear cytology.
- All guidelines recommend only cytology screening for women aged 21 to 29 years.
- Frequency The frequency of testing is dependent upon the screening test used.
- For cytology is the only option for women aged 21 through 29 years, USPSTF, ACS/ASCCP/ASCP, and ACOG guidelines recommend testing every three years.
- For co-testing with cytology and HPV tests for women over 30 years of age, the USPSTF, ACS/ASCCP/ASCP, and ACOG recommend five years intervals.



High Risk Groups

- Certain risk groups that may require more frequent screening: HIV infection, immunosuppression, or in utero DES exposure.
- ACOG recommends annual screening for women who have been treated in the past for CIN 2, CIN 3, or cervical cancer.
- ACOG recommends screening twice in the first year for women who are immunocompromised and annually thereafter.



Trends in Five-year	Relative	Cancer	Survival	Rates	(%),	1975-2008
---------------------	----------	--------	----------	-------	------	-----------

Site	1975-1977	1987-1989	2002-2008
All sites	49	56	68
Breast (female)	75	84	90
Colon	51	61	65
Leukemia	34	43	58
Lung & bronchus	12	13	17
Melanoma	82	88	93
Non-Hodgkin lymphoma	47	51	71
Ovary	36	38	43
Pancreas	2	4	6
Prostate	68	83	100
Rectum	48	58	68
Urinary bladder	73	79	80

5-year relative survival rates based on patients diagnosed from 2002 to 2008, all followed through 2009. Source: SEER Cancer Statistics Review 1975-2009 (SEER 9 registries), National Cancer Institute, 2012.

