

Screening Tests in Older Individuals

Preventive Medicine in Adults

- Which conditions cause the largest burden of suffering for older adults?
- For these conditions, identify preventive services which have demonstrated effectiveness in improving patient outcomes

Cancers With Greatest Mortality in US

- Lung
- Colorectal
- Breast
- prostate

US Preventive Services Task Force

- Convened by US Public Health Service in 1984
- Now sponsored by the Agency for Health Care Research and Quality
- Mission is to:
 - Evaluate the benefits of individual services based on age, gender, and risk factors for disease
 - Make recommendations about which preventive services should be incorporated routinely into primary health care.

- Supported by Evidence-based Practice Center (EPC) which conducts systematic reviews of the evidence on specific topics in clinical prevention

Preventive Measures

- Primary Prevention, avert the development of disease
 - Immunization
 - Life-style adaptations
 - Smoking cessation
 - Exercise
 - Chemoprophylaxis
 - Aspirin to prevent heart disease and stroke

- Secondary prevention – early detection and treatment of asymptomatic disease – screening for:
 - Cancer
 - Hearing and vision impairment
 - Osteoporosis
 - Hypertension
 - Abdominal aortic aneurysm

- Tertiary prevention – identifying established conditions to prevent further morbidity or functional decline
 - Cognitive problems
 - Disorders of gait and balance
 - Malnutrition
 - Urinary incontinence

Cancer Screening in Elderly Patients

- Decisions depend upon:
 - Quantitative estimates of life expectancy
 - Risk of cancer death
 - Screening outcomes from published data

Bias in Cancer Screening Research

- Lead time bias – underlining disease is not able to be affected by treatment
 - Earlier diagnosis – but does not alter time until death
- Length bias – a test identifies a clinically slowly progressive or non-progressive disease that would never have become a symptomatic problem
- Selection bias – people willing to be screened for cancer may not reflect the population as a whole

Risk of Dying

- Maximum potential benefit of screening – patient's risk of dying of a screen-detectable cancer
 - Not risk of diagnosis of cancer
- Risk of death due to cancer
 - Life expectancy of individual (decreases with age)
 - Age-specific mortality rate of particular cancer (increases with age)

Estimating Life Expectancy

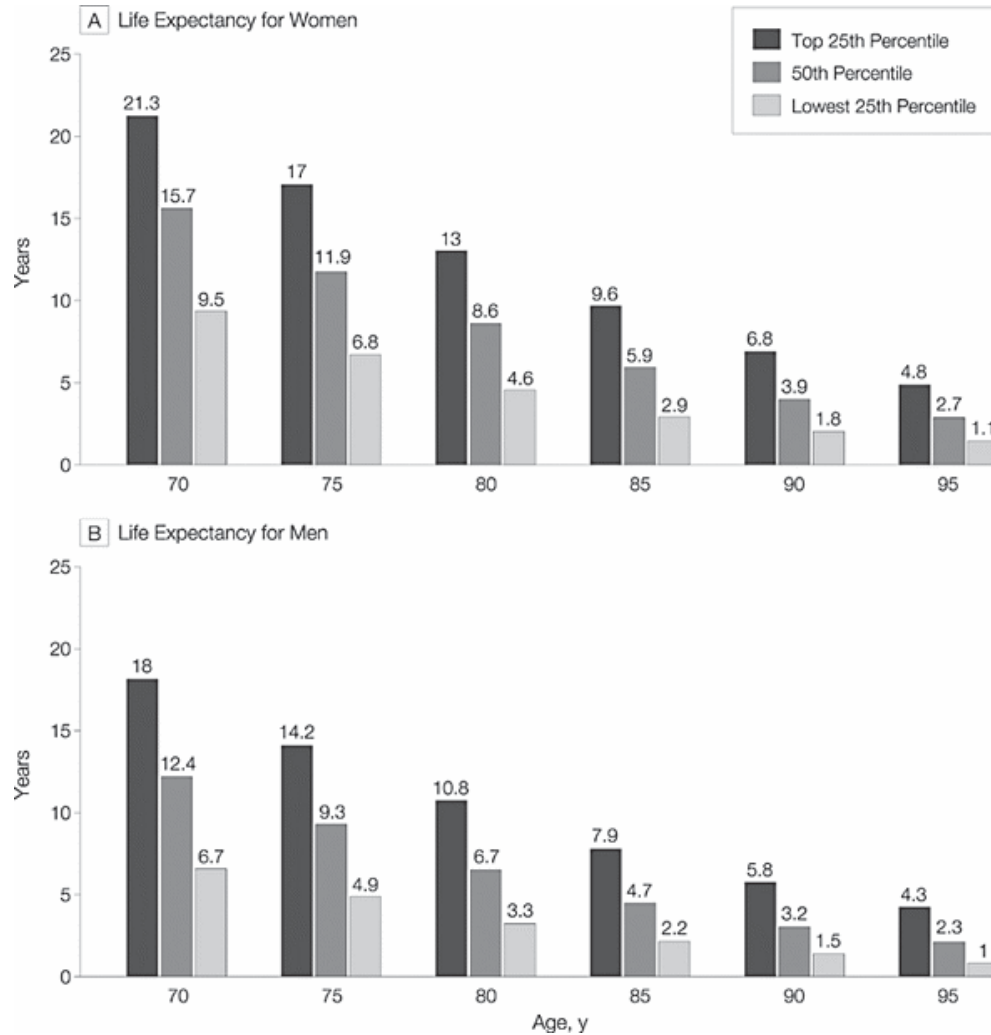
- Is patient at middle of cohort or at upper or lower limits?
- Useful variables
 - Number and severity of co-morbid conditions
 - Congestive heart failure
 - Renal disease
 - Chronic lung disease
 - Functional status
 - Cognitive status
 - Nutritional status

- Absence of comorbid conditions and functional status considerably better than average – upper level for life expectancy

Life Expectancy

Age	Male	Female
60	20.36	23.53
70	13.27	15.72
75	10.24	12.29
80	7.62	9.22
85	5.45	6.62
90	3.80	4.60

Figure. Upper, Middle, and Lower Quartiles of Life Expectancy for Women and Men at Selected Ages Data from the Life Tables of the United States.⁹



Walter, L. C. et al. JAMA 2001;285:2750-2756

JAMA

Benefits of Cancer Screening

- If screening were 100% effective in preventing cancer death, the patient's benefit would approximate his/her risk of dying of a screened-detectable cancer
- Benefit likely to be less than this value
 - Screening may miss early stage malignancies
 - Screening may detect disease too advanced or too aggressive to respond to therapy
 - May detect indolent cancer not likely to become symptomatic

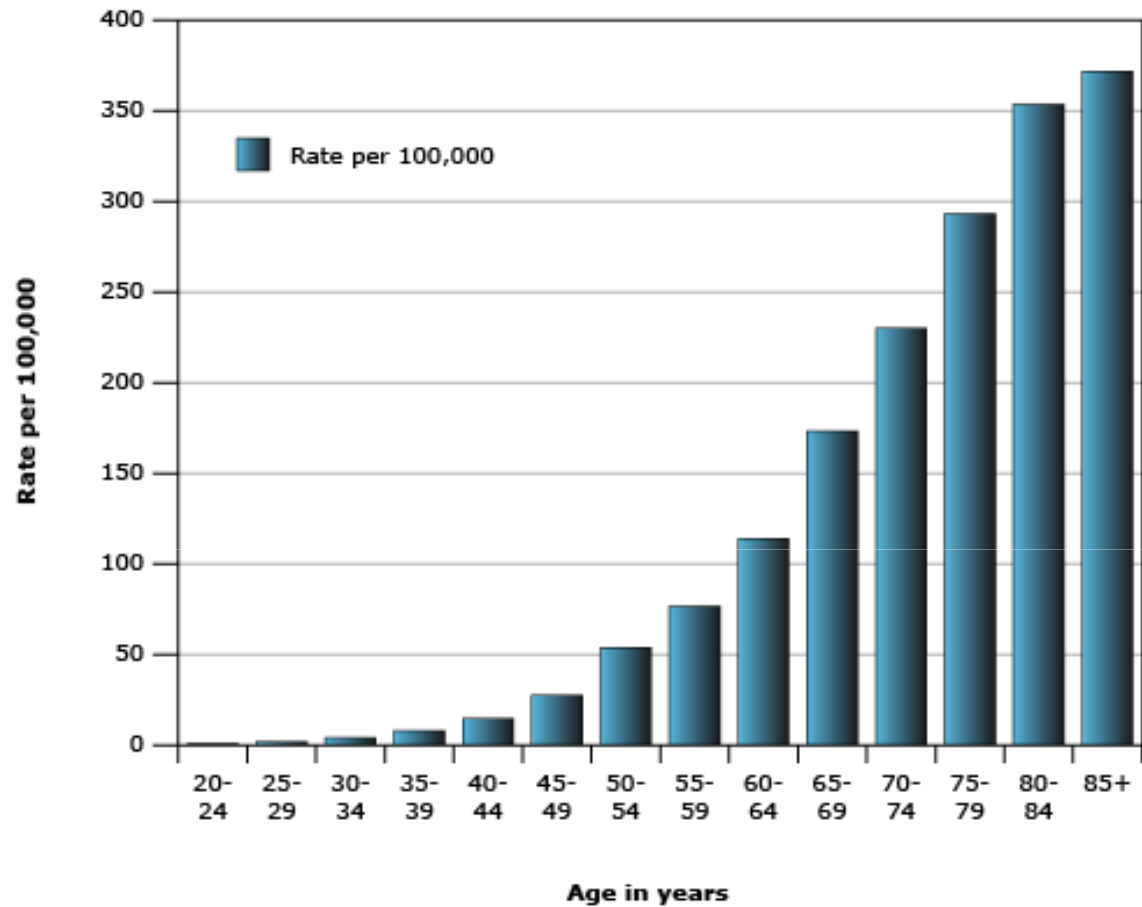
Time to Benefit from Screening

- In studies of fecal occult blood testing and mammography, cancer-specific survival curves between screened and unscreened groups do not separate significantly until at least five years after start of screening.
- Survival benefit from detecting cancer that would have resulted in death only after five years or more
- Cancers causing death before five years may be too aggressive to benefit from early detection and treatment

Harms from Screening

- Complication from additional diagnostic procedures due to inaccurate test results
- Identification and treatment of clinically unimportant cancer
- Psychological stress from screening

Increasing incidence of colorectal cancer with age



The age-specific incidence of colorectal cancer was measured between 2002 and 2006 in men and women of all races.
Data from: Surveillance, Epidemiology, and End Results (SEER) Program, 2002-2006.
Available online at <http://seer.cancer.gov>.

Screening for Colorectal Cancer

- Colorectal cancer is a leading cause of cancer death in the United States – 9% of cancer deaths
- Incidence rises progressively with age
- Most colorectal cancers arise from adenomatous polyps that progress from small → large → dysplasia → cancer
- Progression from adenoma to cancer, when it occurs, takes at least ten years on average
- Two thirds of polyps are adenomas
 - Hyperplastic polyps usually do not progress to cancer

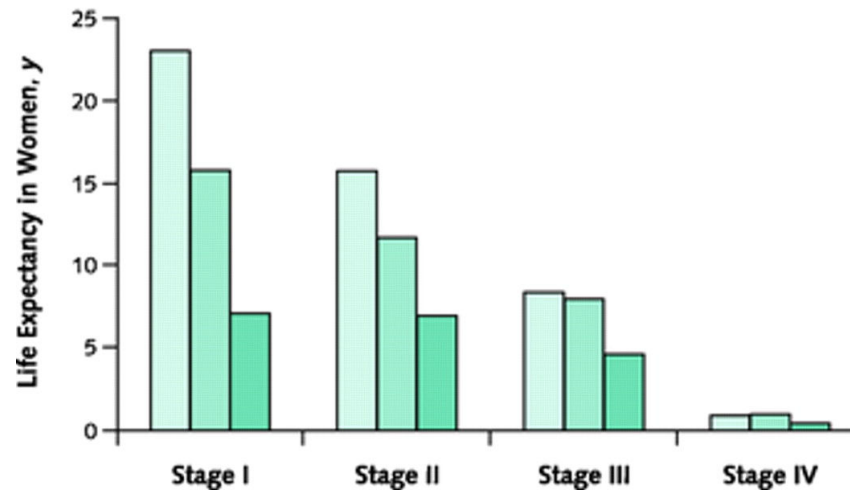
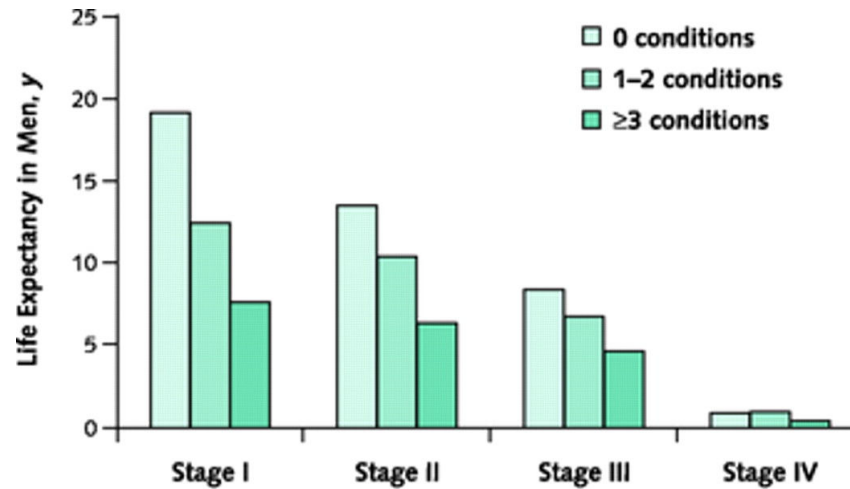
Increased Risk of Colorectal Cancer

- Hereditary nonpolyposis colon cancer
- Familial adenomatous polyposis
- Prior colorectal cancer or polyps
- Inflammatory bowel disease
- Family history of colorectal cancer
- Race (black > white)

Effectiveness for Screening for Colorectal Cancer

- Screening for fecal occult blood
 - 15-33% decreased mortality in screened group
- Flexible sigmoidoscopy
 - Age 55 to 64 – one time screening with sigmoidoscopy with 11 year follow-up
 - 23% decrease in colorectal cancer
 - 31% decrease in mortality
- No data for other tests or procedures

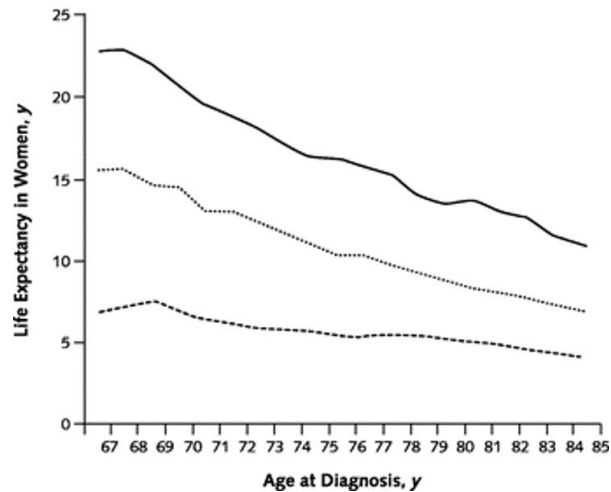
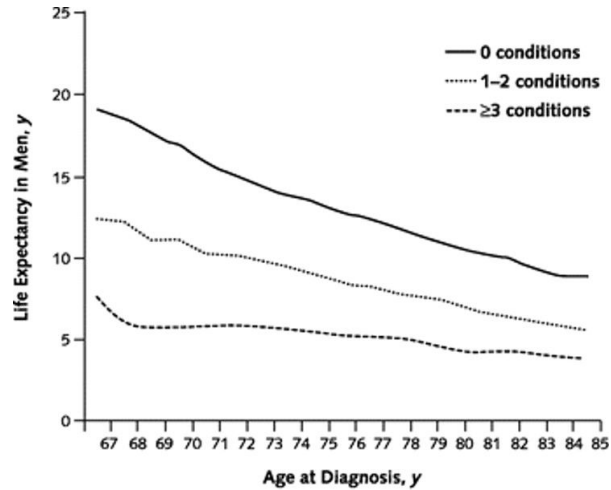
Life expectancy after diagnosis of colorectal cancer at age 67 years according to cancer stage and number of chronic conditions.



Gross C P et al. Ann Intern Med 2006;145:646-653

Annals of Internal Medicine

Life expectancy after stage I cancer diagnosis according to age, number of chronic conditions, and sex.



Gross C P et al. Ann Intern Med 2006;145:646-653

Annals of Internal Medicine

Risk of Dying of Colorectal Cancer by Age

Women

Age	life expectancy	Risk of dying from colorectal cancer
50	40	3.8
	33	2.2
	24.5	1.0
70	21.3	3.5
	15.7	2.0
	9.5	0.9

Women

Age	life expectancy	Risk of dying from colorectal cancer
75	17	3.3
	11.9	1.9
	6.8	0.9
80	13	3.0
	8.6	1.8
	4.6	0.8

Women

Age	life expectancy	Risk of dying from colorectal cancer
85	9.6	2.5
	5.9	1.6
	2.9	0.8
90	6.8	1.8
	3.9	1.0
	1.8	0.5

Risk of Dying of Colorectal Cancer for Men

Men

Age	life expectancy	Risk of dying from colorectal cancer
50	36	4.1
	28.5	2.3
	19.6	1.0
70	18	3.8
	12.4	2.1
	6.7	0.9

Men

Age	life expectancy	Risk of dying from colorectal cancer
75	14.2	3.5
	9.3	1.9
	4.9	0.8
80	10.8	3.2
	6.7	1.8
	3.3	0.8

Men

Age	life expectancy	Risk of dying from colorectal cancer
85	7.9	2.7
	4.7	1.6
	2.2	0.8
90	5.8	2.0
	3.2	1.1
	1.5	0.5

Colorectal Screening in Older Adults

- Screening trials have included too few elderly people to provide reliable estimates of screening effectiveness for this age group
- Study model
 - Colonoscopy would increase survival by 0.13 years for those 80 and older
 - Increase survival by 0.85 years for those 50-54.
 - Colonoscopy carries increased risk in elderly
 - USPSTF guidelines recommend against screening those 75 and older

2008 Colorectal Guidelines – ACS and Multi-society Task Force

- Offer screening beginning at age 50 for average risk patient
- Discontinue screening when life expectancy < ten years
- No single test is of unequivocal superiority
- Screening should be supported by a program which assures proper follow-up of abnormal findings and ongoing testing of identified levels

Screening for Breast Cancer

- Increasing age is the primary risk factor for breast cancer in most women
- 85% of breast cancers occur after women 50 yrs. of age.
- Does screening with mammography decrease breast cancer mortality?
- Protective effect occurs relatively quickly among women age 50-69
 - Decrease in all cause mortality for screened women in 4 Swedish studies

- 28% reduction in breast cancer mortality in USA since 1990
 - Decreased use of estrogen?
 - More effective treatment?
 - Screening – possible reduction in mortality by 10%
- Only 8% relative reduction in breast cancer mortality for women > 70

Frequency of Mammography

- Observation study
 - Screened annually vs. every two years
 - No significant difference in breast cancer detection rate or prognostic stage
- Breast cancer grows more slowly in older women – longer interval between screening may be reasonable in older women

Breast Palpation

- Clinical breast exam did not add to screening effectiveness of mammography
- No benefits of regular breast self-examination in results of:
 - Rates of breast cancer diagnosis
 - Rates of breast cancer deaths
 - Tumor stage or size

Screening for Breast Cancer in Those 70 and Older

- Shorter life expectancy decreases the potential for screening to prolong life
- Data from randomized control trials in women older than 70 are limited
 - Mortality unchanged for women screened age 70 – 74 in one study
 - Case controlled studies in Holland showed effect of screening in those 65 – 74, but no effect after age 75
 - Cohort study of 2011 women – no effect of screening past age 80

Screening Mammography in Women 75 yrs and Older

- No women 75 years and older have been included in multiple randomized clinical trials of breast cancer screening
- Breast cancer is a leading cause of death in older women
- Screening benefit probably decreases with increased age
 - Benefits of screening occur several years after screening – decrease survivorship limits benefits
 - Higher percentage of breast cancer in elderly is more easily treated estrogen receptor-positive type
 - Women of this age are a great risk for dying from other conditions.

Benefits vs. Burdens of Mammography Screening in Women 80 and Older

- Several community health practices
- 2011 – women 80 and older
 - 1034 screened with mammography
 - 977 not screened
- Many false positive biopsies in screened group
- No significant difference in rate, stages, recurrence rates, or deaths due to breast cancer between women who were screened and those who were not screened

False Positive Tests

- A mammogram that prompted a recommendation for additional workup in a woman with no finding of breast cancer within one year
- In USA, 11% of mammograms require additional evaluation – lesion is benign in 90% of cases
- Over diagnosis leads to unnecessary testing and treatment and psychological and other consequences of being diagnosed and being treated for cancer

Breast Cancer Screening in Women Over 70

Age	Life Expectancy	Risk of Dying from breast cancer	Number needed to screen over lifetime
50	40	4.4	95
	33	3.1	133
	24.5	2.0	226
70	21.3	3.3	142
	15.7	2.2	242
	9.5	1.2	642
80	13	2.4	240
	8.6	1.5	533
	4.6	0.7	—

Age	Life Expectancy	Risk of Dying from breast cancer	Number needed to screen over lifetime
85	9.6	1.9	417
	5.9	1.2	2,131
	2.9	0.6	—
90	6.8	1.4	1,066
	3.9	0.8	—
	1.8	0.4	—

Breast Screening Recommendation in Older Women

- Data limited on effectiveness of screening in those 75 and older
- Age, however, should not be the sole determining factor for determining the indication for screening
- Should take into account individual estimates of risk and benefit, and take into account patient preferences
- One suggestion – breast screening with mammography be continued as long as life expectancy is at least ten years.

Sensitivity and Specificity of PSA

- PSA cutoff of 4.0
 - 21% sensitive for detecting any prostate cancer
 - 51% sensitive for detecting high grade cancer
 - 91% specificity
- PSA cutoff – 3.0
 - 32% sensitivity for any prostate cancer
 - 68% sensitivity for high grade cancer
 - 85% specificity

- Positive predictive value:
 - PSA >4 – 30%
 - PSA 4-10 – 25%
 - PSA > 10 – 42-64%
- 75% of cancers detected with PSA 4-10 are organ confined and potentially curable

Effectiveness of Prostate Cancer Screening

- European randomized study of screening for prostate cancer (ERSPC)
 - 182,160 men age 50-74 – PSA screening every four years vs. control
 - PSA cutoff 2.5 – 4
 - Primary outcome of prostate cancer mortality – 20% lower in group offered screening
 - ERSPC site from Goteborg, Sweden
 - Cumulative mortality reduction of 44% for PSA screening over 14 year follow-up

- United States prostate, lung, colorectal, and ovarian cancer trial
 - 76,693 men 55-74 – screened with PSA and digital exam vs. usual care
 - PSA level 4 and above – biopsy
 - 11 years – no reduction in prostate cancer mortality

Meta-analysis

- 6 randomized trials
 - 387,286 participants
 - Screening with PSA with and without digital rectal exam did not reduce deaths from prostate cancer
- A large nested case-control study found no evidence that PSA screening for prostate cancer reduced all cause mortality

Overdiagnosis

- Detection by screening of condition that would not have become clinically significant
- Lifetime risk of being diagnosed with prostate cancer has gone from 1 in 11 to 1 in 6 with screening; the lifetime risk of dying from prostate cancer remains unchanged at 1 in 34

Risk of Therapy for Prostate Cancer

- Common complications of therapy
 - Urinary incontinence
 - Sexual dysfunction
 - bowel problems

Approach for Screening for Prostate Cancer

- Absolute risk reduction is very low
- Do the benefits of screening outweigh the potential harm to the quality of life?
- Patients must make their own informed decision about screening
- Screening for prostate cancer is unlikely to benefit men with less than a ten year life expectancy (75 and older)

Screening for Prostate Cancer - 2008

- The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of prostate cancer screening in men younger than 75 years
- The USPSTF recommends against screening for prostate cancer in men age 75 or older
- Given the uncertainties and controversies surrounding prostate cancer screening in men younger than age 75 years, a clinician should not order the PSA test without first discussing with the patient the potential but uncertain benefits and the known harms of prostate cancer screening and treatment

- Because of the uncertainty about the benefits of treating prostate cancer detected by screening men younger than age 75 years, there is no consensus regarding optimal treatment
- Even if prostate screening is determined to be effective, the length of time required to experience a mortality benefit is > 10 years. Because a 75 year old man has an average life expectancy of about 10 years, very few men age 75 years and older would experience a mortality benefit.

Oct 10, 2011 USPTSF Draft Recommendation

- The US Preventive Services Task Force recommended against Prostate Specific Antigen (PSA) based screening for prostate cancer

USPSTF Rationale

- The majority of men who have asymptomatic prostate cancer detected by PSA screening have a tumor that meets the histologic criteria for prostate cancer, but the tumor either will not progress or is so indolent and slow-growing that it will not affect the man's lifespan or cause adverse health effects
- For men over 70. screening has no mortality benefit

Rationale (cont)

- For men aged 50-69 – reduction in prostate cancer mortality 10 years after screening – small to none
- 95% of men with PSA-detected cancer who are followed for 12 years do not die from that cancer
- No prostate cancer screening study has demonstrated a reduction in all cause mortality

Harms Related to Screening

- Anxiety over the diagnosis of cancer
- Morbidity of prostate biopsy
- Over-diagnosis – a patient with an indolent lesion may experience associated harms of a therapy without benefiting from the intervention

Harms related to treatment

- 90% of men with a PSA-detected prostate cancer undergo early treatment with surgery, radiation, or androgen deprivation therapy
 - 5/1000 – die in 1 month
 - 10-70/1000 – severe complications
 - 200-300/1000 urinary incontinence or erectile dysfunction
- PSA-based screening for prostate cancer results in considerable overtreatment

Does PSA-Based Early Detection of Prostate Cancer Save Lives?

- European Trial – statistically insignificant 0.06% absolute reduction in prostate cancer deaths for men aged 50-74.
- US Trial – statistically insignificant 0.03% absolute increase in prostate cancer deaths in screened men.
- Meta-analysis of all published trials – no significant reduction in prostate cancer deaths from screening

Conclusion - USPSTF

- The vast majority of men who are treated for PSA-screened prostate cancer do not have prostate cancer death prevented or lives extended from that treatment, but are exposed to significant harms
- The USPSTF concludes that there is moderate certainty that the harms of PSA screening for prostate cancer outweigh the benefits

Screening for Cervical Cancer

- The USPSTF recommends against routine screening women older than 65 yrs for cervical cancer if they have had adequate recent screening with normal PAP smears and are not otherwise at high risk for cervical cancer
- American Cancer Society recommendation suggests stopping cervical cancer screening at age 70 yrs
- Screening is recommended in older women who have not been previously screened, when information about previous screening is unavailable, or when screening is unlikely to have occurred in the past

Bone Mineral Density Screening

- Suggest BMD assessment in all women age 65 and older
- BMD in post-menopausal women under 65 and men with the following risk factors:
 - Previous fracture
 - Glucocorticoid therapy
 - Parental history of hip fracture
 - Low body weight
 - Current cigarette smoking
 - Excessive alcohol consumption
 - Rheumatoid arthritis

- Risk factors – BMD measurement every two years
- No risk factors and normal study – BMD measurement every three to five years

Bladder Cancer

- 4th most common cancer in men
- 9th most common cancer in women
- 7th leading cause of solid-cancer related death

- Detection
 - Inadequate evidence regarding diagnostic accuracy of
 - Urinalysis
 - Urine cytology
 - Tests for urine biomarkers

- USPSTF
 - Inadequate evidence that screening for bladder cancer leads to improved disease-specific or overall morbidity and mortality
 - Difficult to identify early cases with high risk of progression
- Increased risk for bladder cancer
 - Male
 - Smoker
 - Older individuals
 - Family history

Screening for Ovarian Cancer

- The US Preventative Task Force (USPSTF) recommends against routine screening for ovarian cancer.
 - There is no existing evidence that any screening test, including CA-125, ultrasound, or pelvic examination reduces mortality from ovarian cancer. Existing evidence that screening can detect early stage ovarian cancer is insufficient to indicate that this early diagnosis will reduce mortality
 - Because there is a low incidence of ovarian cancer in the general population (age-adjusted incidence of 17 per 100,000) screening for ovarian cancer is likely to have a relatively low yield.

Screening for Pancreatic Cancer

- USPSTF recommends against routine screening for pancreatic cancer in asymptomatic adults using abdominal palpation, ultrasonography, or serologic markers
- Due to the poor prognosis of those diagnosed with pancreatic cancer, there is interest in primary prevention. The evidence for diet-based prevention of pancreatic cancer is limited and conflicting. Some experts recommend lifestyle changes that may help to prevent pancreatic cancer, such as stopping the use of tobacco products, moderating alcohol intake, and eating a balanced diet with sufficient fruit and vegetables.

Screening for Skin Cancer

- The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of using whole-body skin examination by a primary care physician or patient skin self examination for the early detection of cutaneous melanoma, basal cell cancer, or squamous cell skin cancer in the adult general population

- Clinician should remain alert for skin lesions with malignant features noted in the context of physical examination performed for other purposes. Asymmetry, border irregularity, color variability, diameter > 6mm or rapidly changing lesions are features associated with an increased risk of cancer. Biopsy of suspicious lesions is warranted.

- Clinicians should be aware that fair-skin men and women older than 65 years, patients with atypical moles, and those with more than 50 moles, constitute known groups at substantially increased risk for melanoma.

Screening for Abdominal Aortic Aneurysm

- The USPSTF recommends one time screening for abdominal aortic aneurysm by ultrasonography in men 65 to 75 who have ever smoked.
- The USPSTF makes no recommendation for or against screening for abdominal aortic aneurysm in men age 65 to 75 who have never smoked
- The USPSTF recommends against routine screening for abdominal aortic aneurysm in women
- The major risk factors for abdominal aortic aneurysm include age (being 65 or older), male sex, and a history of ever smoking (at least 100 cigarettes in a person's lifetime)

- For most men, 75 years may be considered an upper age limit for screening. The increased presence of co-morbidities for people age 75 and older decreases the likelihood that they will benefit from screening.
- One time screening to detect an abdominal aortic aneurysm using ultrasonography is sufficient. There is negligible health benefit in rescreening those who have a normal aortic diameter on initial screening.

- Open surgical repair for abdominal aortic aneurysm of at least 5.5 cm leads to an estimated 43% reduction in aneurysms' specific mortality in older men who undergo screening
- In men with intermediate size aneurysms (4.0 – 5.4 cm), periodic surveillance offers comparable mortality benefit to routine elective surgery with the benefit of fewer operations

Screening for Carotid Artery Stenosis

- USPSTF recommends against screening for asymptomatic carotid artery stenosis in the general adult population
- This recommendation applies to adults without neurologic signs or symptoms, including a history of transient ischemic attacks or strokes. An individual who has a carotid-area transient ischemic attack should be evaluated promptly for consideration of carotid endarterectomy

- In the setting of excellent surgical care and low complication rates, screening may benefit patients who have a very high risk of stroke. It is not clear, however, how to identify people who are at risk for stroke that is high enough to justify screening, yet do not also have a high risk for surgical complications.

Screening for Coronary Heart Disease

- The USPSTF recommends against routine screening with resting electrocardiography (ECG), exercise treadmill tests (ETT), or electron beam computerized tomography (EBCT) scanning for coronary calcium for either the presence of severe coronary artery stenosis or the prediction of coronary heart disease events in adults at low risk for coronary heart disease events.
- The USPSTF found insufficient evidence to recommend for or against routine screening with EKG, ETT, or EBCT scanning for coronary calcium for either the presence of severe CAS or the prediction of CHD events in adults and increased risk for CHD events.

US Preventive Services Task Force (USPSTF) – Screening for Breast Cancer

- Recommend biennial screening mammography for women age 50-74 years.
- Decision to start regular mammography before age 50- an individual one
- Current evidence is insufficient to assess the additional benefits and harms of screening mammography in women 75 yrs and older.
- Current evidence is insufficient to assess the additional benefit and harms of clinical breast examination beyond screening mammography in women 40 yrs and older

Screening for Colorectal Cancer

- USPSTF recommends screening for colorectal cancer using fecal occult blood testing, sigmoidoscopy or colonoscopy in adults, beginning at age 50 yrs and continuing until age 75 yrs
- The USPSTF recommends against routine screening for colorectal in adults 76 – 85 years of age.
- USPSTF recommends against screening for colorectal cancer in adults older than 85 yrs
- These recommendations exclude individuals with specific inherited syndromes (familial polyposis, etc.) and those with inflammatory bowel disease

- For individuals age 75 – 85, the *gain* in life-years associated with extending screening was small in comparison to the *risk* of screening people in this decade.
- For persons older than 85 yrs, competing causes for mortality preclude a mortality benefit that outweighs the harms

Screening In Older Patients

- Cervical cancer – no screening after age 65 if Pap smears have been negative
- Breast cancer – stop screening when life expectancy, adjusted for co-morbidity, less than 10 years.
- Colon cancer – stop screening when life expectancy, adjusted for co-morbidity, less than 10 years.
- Prostate cancer – no evidence for screening at any age
- Abdominal aortic aneurysm – one time screening test for men who are current or past smokers, age 65 to 74

Screening for Lung Cancer (NEJM August 4, 2011)

- 53,454 persons at high risk for lung cancer
 - Current or former (30 pack/yr smokers)
 - Age 55-74
- Randomized to three annual screens
 - Low dose CT scan
 - Single PA chest film
- 247 deaths from lung cancer/100,000 patient years – CT group
- 309 deaths from lung cancer/100,000 patient years – plain chest film group

- 20% relative reduction in mortality from lung cancer in CT group
- 6.7% overall mortality reduction in CT group
- 96.4% of CT scans and 94.5% of plain film x-ray findings were false positive
- Number needed to screen with low dose CT to prevent one death from lung cancer-
320