

Cancer Screening & Prevention

(See also *Harrison's Principles of Internal Medicine*, 17th Edition, Chapter 390)

Definition

- Cancer prevention and control has grown, based on increased understanding of the biology of carcinogenesis.
- Primary prevention: identification and manipulation of genetic, biologic, and environmental factors that cause cancer
 - Primary areas of concentration
 - Smoking cessation
 - Diet modification
 - Chemoprevention: natural or synthetic chemical agents to reverse, suppress, or prevent development of invasive cancer
- Secondary prevention: identification and treatment of asymptomatic neoplastic lesions
 - Cancer screening: method for detecting disease early in asymptomatic persons in order to decrease morbidity and mortality
- Terms used to define a screening test's accuracy in discrimination of disease
 - Sensitivity: the proportion of persons with the condition who test positive
 - Specificity: the proportion of persons without the condition who test negative
 - Positive predictive value: the proportion of persons with a positive test who have the condition
 - Negative predictive value: the proportion of persons who test negative and do not have the disease
 - Sensitivity and specificity are relatively independent of underlying prevalence (risk) of the disease in the population screened.
 - Predictive values (expressed as a percentage) are influenced by sensitivity and specificity of the screening test as well as the prevalence of the disease.

Goals

- Cancer prevention includes:
 - Identification and avoidance of carcinogens
 - Specific interventions to reduce cancer risk
 - Screening for early detection of cancer
- Cancer screening tests
 - To be valuable, screening must detect disease earlier, and treatment of earlier disease must yield a better outcome than treatment at the onset of symptoms.
 - Likelihood of benefit from screening should outweigh harm.
 - A test is most beneficial, efficient, and economical when target disease is common in the population being screened.
 - Should also have a high specificity

Mechanism of Action

General

- Cancer develops through accumulation of genetic changes.
 - *Initiators* are initial genetic changes.
 - *Promoters* are influences that cause a cell to progress through the carcinogenic process and change phenotypically.
- Cancer can be prevented by interference with factors that cause initiation, promotion, or progression.
 - Chemopreventive compounds often have antimutagenic, antioxidant, antiproliferative, or pro-apoptotic actions.

Carcinogens and associated cancers

- Alkylating agents
 - Acute myeloid leukemia, bladder cancer
- Androgens
 - Prostate cancer
- Aromatic amines (dyes)
 - Bladder cancer
- Arsenic
 - Cancer of the lung, skin
- Asbestos
 - Cancer of the lung, pleural and peritoneal mesothelioma
- Benzene
 - Acute myeloid leukemia
- Chromium
 - Lung cancer
- Diethylstilbestrol (prenatal)
 - Vaginal cancer (clear cell)
- Epstein–Barr virus
 - Burkitt’s lymphoma, nasal T-cell lymphoma, post-transplantation lymphoma, AIDS-associated lymphoma, perhaps some cases of Hodgkin’s disease, nasopharyngeal carcinoma in China
- Estrogens
 - Cancer of the endometrium, liver, breast
- Ethyl alcohol
 - Cancer of the liver, esophagus, head and neck
- *Helicobacter pylori*
 - Gastric cancer
- Hepatitis B or C virus
 - Liver cancer
- HIV
 - Non-Hodgkin’s lymphoma, Kaposi’s sarcoma, squamous-cell carcinomas (especially of the urogenital tract)
- Human T-cell lymphotropic virus type 1
 - Adult T-cell leukemia/lymphoma
- Immunosuppressive agents (azathioprine, cyclosporine, glucocorticoids)
 - Non-Hodgkin’s lymphoma
- Nitrogen mustard gas
 - Cancer of the lung, head and neck, nasal sinuses

- Nickel dust
 - Cancer of the lung, nasal sinuses
- Phenacetin
 - Cancer of the renal pelvis and bladder
- Polycyclic hydrocarbons
 - Cancer of the lung, skin (especially squamous-cell carcinoma of scrotal skin)
- Schistosomiasis
 - Bladder cancer (squamous-cell carcinoma)
- Sunlight (ultraviolet)
 - Skin cancer (squamous-cell carcinoma and melanoma)
- Tobacco (including smokeless)
 - Cancer of the upper aerodigestive tract, bladder
- Vinyl chloride
 - Liver cancer (angiosarcoma)

Smoking

- The most avoidable risk factor for cancer
- Smoking causes diffuse epithelial injury in the head, neck, esophagus, and lung.
- Smoking cessation may halt early stages of the carcinogenic process (e.g., metaplasia); it may have no effect on late stages of carcinogenesis.
- Degree of smoke exposure is correlated with risk of death from lung cancer.
 - Number of cigarettes smoked per day as well as the level of smoke inhalation.
- Cigarette smoking is a causative agent in cancers of the larynx, oropharynx, esophagus, bladder, and pancreas.
- The risk of tobacco smoke is not necessarily limited to the smoker.
 - Studies suggest environmental tobacco smoke may cause lung cancer and other pulmonary diseases in nonsmokers.
- Health risks of cigars similar to cigarettes
 - 2 cigars per day doubles the risk for oral and esophageal cancer.
 - 3–4 cigars per day increases risk of oral cancer 8-fold and esophageal cancer 4-fold.
- Smokeless tobacco is the fastest growing part of the tobacco industry.
 - Carcinogen linked to dental caries, gingivitis, oral leukoplakia, and oral cancer
 - Systemic effects may increase risk for other cancers.

Diet modification

- May have significant potential for lowering cancer risk in western culture
 - Studies suggest that diets high in fat increase the risk for cancers of the breast, colon, prostate, and endometrium.
 - Highest incidence and mortality rates in western countries, where fat comprises an average of 40–45% of the total calories consumed.
 - In populations at low risk for these cancers, fat accounts for <20% of calories.
- Dietary fat has not been proven to cause cancer.
 - Diet is a highly complex exposure to many nutrients and chemicals.
 - Low-fat diets may offer some protection through anticarcinogens found in vegetables, fruits, legumes, nuts, and grains.
 - Protective substances include phenols, sulfur-containing compounds, flavones, and fiber.

- Evidence points to a preventive effect of vegetable and fruit consumption.
 - Specific protective factors remain uncertain.
 - Best evidence of benefit is for cancers of mouth, pharynx, esophagus, larynx, lung, stomach, kidney, colon and rectum, ovary (vegetables only), and bladder (fruit only).
- Dietary fiber appears protective against colonic polyps and invasive cancer of the colon.
 - Mechanisms involved are complex and speculative.
 - Binding of oxidized bile acids
 - Generation of soluble fiber products, such as butyrate, that may have differentiating properties
- High-fiber diets may also protect against breast and prostate cancer.
 - May absorb and inactivate dietary estrogenic and androgenic cancer promoters.
- Protective effects of fiber have not been proved in a prospective clinical trial.

Sun avoidance

- Nonmelanoma skin cancers (basal cell and squamous cell) are induced by cumulative exposure to ultraviolet radiation.
- Intermittent acute sun exposure and sun damage have been linked to melanoma.
 - Sunburns, especially in childhood and adolescence, are associated with an increased risk of melanoma in adulthood.
- Recommendations include wearing hats and long sleeves and use of sunblock with at least SPF 15.

Cancer chemoprevention

- Calcium may lower colon cancer risk.
 - Binds bile and fatty acids causing hyperproliferation of colonic epithelium, reducing intraluminal exposure to these compounds
 - May not be an adequate surrogate marker; trials still under way
- Hormonally driven cancers
 - Hormonal manipulation may be feasible in primary prevention of breast and prostate cancer.
 - Tamoxifen is an antiestrogen with partial estrogen agonistic activity in some tissues, such as endometrium and bone.
 - Upregulates transforming growth factor β , decreasing breast-cell proliferation
 - Reduces risk of breast cancer by 50% in women at moderately high risk (>1.66% risk in next 5 years)
 - Women with *BRCA1* or *BRCA2* mutations require bilateral prophylactic mastectomy for maximum risk reduction (>90%)
 - Finasteride is a 5 α -reductase inhibitor that inhibits the conversion of testosterone to dihydrotestosterone, a more potent stimulator of prostate cell proliferation than testosterone.
 - Reduces the risk of prostate cancer by 25%
 - The prostate cancers that did occur during finasteride therapy had a somewhat higher Gleason grade.
 - Selenium and β -carotene are being evaluated for their effects on prostate cancer incidence.

Indications

Smoking cessation

- Prevention among young people is critical; >80% of American smokers begin before 18 years of age.
- Nearly 20% of Americans 12–18 years of age have smoked a cigarette in the past month.
- Cigar smoking and use of smokeless tobacco products are increasing.
- Cessation of smoking lowers cancer risk in those who have not developed cancer.

Diet and lifestyle

- Dietary fat has not been proven to cause cancer; epidemiologic studies give conflicting results.
- Cancer Prevention Study II showed association between excess body weight and cancer mortality.
 - Higher relative risk in men with high body mass index for all cancers and for the following specific cancers:
 - Prostate
 - Non-Hodgkin lymphoma
 - Kidney
 - Multiple myeloma
 - Gallbladder
 - Colon and rectum
 - Esophagus
 - Stomach
 - Pancreas
 - Liver
 - Higher relative risk in women with high body mass index for all cancers and for the following specific cancers:
 - Multiple myeloma
 - Colon and rectum
 - Ovary
 - Liver
 - Non-Hodgkin lymphoma
 - Breast
 - Gallbladder
 - Esophagus
 - Pancreas
 - Cervix
 - Kidney
 - Uterus
- A U.S. National Institutes of Health Women's Health initiative enrolled >100,000 women in a long-term clinical trial of cancer-preventing effects of low-fat diet and vitamin supplementation.
 - Full results are not yet available.
 - A nearly 11% reduction in dietary fat did not affect the incidence of colorectal cancer in the Women's Health Initiative.
- There is no current evidence to establish anticarcinogenic value of vitamin, mineral, or nutritional supplements beyond those of a good diet.

- Regular physical exercise may prevent some cancers.
 - Ovary
 - Breast
 - Colorectal
 - Prostate
 - Lung

Sun avoidance

- Indicated especially in those with risk factors for melanoma, including:
 - Propensity to sunburn
 - Large number of benign melanocytic nevi
 - Atypical nevi

Chemoprevention

- Tamoxifen is the only chemoprevention currently approved by the U.S. Food and Drug Administration.
 - Indicated for reducing risk of breast cancer in high-risk women
 - Given the superiority of aromatase inhibitors to tamoxifen in adjuvant therapy, it is expected that further benefit will be associated with their use in chemoprevention when ongoing clinical trials are completed.
- Treatment of chronic hepatitis C with interferon lowers the risk of hepatocellular carcinoma.

Surgical prevention

- Organ removal in persons at very high risk of developing cancer
 - Cervical dysplasia
 - Women treated with conization and possibly hysterectomy
 - Colectomy to prevent colon cancer in people with familial polyposis, ulcerative colitis, and hereditary nonpolyposis colorectal cancer
 - Women with genetic predisposition to breast cancer (*BRCA1*, *BRCA2*) may opt for bilateral mastectomy and oophorectomy.

Cancer screening

- Widespread screening is beneficial for certain age groups for:
 - Cervical cancer
 - Colorectal cancer
 - Breast cancer

High-risk persons

- Special surveillance for a specific cancer because of family history or genetic risk may be prudent.
- Few studies have been carried out to assess impact on mortality in these groups.

Asymptomatic normal-risk persons

- Recommended screening differs among organizations that study and promote such activities.
- Sigmoidoscopy
 - U.S. Preventive Services Task Force: >50 years, periodically; <50 years, not recommended
 - American Cancer Society: ≥50 years, every 3-5 years
 - Canadian Task Force on Prevention Health Care: insufficient evidence
- Fecal occult blood testing
 - U.S. Preventive Services Task Force: ≥50 years, every year
 - American Cancer Society: ≥50 years, every year
 - Canadian Task Force on Prevention Health Care: insufficient evidence
- Digital rectal examination
 - U.S. Preventive Services Task Force: no recommendation
 - American Cancer Society: ≥40 years, every year
 - Canadian Task Force on Prevention Health Care: poor evidence to include or exclude
- Prostate-specific antigen
 - U.S. Preventive Services Task Force: insufficient evidence to recommend
 - American Cancer Society: men ≥50 years, every year
 - Canadian Task Force on Prevention Health Care: recommendation against
- Papanicolaou (Pap) test
 - U.S. Preventive Services Task Force: women 18–65 years, every 1–3 years
 - American Cancer Society: women with uterine cervix, beginning 3 years after first intercourse or by 21. years of age; yearly for standard Pap; every 2 years with liquid test
 - Canadian Task Force on Prevention Health Care: fair evidence to include in examination of sexually active women
- Pelvic examination
 - U.S. Preventive Services Task Force: do not recommend, advise adnexal palpation during examination for other reasons
 - American Cancer Society: women 18–40 years, every 1–3 years with Pap test; >40 years, every year
 - Canadian Task Force on Prevention Health Care: not considered
- Endometrial tissue sampling
 - U.S. Preventive Services Task Force: not considered
 - American Cancer Society: at menopause if obese or a history of unopposed estrogen use
 - Canadian Task Force on Prevention Health Care: not considered
- Breast self-examination
 - U.S. Preventive Services Task Force: no recommendation
 - American Cancer Society: ≥20 years, monthly
 - Canadian Task Force on Prevention Health Care: insufficient evidence to make a recommendation
- Mammography
 - U.S. Preventive Services Task Force: women 40–75 years, every 1–2 years
 - American Cancer Society: ≥40 years, every year
 - Canadian Task Force on Prevention Health Care: 50–69 years, every year
 - Familial breast cancer is more readily detected by MRI than mammography.
 - Digital mammography is said to be more sensitive, but the benefit, if any, is small and mainly seen in young women, in whom breast cancer is very rare.

- Complete skin examination
 - U.S. Preventive Services Task Force: not recommended
 - American Cancer Society: 20–39 years, every 3 years
 - Canadian Task Force on Prevention Health Care: poor evidence to include or exclude

Contraindications

- Cancer screening risks include:
 - Harm caused by the screening intervention itself
 - Harm from further investigation (diagnostic tests) of persons with positive test results (both true and false positive)
 - Harm from treatment of persons with true-positive result, even if life is extended by treatment
 - Psychological impact of cancer screening itself

Technique

Smoking cessation

- Nonsmoking persons should be encouraged not to start.
 - >80% of American smokers begin smoking before 18 years of age.
 - Counseling adolescents and young adults is critical to prevent smoking.
- Persons who smoke should be encouraged to stop.
 - Light and low-tar cigarettes are not safer because smokers tend to inhale them more frequently and deeply.
- Current approaches recognize that smoking is an addiction.
 - Smokers who are quitting go through a process with identifiable stages.
 - Contemplation of quitting
 - Action phase in which the smoker quits
 - Maintenance phase
 - Smokers who quit completely are most likely to be successful compared to:
 - Those who gradually reduce the number of cigarettes smoked
 - Those who change to lower tar or nicotine cigarettes
- The "5-A" behavioral counseling framework provides a useful strategy for engaging patients in smoking cessation discussions.
 - Ask about tobacco use.
 - Advise to quit through clear personalized messages.
 - Assess willingness to quit.
 - Assist to quit.
 - Arrange follow-up and support.
 - Provide pharmacologic measures, such as nicotine gum and patches and bupropion, to manage withdrawal.

Diet and lifestyle

- Diet should contain a variety of healthful foods, emphasizing plant sources.
 - ≥5 servings of fruits and vegetables daily
 - Wholegrains rather than processed or refined grains and sugars
 - Limited red meat, especially high-fat or processed meats
 - Balance caloric intake with physical activity.
 - Maintain a healthy weight, losing weight if necessary.

- Limit consumption of alcohol.
- Benefits of fish oil (3-omega fatty acids) are being defined.
- Physically active lifestyle
 - Adults should have moderate activity for ≥ 30 minutes at least 3–5 days a week.
 - ≥ 45 minutes of moderate or vigorous activity may further reduce risk of breast, colon, and ovarian cancer.

Sun avoidance

- Reduction of sun exposure can reduce skin cancer risk.
 - Protective clothing
 - Changes in the pattern of outdoor activities
 - Sunscreens
 - Prevent burning and may encourage more prolonged exposure
 - May not filter out wavelengths of energy that cause melanoma
- Self-examination or examination by a health care provider for skin pigment characteristics associated with melanoma
 - Propensity to sunburn
 - Numerous benign melanocytic nevi
 - Atypical nevi
- Identification of those at risk
 - Those who know they are at risk tend to be more compliant with preventive measures.

Cancer chemoprevention

- Tamoxifen
 - Approved by the U.S. Food and Drug Administration for reducing the likelihood of breast cancer in high-risk women
 - Dosage: 20 mg PO qd for 5 years
- Use of NSAIDs to prevent formation of colonic adenomas or to cause regression of adenomatous polyps is under study.
 - The presumed mechanism is through blocking the cyclooxygenase pathway.
- Selective cyclooxygenase 2 inhibitors may be more effective at colon cancer prevention.
 - High-dose celecoxib reduces the number of colorectal polyps in patients with familial adenomatous polyposis and is under study.
 - Risk of coronary events is modestly increased for some cyclooxygenase 2 inhibitors, but possibly not all of them.

Efficacy

Smoking cessation

- $>90\%$ of Americans who successfully quit smoking do so without participation in organized cessation program.
 - Cessation programs helpful for some.
- Community Intervention Trial for Smoking Cessation
 - Community-based 4-year program
 - Demonstrated that light smokers (<25 cigarettes per day) can benefit from simple cessation messages and programs

- Quit rate was 30.5% in intervention communities and 27.5% in controls.
 - Quit rate: fraction of participants who achieved and maintained cessation at end of trial
 - Statistically significant, but modestly so
- Not successful for heavy smokers (≥ 25 cigarettes per day)
 - Intensive, broad-based cessation program needed
 - Require counseling, behavioral strategies, pharmacologic adjuncts (e.g., nicotine replacement and bupropion)
- Efficacy in cancer risk reduction
 - Smoking cessation lowers cancer risk in those who have never developed cancer.
 - Those who stop smoking have a lower lung cancer mortality rate than those who continue.
 - However, some carcinogen-induced genetic mutations persist for years.
 - Does not markedly decrease the cured cancer patient's risk of second cancer

Diet modification

- The Polyp Prevention Trial randomly assigned 2,000 elderly persons to a low-fat, high-fiber diet versus routine diet for 4 years.
 - No differences were noted in colon polyp formation.
- The U.S. National Institutes of Health Women's Health Initiative
 - Launched in 1994
 - Long-term clinical trial with $>100,000$ women 45–69 years of age
 - Potential cancer-preventing effects of a low-fat diet and vitamin supplementation are being studied.
 - Results are not yet available.
- Evidence does not currently establish the anticarcinogenic value of vitamin, mineral, or nutritional supplements in amounts greater than that provided by a good diet.
 - At least 5 servings of fruits and vegetables daily decreases dietary fat and increases fiber.
 - May lower the risk of cardiovascular disease and cancer

Sun avoidance

- Sunscreens
 - Decrease the risk of actinic keratoses, the precursor to squamous-cell skin cancer
 - Melanoma risk may be increased.
 - Sunscreens may encourage more prolonged exposure.
 - May not filter out wavelengths of energy that cause melanoma
 - Paradoxically, sunscreen use may lead people to spend more time in the sun.
- Educational interventions have some impact.
 - Those who recognize themselves as being at risk tend to be more compliant with sun-avoidance techniques.

Cancer chemoprevention trials

- Isoretinoin (13-*cis*-retinoic acid)
 - A clinical trial has shown that adjuvant isoretinoin can reduce the incidence of second primary tumors in patients treated with local therapy for head and neck cancer.
 - Overall survival was not improved due to mortality from recurrences of the primary tumor.
 - Beneficial effects were not replicated in other studies.

- NSAIDs
 - Early clinical trial results suggest that such agents as piroxicam, sulindac, and aspirin may prevent adenoma formation or cause regression of adenomatous polyps.
 - In the Physicians' Health Trial, aspirin had no effect on colon cancer incidence, although the 6-year assessment period may not have been long enough to evaluate this end point definitively.
 - Studies evaluating NSAIDs as colon cancer chemopreventive agents have not yet been completed.
- Cyclooxygenase 2 inhibitors
 - May be effective at colon cancer prevention
 - High-dose celecoxib reduces the number of colorectal polyps in patients with familial adenomatous polyposis.
 - Under study for prevention of sporadic colorectal cancer
 - Risk of coronary events is increased (~4 cases per 1,000 patients).
- Calcium supplementation
 - Early data from randomized studies suggest that calcium supplementation decreases risk of adenomatous polyp recurrence by ~20%.
 - Does not decrease the proliferative rate of the colonic epithelium
 - Vitamin D may also reduce the risk.
- β -Carotene
 - In the Physician's Health Trial, β -carotene was not associated with a decreased cancer risk compared to placebo.
- Alpha-Tocopherol/Beta-Carotene Lung Cancer Prevention Trial
 - Participants received α -tocopherol, β -carotene, and/or placebo.
 - After a median follow-up of 6.1 years:
 - Lung cancer incidence and mortality were statistically significantly increased in those receiving β -carotene.
 - α -Tocopherol had no effect on lung cancer mortality, but there was higher incidence of hemorrhagic stroke.
 - No evidence suggested interaction between the 2 drugs.
 - An unplanned analysis suggested that prostate cancers might have been reduced.
- Interferon α alone in chronic hepatitis B and combined with ribavirin in chronic hepatitis C lowers the risk of hepatocellular carcinoma.

Hormonally induced cancers

- Finasteride
 - Produced a 25% decrease in overall prostate cancer, but a slight increase in high-grade (Gleason score 7–10) prostate cancer in men >55 years of age.
 - It remains unclear whether the higher Gleason grade means more aggressive tumor progression in the setting of androgen deprivation.
- Tamoxifen
 - Adjuvant in breast cancer treatment
 - Reduced the number of new breast cancers in the uninvolved breast by more than one-third
 - Patients at high risk for breast cancer
 - In a randomized placebo-controlled trial involving > 13,000 women at high risk, tamoxifen decreased the risk of developing cancer by 49% compared to placebo.
 - Small increase in risk of endometrial cancer, stroke, pulmonary emboli, and deep venous thrombosis

- A trial to compare tamoxifen with another selective estrogen receptor modulator, raloxifene, is ongoing.
 - Raloxifene may have less risk of endometrial cancer.
- Selenium and vitamin E
 - Men taking selenium to prevent skin cancer were found to have a significantly reduced incidence of prostate cancer.
 - Another trial showed risk of prostate cancer was reduced in those taking vitamin E.
 - The findings on selenium and vitamin E were serendipitous and based on secondary analysis; a prospective study is under way.

Surgical prevention

- A study evaluated 139 women with *BRCA1* and *BRCA2* mutations to evaluate option of bilateral mastectomy rather than close surveillance.
 - 76 chose mastectomy and 63 chose surveillance.
 - None of the 76 women who underwent mastectomy developed breast cancer.
 - 8 of the 63 women under careful surveillance developed breast cancer.
 - A randomized study is unlikely to be done, and assessment of the effects of prophylactic mastectomy on mortality is also unlikely to be done.

Cancer screening

General

- Clearly saves lives in cervical cancer, colorectal cancer, and breast cancer
- Subject to biases that can suggest a benefit when there is none, possibly even masking net harm
- Lead-time bias occurs when slow-growing, less aggressive cancers are detected during screening.
 - Cancers diagnosed due to the onset of symptoms are on average more aggressive, and treatment outcomes are not as favorable.
 - In overdiagnosis, undetected slow-growing tumors are discovered.
 - Many of these tumors fulfill the histologic criteria of cancer but will never become clinically significant or cause death.
 - Most common cancers appear most frequently at ages when competing causes of death are more frequent.
- Selection bias results when the group most likely to seek screening may differ from the general population.
 - Those screened may have volunteered because of a particular risk factor not found in the general population, such as a strong family history.
 - Volunteers for studies may be more health conscious and likely have a better prognosis or lower mortality rate, irrespective of the screening result.

Breast cancer

- Mammography or mammography plus clinical examination in women >50 years of age
 - Trials have shown that mortality decreased by 20–30%, but each study has design flaws.
 - In women 40–49 years of age, the result depends on the statistical test used.
 - Analysis of 8 large randomized trials showed no benefit from mammographic screening for women 40–49 years of age when assessed 5–7 years after trial entry.

- A small benefit emerged 10–12 years after study entry.
 - What proportion of this benefit is due to screening after these women turned 50 years of age is not known.
- Nearly half of women 40–49 years of age screened annually will have false-positive mammograms necessitating further evaluation, often including biopsy.
 - The risk of false-positive testing should be discussed with the patient.
- In randomized screening studies of women 50–69 years of age, the decline in mortality begins about 5 years after initiation of screening.
- A substantial fraction of breast cancers are first detected by patients.
 - Self-examination leads to increased biopsy rate without reduction in cancer mortality.
- Genetic screening for *BRCA1* and *BRCA2* mutations and other markers of breast cancer risk has identified a group of women at high risk for breast cancer.
 - When to begin and the optimal frequency of screening have not been defined.
 - Mammography is less sensitive at detecting breast cancers in women carrying *BRCA* mutations.
 - Such cancers occur in younger women, in whom mammography is known to be less sensitive.

Cervical cancer

- The cervical cancer mortality rate has decreased substantially since the widespread use of the Pap smear.

Colorectal cancer

- Annual fecal occult blood testing could reduce colorectal cancer mortality by one-third.
 - Sensitivity increases if specimens are rehydrated before testing, but specificity is reduced.
- 2 studies of sigmoidoscopy in persons >50 years of age shows decreased mortality, but the study design was prone to selection bias.
 - One-quarter to one-third of polyps can be discovered with the rigid sigmoidoscope, half are found with a 35-cm flexible scope, and two-thirds to three-quarters are found with a 60-cm scope.
 - Diagnosis of polyposis by sigmoidoscopy should lead to evaluation of the entire colon with colonoscopy and/or barium enema.
 - The most efficient interval for screening sigmoidoscopy is unknown.
 - Case-control studies suggest that testing at intervals of up to 15 years may confer benefit.
- One-time colonoscopy detects about 25% more advanced lesions (polyps >10 mm, villous adenomas, polyps with high-grade dysplasia, invasive cancer) than does one-time fecal occult blood testing with sigmoidoscopy.
 - Well suited to screening subjects at high risk, e.g., with ulcerative colitis or family predisposition
 - Debate continues on whether full colonoscopy is too expensive and invasive for widespread use as a screening tool in standard-risk groups.
- Data are not available on digital rectal examination or barium enema as colon cancer screening tools, but both are insensitive.

Lung cancer

- Chest radiography and sputum cytology
 - No reduction in lung cancer mortality found, including in high-risk persons
 - Spiral CT increases number of lesions detected at early stage, but with high false-positive rates.

Ovarian cancer

- Adnexal palpation is too insensitive to detect ovarian cancer at an early enough stage to affect mortality substantially.
- Neither transvaginal ultrasonography nor CA-125 screening has been tested in a completed randomized prospective trial.
 - Ovarian cancer screening can lead to an invasive diagnostic work-up, which may include laparotomy.
 - A large proportion of women identified would have advanced, incurable disease and thus not benefit from screening.
 - A National Institutes of Health consensus conference in 1994 concluded that routine screening for ovarian cancer is:
 - Not indicated for standard-risk women
 - Not indicated for those with a single affected family member
 - Probably worthwhile in families with genetic ovarian cancer syndromes, where prophylactic oophorectomy can save lives

Prostate cancer

- Prostate-specific antigen screening has caused prostate cancer to become the most common nonskin cancer diagnosed in American men.
 - Very prone to lead-time bias, length bias, and overdiagnosis
 - Substantial debate rages among experts on whether it is effective.
 - Some experts are concerned that prostate cancer screening, more than screening for other cancers, may cause net harm on the basis of serious side effects of treatment.
 - Clearly detects many asymptomatic cancers, but ability to distinguish tumors that are lethal but curable from those that pose little or no threat is limited
 - Men >50 years of age have a very high prevalence of indolent, clinically insignificant prostate cancers.
 - No well-designed trial has demonstrated the benefit of prostate cancer screening and treatment.

Endometrial cancer

- Benefits from routine screening (transvaginal ultrasonography or endometrial sampling) have not been shown.

Skin cancer

- No prospective randomized studies have evaluated the impact on mortality of visual examination of skin surfaces by a health care provider.

- Observational evidence suggests that screening programs have resulted in a stage shift in melanoma diagnosis.
 - May reinforce sun avoidance and other cancer prevention behaviors

Complications

- Complications of the screening procedure
 - Example: colonoscopy
 - Occurs in 1–3 persons per 1,000 colonoscopies
 - Bleeding
 - Infection
 - Colonic perforation
 - Anesthesia complications
 - Stroke, myocardial infarction
- Complications of follow-up tests after abnormal screening test
- Emotional distress from screening and false-positive results

ICD-9-CM

- 199.1 Malignant neoplasm without specification of site (includes cancer, unspecified site either primary or secondary) Cancer Screening & Prevention
- 234.9 Carcinoma in situ of other and unspecified sites, site unspecified Cancer Screening & Prevention

See Also

- Approach to the Patient with Cancer
- Breast Cancer
- Cervical Cancer
- Colorectal Cancer
- Endometrial Cancer
- Gastrointestinal Endoscopy
- Head and Neck Cancer
- Health Care Screening and Disease Prevention
- Lung Cancer, General
- Nicotine Addiction
- Prostate Cancer
- Squamous Cell Cancer of the Skin
- Testicular Cancer

Internet Sites

- Professionals
 - Screening and Testing to Detect Cancer
National Cancer Institute
 - U.S. Preventive Services Task Force (USPSTF)
Agency for Healthcare Research and Quality

- Homepage
Canadian Taskforce on Preventive Health Care
- Cancer Prevention and Control
Centers for Disease Control and Prevention
- Patients
 - Homepage
American Cancer Society
 - American Cancer Society Guidelines for the Early Detection of Cancer
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Pearls

- Cancer detection is among the most litigious activities physicians undertake.
 - It is imperative that a patient's medical history be thorough, updated frequently, verified by the physician, and signed in acknowledgement by the patient.
 - In addition, the patient should be informed that family history can influence decisions about screening, prevention, and diagnostic procedures and therefore, it is in the patient's best interest for the family history to be as accurate and complete as possible.
- A common belief is that cancers detected in asymptomatic people are generally curable.
 - However, even the smallest detectable primary cancers may have spread to regional lymphatics or hematogenously.
 - Discussion with the patient about probabilities is important to maintain realistic expectations of the value of screening.

- In discussions of cancer risk factors, prior exposure to radiation therapy is often not considered.
 - However, with the increase in cancer survival from effective therapies, an increasing number of persons are surviving a first cancer and are at risk of a second cancer as a consequence of the treatment.
 - People who have received radiation therapy to the chest are at increased risk of breast cancer, lung cancer, and other cancers in or adjacent to the radiation field.
 - A woman who received mediastinal radiation therapy for Hodgkin's disease at age 25 years has a 30% of risk of developing breast cancer by age 55 years.
 - Heightened surveillance and chemoprevention are important considerations in the setting of such high risk.
- The risks and benefits of a screening test should always be discussed with a patient in advance or performing the test, even a blood test (such as prostate-specific antigen).
 - In addition, the physician also needs to discuss the risks of not taking the test.
- While in general, little evidence supports the use of vitamin supplementation in the prevention of cancer, 2 exceptions to this statement are emerging.
 - Vitamin D and vitamin B₆ appear to prevent the development of colorectal cancer.
 - Vitamin D inhibits the development of polyps and vitamin B₆ decreased the risk of colorectal cancer by one-third, especially in women who drink alcohol.