7-10-2017

Cancer Prevention and Screening

James Liebmann

University of Massachusetts Medical School

Recommended Citation

James Liebmann, MD

Summary and Key Points

Prevention

1. Currently in the United States, tobacco use is the single greatest preventable cause of cancer. Physicians should strongly encourage patients to quit smoking or chewing tobacco or, even better, to never take up these habits.

2. Some viral and bacterial infections can cause cancer. It is hoped that vaccines against specific infectious agents (e.g., Hepatitis B, human papilloma virus) will result in reductions in cancers associated with these infections.

3. Obesity is associated with an increased risk of a number of malignancies. While it makes sense to urge patients to adopt "healthy lifestyles" with attention to sensible diets and moderate exercise, no study has shown any particular diet or nutritional supplement capable of lowering the risk of developing cancer.

4. Some cancers can be prevented by taking drugs that block carcinogenic pathways (chemoprevention). In individuals at high risk of developing certain cancers, prophylactic removal of the organ at risk (e.g., mastectomy, oophorectomy, and colectomy) can prevent subsequent cancer.

Screening

1. The goal of cancer screening tests is to lower the morbidity and mortality from cancer by discovering cancers at an early, treatable stage.

2. Effective cancer screening currently exists for breast, cervical, and colorectal cancers.

Introduction

Current treatments of cancer are imperfect and entail risks. For many malignancies, the best "treatment" is to prevent the cancer from ever appearing in the first place. Cancer prevention refers to interventions that reduce the incidence of cancer. Such interventions can include reduction of exposure to known carcinogens (e.g., tobacco), treatment with drugs that lower cancer risk (chemoprevention), vaccination against infectious agents that cause cancer, surgery to remove organs at high risk of developing cancer in individuals with familial cancer syndromes, or the adoption of a "healthy lifestyle" that modifies cancer risk. Cancer screening shares some concepts with cancer prevention. A screening test like colonoscopy that results in the removal of polyps that have the potential of progressing to cancer can be a form of cancer prevention. Cancer screening is also utilized to find an established cancer at an early, treatable stage.

Cancer screening tests are employed in healthy, asymptomatic patients so it is imperative that these tests are safe and effective. A "positive" screening test will invariably lead to additional, increasingly invasive tests. It is not good enough to find a cancer early in its growth if no effective treatment exists for it or if the cancer was never going to grow and harm the patient during the course of the patient's life. An effective screening test should not just find a cancer early; it should lead to a reduction in morbidity and mortality from the malignancy.

This chapter will provide a brief review of cancer prevention and screening. It should be noted that preventive care literature frequently refers to "primary", "secondary", and "tertiary" prevention measures. The U.S. Preventive Services Task Force defines primary prevention as measures designed to prevent the occurrence of a disease; the discussion of cancer prevention in this section will be restricted to primary prevention. Secondary prevention includes anything that detects disease at a stage before it becomes clinically apparent when

interventions might be more effective – this definition typically applies to cancer screening. Tertiary prevention includes the care of active disease and will not be covered in this chapter. Interested students can acquire additional information through the National Cancer Institute, the American Cancer Society, or the Centers for Disease Control and Prevention web sites.

Cancer Prevention

Smoking Cessation

It is impossible to exaggerate the impact of tobacco use on cancer incidence and mortality.[1] Tobacco consumption by men in the United States began to skyrocket after the introduction of industrial production of cigarettes in the early 20th Century. In the 1960's, over 50% of men in the United States were smoking. Women took up the smoking habit during and after World War II, and over one-quarter of women in the United States were smoking by the 1980's. The incidence of lung cancer, a once rare disease, began to rise about 20-30 years after the increase in tobacco consumption. Today, thanks to decades of anti-smoking awareness, smoking rates among both sexes in the United States are now down to about 20%. Lung cancer incidence and mortality in men have fallen by over 20% since reaching peak levels in 1990.

Although lung cancer is the leading cause of tobacco-induced cancer mortality, smoking increases the risk of a variety of other disorders. Table 1 lists the variety of cancers which are linked to smoking. Some cancers (e.g., larynx, esophagus), like lung cancer, occur because of direct exposure to the carcinogens in cigarette smoke. Others (e.g., renal, bladder) are due to exposure of carcinogens that are absorbed from cigarette smoke and concentrated in excretory organs. Besides cancer, cigarette smoking markedly increases morbidity and mortality from other diseases, including stroke, heart disease, peripheral vascular disease, and chronic lung disease.

Table 1. Cancers Strongly Associated With Tobacco Use
Lung Cancer
Esophageal Cancer
Kidney Cancer
Bladder Cancer
Cancers of the Head & Neck (Tobacco Smoking & Chewing)

Smoking cessation lowers the risk of smoking related cancers and other diseases. Smoking cessation is, therefore, the single most effective measure that can be taken in any smoking patient to lower the risk of premature death. Because of the addictive potency of nicotine, smoking cessation can be very difficult. A variety of techniques (Table 2), including pharmacological intervention, have been shown to have some effectiveness in helping smokers quit. Importantly, the simple acts of a physician asking a patient about their desire to quit and encouraging the patient to try to quit can increase the probability that a patient will successfully stop smoking.

Table 2. Strategies to Aid Smoking Cessation
Pharmacological
Nicotine Replacement – Transdermal Patch, Gum, Lozenge, Inhaler
Nasal Spray
Nicotinic Acetylcholine Receptor Binding – Varenicline
Antidepressant - Bupropion
Behavioral
Hypnosis
Support Groups/Counseling

Infections and Cancer

A number of infectious agents can cause cancer. Some strains of human papilloma virus are associated with cancers of the cervix, anus, penis, and oropharynx. Hepatitis B and C infections can cause hepatocellular carcinoma. Epstein-Barr virus is associated with the epidemic form of Burkitt's lymphoma and *Helicobacter pylori* infection contributes to gastric cancer. It is hoped that vaccines may reduce the risk of cancer from some infections. A vaccine against oncogenic strains of human papilloma virus has been shown to reduce the incidence of precancerous cervical lesions. Similarly, effective use of the vaccine against hepatitis B may result in a reduction in the incidence of hepatocellular carcinoma.

Obesity and Healthy Lifestyles

The rising incidence of obesity in industrialized countries over the last quarter-century has been recognized as a major public health problem.

In addition to contributing to increased rates of diabetes, heart disease, and joint disease, obesity is associated with an increased risk of a variety of malignancies.[2] Cancers of the breast, colon, esophagus, uterus, and kidney all appear at increased frequency in obese individuals. Additionally, obese women with a history of early stage breast cancer appear to have an increased risk of relapse of their disease compared to women of ideal body weight with breast cancers of similar stage. The exact reasons for the higher cancer risks resulting from obesity are not clear. However, a number of hormones and growth factors are elevated in obese individuals, including estrogen, insulin, insulin-like growth factor, and leptin and these may help promote cancer cell growth.

There are probably many factors that have contributed to the increasing incidence of obesity. These include the availability of cheap, high calorie foods. Additionally, labor-saving devices and sedentary jobs and habits result in decreased caloric expenditure. Unlike vaccines that prevent infections, there is unlikely to be a "magic pill" that will safely curb obesity. Rather, patients should be encouraged to adopt life-long "healthy lifestyles" that include both sensible dietary habits combined with regular moderate exercise.

It is impossible to point to any one diet as the "perfect" diet.[3] However; it appears that a well-balanced diet, rich in fresh fruits and vegetables, is a good starting point. Dietary recall studies have demonstrated that individuals who take in large amounts of fresh fruits and vegetables have a lower risk of some cancers than those who take low amounts of such foods. By contrast, no large randomized trial of dietary supplements, including vitamins, has shown a reduction in the risk of developing cancer (Table 3). One explanation for this apparent paradox may be that it is more beneficial to obtain a variety of nutrients from whole foods than individual purified nutrients from pills.

Table 3. Dietary Supplement Trials and Cancer Risk

Dietary Supplement	Cancer	Effect	Study	Reference
Multi Vitamin (MV)	Cancer in women	No effect	Observational (WHI)	Neuhouser et al., Arch Int Med, Feb. 2009
Selenium (Se)	Prostate	No effect	Prospective intervention (SELECT)	Lippman, et al., *JAMA*, Jan. 2009
Vitamin C	All cancer in men	No effect	Prospective intervention (Physicians' Health Study II)	Gaziano et al., *JAMA*, Jan. 2009
Vitamin E	Prostate, all cancer in men	No effect	Prospective intervention, two trials (SELECT and Physicians' Health Study II)	Lippman et al. Gaziano et al., *JAMA*, Jan. 2009
Calcium + Vitamin D	Breast cancer in women	No effect	Prospective observational (WHI)	Chlebowski et al., *JNCI*, Nov. 2008
Folate	Prostate	More incidence	Prospective intervention (Aspirin/Folate Polyp Prevention Study)	Figueiredo et al., *JNCI*, March 2009
Se + Vit E + βcarotene	Gastric	Less death	Prospective intervention (Linxian Nutrition Intervention Trial)	Qiao et al., *JNCI*, April 2009

Chemoprevention

Chemoprevention refers to the use of pharmacologic agents to prevent cancer. At present, the only drugs shown to prevent the development of cancer block the formation of tumors dependent on hormones for their growth. Tamoxifen and raloxifene are approved for breast cancer prevention. They are selective estrogen receptor modulators (SERM) that prevent carcinogenesis in breast cells by binding to the estrogen receptor in those cells. Finasteride is a 5-α reductase inhibitor that blocks the conversion of testosterone to dihydrotesterone (DHT). Reduction of

DHT prevents progression of prostate cells to cancer cells. While the American Society of Clinical Oncology (ASCO) and the American Urological Association (AUA) have issued guidelines that support the use of finasteride for prostate cancer prevention, finasteride has not yet received FDA approval for that indication.

It is important to appreciate that when tamoxifen, raloxifene, and finasteride are given to patients for cancer prevention, it is healthy people who do not have a disease who are being exposed to the drugs. Accordingly, side effects of any chemopreventive drug should be minimal. Tamoxifen and raloxifene can cause hot flashes and deep vein thromboses and tamoxifen can increase the risk of endometrial cancer. Finasteride can cause gynecomastia, impotence, and reduced libido. Any patient and physician considering using these drugs for chemoprevention has to weigh the potential benefit of cancer risk reduction against the risk of side effects of the drugs.[4]

Surgery and Cancer Prevention

A number of inherited genetic mutations have been identified that markedly increase the risk of developing certain cancers. Some of these cancers occur in organs that can be removed with no impact on life span. For example, women who inherit mutations in BRCA1 or BRCA2 have an elevated risk of developing breast and ovarian cancers. These women can be offered bilateral mastectomy and oophorectomy and those operations will markedly lower the risk of developing breast or ovarian cancer. Similarly, familial adenomatous polyposis coli syndrome is due to an inherited mutation in the APC gene and typically results in the development of colon cancer before the age of 40. Individuals with this syndrome are routinely offered total colectomy at a young age.

Just as the risks and benefits of chemoprevention need to be carefully considered for each individual patient, it is important to consider the implications of the surgical removal of an organ to prevent the subsequent development of cancer. Besides the immediate surgical risks (e.g., infection, bleeding), there may be long-term physical and psychological risks associated with prophylactic surgery. It is vital that patients be thoroughly counseled about the short and long-term risks before embarking on such surgery.

Cancer Screening

The primary goal of cancer screening is to improve survival from a cancer by finding the cancer at an early stage when it is more likely to be cured. Because large numbers of healthy people may undergo cancer screening, it is important that screening be affordable and safe.[5] In the United States, there is wide acceptance of screening for three cancers – breast, colorectal, and uterine cervix. More controversial is the value of current screening for prostate cancer and lung cancer.

No test is perfect. Statistical terms that mathematically assess tests include sensitivity and specificity. In the case of cancer screening, sensitivity refers to the ability of a test to find a cancer in those individuals who are afflicted with the disease and specificity is the measure of how well a test correctly identifies those individuals who do **not** have cancer (Figure 1). To be effective, a screening test should not only be sensitive (able to find cancer), but should also be very specific (able to identify healthy persons). The following example provides some idea of the need for high specificity. About 20% - roughly 40 million people - of the adult population smokes and there will be about 200,000 cases of lung cancer diagnosed this year in the United States. If a screening test for lung cancer has sensitivity and specificity both of 99% and all 40 million smokers are screened, then the screening test will miss about 2000 cases of cancer (99% sensitivity means 1% of cancers are missed – this result is called a false-negative). However, it will incorrectly identify almost 400,000 healthy people as having lung cancer (99% specificity means 1% of healthy people are mislabeled – this result is called a false-positive). Those 400,000 people without lung cancer may undergo further tests, including lung biopsies that can be costly, invasive, and risky. Thus, even a test with 99% sensitivity and specificity can result in twice as many people being given an incorrect diagnosis that they have cancer than are correctly diagnosed with cancer[1].

This example also highlights another aspect of screening, which is that the incidence of the screened condition will also affect the outcome of screening tests. For example, if lung cancer was a rare disorder with only 10,000 cases annually, a screening test with 99% sensitivity and specificity, if applied to 40 million people, will still incorrectly identify about 400,000 people as having lung cancer, so the ratio of false-positive results to true-positive results will now be 40:1 – forty people will be incorrectly identified as having lung cancer for every patient correctly diagnosed with the disease! This exercise illustrates the importance of

screening tests being highly specific, particularly when they are employed to find uncommon diseases. The mathematical concept that explores the effect of disease incidence on screening test outcome in detail is known as Baye's Theorum.

Breast Cancer Screening

Breast cancer is, in many ways, an ideal malignancy to screen for. It is the most common non-skin cancer diagnosed in women in the United States. Most breast cancers grow at rates that permit detection by mammography before they become symptomatic. Mammography trials date back almost half a century to the HIP trial from the 1960's. At this point, trials in North America and Europe have enrolled over 500,000 women randomly assigned to mammographic screening or no screening for breast cancer. Taken together, these studies have shown that mammography lowers the risk of dying of breast cancer by at least 15%.

That mammography lowers the risk of dying from breast cancer is not controversial. However, many issues regarding mammography continue to be subjects of debate and research. Mammography has been extensively studied in women between the ages of 50 and 70 and is strongly recommended for them. Very few women over the age of 70 have been included in randomized trials of screening so it is not known what benefit elderly women may realize from screening. There are also differences of opinion over the age at which women should begin screening. Because breast cancer is less common in younger women, there is concern over the increased number of false-positive mammograms relative to true-positive studies in younger age groups. It is also not clear what the optimal interval should be between mammograms. Randomized trials have had women undergo mammograms at intervals ranging between 12 and 33 months and it is not obvious that more frequent intervals provide enhanced benefit compared to longer intervals. Finally, the technology used for breast cancer screening has changed over the last fifty years. Breast MRI, widely used in the evaluation of women with an established diagnosis of breast cancer, is now recommended for screening women at very high risk of developing breast cancer (e.g., women harboring mutations in BRCA1 or BRCA2). Whether breast MRI, or any other technology, will replace mammography for screening the general population will depend on the results of well done trials comparing the different techniques.

Currently, the most commonly accepted standard in the United States is to recommend to women that they begin annual mammography sometime between the age of 40 and 50 and continue to at least the age of 75. Older women in good health could consider continuing annual or biannual mammogram screening past the age of 70.

Cervical Cancer Screening

Cervical cancer is almost entirely due to infection by oncogenic strains of the human papillomavirus (HPV). The virus is sexually transmitted, so screening for cervical cancer should begin after a woman becomes sexually active. The current screening test is the Papanicolaou smear (Pap test) in which cells scraped from the cervix are viewed for evidence of dysplasia. The Pap test has a significant incidence of false-positive results due to inflammation. There has never been a randomized trial of cervical cancer screening to clearly define the extent of benefit from the test. However, since the introduction of the Pap smear over fifty years ago, the death rate due to cervical cancer in the United States has fallen by over 70% and continues to decline at the rate of about 4% per year. In 2012 the United States Public Health Service Task Force on Prevention issued new guidelines for cervical cancer screening which have been endorsed by the American College of Obstetricians and Gynecologists (ACOG). Women should begin screening at the age of 21 and should have Pap smears every other year until age 30. At that point, screening should occur every three years. Screening can be discontinued for women at the age of 65 to 70 if they have had three consecutive normal Pap smears and are in a monogamous sexual relationship. These new guidelines replaced earlier standards that called for earlier and more frequent screening. The current guidelines recognize that cervical cancer may take years to develop and therefore the net benefit of screening young women shortly after they become sexually active or screening all women annually will be minimal. Although it is hoped that widespread use of HPV vaccination will reduce the incidence of cervical cancer, at present ACOG recommends that women who have received a HPV vaccine follow the screening guidelines noted above.

Colorectal Cancer Screening

Colorectal cancers arise from colonic epithelial cells as the result of mutations in oncogenes and tumor suppressor genes. As these cells accumulate genetic changes, they may gradually progress from

phenotypically normal cells to adenomatous cells to cancer cells. If these abnormal cells can be detected and removed in the adenomatous (polyp) state, then progression to cancer should be stopped. The tests most commonly used in the United States for colorectal cancer screening are fecal occult blood testing (FOBT) and colonoscopy. FOBT has been studied in five randomized trials in the United States and Europe and has demonstrated a 15-33% reduction in the risk of dying from colorectal cancer in the screened groups.

Screening colonoscopy has never been evaluated in a randomized trial. Cohort studies suggest that screening colonoscopy can also lower the risk of dying from colon cancer. In this regard, note that most patients in FOBT programs would undergo colonoscopy if they were actually found to have a positive FOBT. At present, both the American Cancer Society and the United States Preventive Services Task Force recommend that adults begin screening for colorectal cancer at the age of 50. Acceptable methods of screening include colonoscopy every ten years or annual FOBT.

While screening colonoscopy is routinely pursued in the United States in spite of the lack of data from randomized trials, a trial has now been published that supports the use of flexible sigmoidoscopy for colon cancer screening. In the United Kingdom over 170,000 patients between the ages of 55 and 64 were randomly assigned to one flexible sigmoidoscopy or no screening. The screened group realized a 23% reduction in colon cancer incidence and a 31% reduction in death due to colon cancer after a median follow-up of over 11 years.

Lung Cancer

Lung cancers are often very aggressive cancers that kill most people who are diagnosed with the malignancy. Stage IV (metastatic) lung cancer has a median survival of less than a year. Unlike many cancers that can affect almost any human, lung cancers are found with greatest frequency in smokers. Thus, it makes sense that a screening program restricted to smokers that was able to find lung cancers at an early stage would be an effective way to lower mortality from lung cancer. Unfortunately, until recently, no lung cancer screening program has demonstrated a reduction in lung cancer mortality.

In the 1970's and 1980's studies using either screening chest x-rays, induced sputum cytology, or both tests had remarkably similar findings.

All trials showed that screening resulted in the discovery of more early stage lung cancers than were found in smokers who did not undergo screening. Importantly, screening permitted the surgical resection of many more early stage (stage I and II) tumors. Despite these findings, individuals randomized to screening had no reduction in risk of death due to lung cancer.

Recently, low dose computerized tomography (CT) of the chest has been advocated as a potentially useful screening technique for lung cancer. Like earlier trials of lung cancer screening, chest CT is able to find many early stage cancers before such cancers would come to medical attention by causing symptoms. In November, 2010, the National Cancer Institute (NCI) released initial results from the National Lung Screening Trial, and the study was eventually published in August, 2011.[6] This trial randomized 53,000 smokers between the ages of 55 and 74 to screening with annual chest CT for three years or standard chest x-ray. Data from the trial showed that patients who underwent screening chest CTs had a 20% reduction in lung cancer mortality compared to those patients who only had screening chest x-rays. Published results of the trial have shown that it is necessary to screen 320 patients annually for three years to benefit one patient. A full economic analysis of this screening approach been published and shows a wide range in the potential cost of lung cancer screening.. A number of national organizations (American Cancer Society, American College of Chest Physicians, National Comprehensive Cancer Network) now recommend that physicians consider low dose chest CT screening for some patients who smoke or have a history of smoking. In July 2013, the US Preventive Services Task Force recommended low dose CT screening annually for adults age 55-79 with a 30-pack year smoking history or who have quit in the last 15 years.[7]

Controversies in Cancer Screening

As previously discussed, the principle goal of cancer screening tests is to reduce the mortality from a screened cancer. Simply being able to find cancers at an early stage is not enough to justify a screening test if such a discovery does not result in a decrease in mortality (or morbidity) from the cancer. However, it can be difficult for the public – and physicians – to accept the notion that finding cancer at an early stage may not be beneficial to patients. The current status of screening for prostate cancer can help illustrate this conundrum.

Prostate specific antigen (PSA) is a protease secreted by normal and malignant prostate cells. It is easy to measure with a simple blood test. PSA levels typically rise as men age, reflecting the hypertrophy of the prostate that accompanies aging. However, PSA levels above a certain range are increasingly likely to indicate the presence of prostate cancer. Checking a man's PSA on a regular basis has been advocated by some as a way to find prostate cancer at an early, treatable stage. Indeed, trials that date back two decades have consistently shown that PSA screening can help to find early stage prostate cancer. The widespread use of PSA screening in the United States led to a dramatic increase in the incidence of prostate cancer diagnosis – rising from about 100 new cases per 100,000 men in the late 1970's to about 230 new cases per 100,000 men in the early 1990's.

While PSA screening unquestionably led to the sharp change in the number and stage of newly diagnosed prostate cancer cases, it has been very difficult to show that screening also led to an improvement in survival from prostate cancer. One reason for this is that prostate cancer is frequently a slowly growing tumor that may never cause problems for a man during his lifetime. Consequently, diagnosing prostate cancer at an early stage may merely expose a man to the risks of treatment (surgery or radiation) without affecting his overall life span.

Two large studies, one from the United States and one from Europe, looked at the impact of PSA screening on prostate cancer outcomes and were published recently. Though screened groups in both trials had a higher incidence of prostate cancer diagnosed, the US trial showed no impact of screening on mortality from prostate cancer. The European trial showed a modest improvement in prostate cancer mortality from screening, but concluded that almost 50 screened men would have to be treated for prostate cancer to save one life. The results from these trials have not settled the controversy over the usefulness of screening for prostate cancer. Passionate advocates on both sides of the issue have seized on the recent data to support their positions. At present, no major national body recommends routine prostate cancer screening with PSA testing. The United States Preventive Services Task Force recommends against prostate cancer screening. Some other groups recommend that physicians thoroughly counsel men about the limitations and risks of screening before embarking on a screening program.

Conclusion

Prevention of cancer is surely the most cost-effective way to lower mortality from cancer. Cessation of tobacco use and adoption of a healthy lifestyle are sensible steps that will provide a number of benefits to patients. Vaccines that reduce the risk of infection by oncogenic viruses are also expected to lower the risk of specific cancers. Drug treatment (chemoprevention) and prophylactic surgery can lower the risk of certain cancers in selected populations.

Screening for a cancer should be adopted if the screen lowers the mortality of the cancer. Some screening techniques can do this for selected cancers and national organizations recommend screening for breast, cervix, lung, and colorectal cancers in appropriate populations. However, controversies still exist about some of these screening programs.

Thought Questions

1. A researcher claims to have a blood test that reliably identifies patients with cancer of the pancreas. She argues passionately that this should become a standard test in order to diagnose this usually fatal malignancy at an early stage. What additional information is needed before deciding if such a test is a useful screening test?

    Your answer:

2. The claim has been made that sharks never get cancer and, therefore, shark cartilage can prevent cancer. You wish to test that hypothesis. What populations should you treat with shark cartilage and why? What limitations to drug procurement can you imagine (besides the obvious teeth problem).

    Your answer:

    Expert Answer

    Expert Answer

Glossary

Adenomatous cells (Polyp)– A benign growth resulting from the acquisition of genetic alterations that lead to hyperplasia. Additional mutations may lead to the development of cancer.

APC gene- A tumor suppressor gene located on chromosome 5.

Baye's Theorem- A statistical theorem that states that the probability that a positive test is true is based in part on the frequency of the condition that the test is searching for.

Bilateral mastectomy- Surgical removal of both breasts.

Bilateral oophorectomy- Surgical removal of both ovaries.

BRCA1- A tumor suppressor gene located on chromosome 17.

BRCA2- A tumor suppressor gene located on chromosome 13.

Cancer prevention- Interventions that reduce the incidence of cancer

Cancer screening- Tests to find cancer early; reducing the morbidity and mortality from the malignancy

Chemoprevention- Treatment with drugs that lower cancer risk

Colonoscopy- Direct fiber-optic examination of entire colon

False-negative- A test result that incorrectly states that the condition being tested for does not exist in the subject undergoing the test.

Obesity- Accumulation of excess body fat to the extent that the health of an individual may be adversely affected.

Oncogenes- A mutated gene that can cause cancer.

Phenotypically normal cells- Cells that exhibit normal behavior.

Primary prevention- Measures designed to prevent the occurrence of a disease

Randomized trial- A trial in which subjects are allocated by chance to one intervention or another.

Secondary prevention- Anything that detects disease at a stage before it becomes clinically apparent when interventions might be more effective (cancer screening)

Sensitivity- In the case of cancer screening, refers to the ability of a test to find a cancer in those individuals who are afflicted with the disease

Sigmoidoscopy- Examination of anus, rectum and sigmoid colon

Specificity- In the case of cancer screening, the measure of how well a test correctly identifies those individuals who do **not** have cancer

Tertiary prevention- Care of active disease

Total colectomy- Surgical removal of the entire colon.

Tumor suppressor genes- A gene whose loss of function predisposes a cell to cancer.

References

1. Tobacco Statistics Snapshot. National Cancer Institute website. http://www.cancer.gov/cancertopics/tobacco/statisticssnapshot. Updated 11/12/2010. Accessed 26 December 2010.

2. Flegal KM, Graubard BI, Williamson DF, et al. Cause-specific excess deaths associated with underweight, overweight, and obesity. JAMA. 2007;298 (17): 2028-37.
   PubMed abstract

3. Huang HY, Caballero B, Chang S, et al. The efficacy and safety of multivitamin and mineral supplement use to prevent cancer and chronic disease in adults: a systematic review for a National Institutes of Health state-of-the-science conference. Ann Intern Med. 2006;145(5):372-85.
   PubMed abstract

4. William WN Jr, Heymach JV, Kim ES, et al. Molecular targets for cancer chemoprevention. Nat Rev Drug Discov. 2009;8(3):213-25.
   PubMed abstract

5. Kramer BS. The science of early detection. Urol Oncol. 2004;22(4):344-7.
   PubMed abstract

6. The National Lung Screening Trial Research Team: Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med. 2011; 365(5):395-409.

7. Humphrey L, Deffebach M, Pappas M, Baumann C, Artis K, Mitchell JP, Zakher B, Fu R, Slatore C. Screening for lung cancer: Systematic review to update the U.S. Preventive Services Task Force recommendation. Rockville (MD): Agency for Healthcare Research and Quality (US); 2013. Available from http://www.ncbi.nlm.nih.gov/books/NBK154610/.