CANCER SCREENING

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What is screening?

Screening is the identification of asymptomatic disease or risk factors by history taking, physical examination, laboratory tests or other procedures that can be applied reasonably rapidly to asymptomatic people. Screening tests are part of secondary prevention activities and are NOT intended to be diagnostic. Any individual who has a positive screening test MUST go on to further diagnostic evaluations.

There are several criteria for a good screening test. They are:

- high sensitivity and specificity
- high positive predictive value
- simple and low cost
- safe and relatively non-invasive
- acceptable to patients and clinicians
- must detect disease at a stage where treatment will affect outcome

Examples of good screening tests include: mammography for breast cancer screening and Pap smears for cervical cancer screening.

Unfortunately, screening can lead to possible adverse side effects such as pain, anxiety and unnecessary further testing due to a false positive result, missed diagnosis with a false-negative result or overdiagnosis of a cancer that may never cause problems during the individuals lifetime or for whom screening does not affect the outcome.

Outlines below are the screening methodologies employed for Breast Cancer, Prostate Cancer, Colo-rectal cancer and cervical cancer.

Breast Cancer

The main purpose of breast cancer screening is to detect early disease before it is clinically evident/palpable in an effort to reduce the chance of distant metastasis and ideally to decrease the morbidity of the disease.

There are numerous modalities that have been used for breast cancer screening, such as

- mammography
- MRI
- clinical breast exam (CBE) by a health profession
- breast self exam (BSE)

Mammography is the most common modality used. Approximately 40% of lesions are picked up on mammogram alone and about ½ of these are invasive cancers <1 cm. From US studies, the chance of a mammographic lesion being positive for malignancy is in the range of 20-30%. At least 8 randomized trials have shown a reduction in mortality with the use of mammographic screening. With 14 years of follow-up, patients aged 50-69 have a 22% reduction in mortality from breast cancer compared to the control population. A 15% reduction in mortality was seen with patients aged 40-49.

Technical advances in radiology, such as digital mammography have improved the sensitivity/specificity of mammography in premenopausal woman and those with dense breasts

There may be evidence that the addition of CBE to mammogram as part of the screening may further reduce the mortality from breast cancer. There is no evidence that SBE alone has any impact on mortality reduction.

In terms of older women, there may be a benefit to continued screening of women over the age of 70. Most trials included only a small number of women from this population; therefore, the exact benefit is unknown. However, screening is recommended if the individual is in good health.

Although not proven in clinical trials, MRI screening along with mammography is recommended for young patients at high risk since mammography is not as sensitive for those patients with dense breasts

<u>Recommendations (Canada)</u>
- Mammogram every 1-2 years from age 50-69
- clinical breast exam yearly from ages 50-69
- self-breast exam monthly

<u>Recommendations (USA)</u>
- Mammogram every 2 years from ages 40-49 then yearly to age 75
- Clinical breast exam yearly
- breast self-exam monthly.

<u>High risk patients and patients with BRCA mutations</u>
- High-risk patients (e.g. first degree relative with breast cancer) may benefit from screening at an earlier age depending on the degree of risk. Screening with mammography and MRI is recommended begging at an age 10 years earlier than the affected relative's age at diagnosis.
- Patients with BRCA mutations are counseled regarding their risks and generally offered prophylactic mastectomy and bilateral oophorectomy. Those who decline mastectomy may opt for MRI screening and mammography.

Cervical Cancer

Cervical cancer represents a clinical entity where screening has been very effective. This is a result of the high prevalence of the disease in the unscreened population, the sensitivity of the Pap smear and the long pre-invasive stage of cervical cancer.

Screening tools include cytological screening with PAP smear (introduced by Papanicolaou in 1930) and examination with bimanual pelvic exam. Case control studies indicate that the PAP smear decreases the incidence of invasive cervical cancer by 60-90%. PAP smears and pelvic exams have led to a decrease in the mortality rate of cervical cancer by more than 70% between 1940 and 1970.

A positive PAP test can indicate a high probability of invasive disease, but a diagnosis of invasive cancer cannot be made based on this test.

<u>Recommendations:</u>

- Canadian and American recommendations are similar with respect to time of first PAP. Generally 3 years after the onset of sexual activity and no later than age 21.

- screening should be annually for at least 3 consecutive normal smears , then every 3 years or at the discretion of the physician. (some evidence to suggest that the yield is low after normal smears). High-risk patients should continue to have yearly smears. The American College of Obstetrics and Gynecology recommends that smears continue annually.

- American Cancer Society and the Canadian Task Force recommend screening until age 65 and 70 respectively.

- Screening should be performed using either the conventional Papanicolaou smear or liquid based cytology

- Screening is not recommended for women who have had total hysterectomies for benign indications

- <u>Canadian recommendations for abnormal PAP</u>:

    - LSIL/ASCUS - every 6 mos if no evidence of progression. If persists, then colposcopy.
    - HSIL or malignant cells - colposcopy and biospy
    - AGUS – colposcopy and biopsy

Because the mortality from cervical cancer increases with increasing age, it may be prudent to continue screening in the elderly.

Screening post radiotherapy:

- controversial issue.
- dysplasia / epithelial changes can be seen after radiation.
- normal PAP 4-12 months if stage I and II is a good prognosticator; this is not true for stages III and IV.
- presence of tumour cells on PAP three months after radiation requires further investigation.

HPV vaccine

Human papillomaviruses (HPV) are highly prevalent, tissue-specific, DNA viruses that infect epithelial cells. Persistent viral infection with oncogenic types of HPV leads to cancer of the cervix, anus, vagina, vulva, penis, mouth, and sinuses.

In 2006, a two HPV vaccines were introduced. The bivalent vaccine is directed towards the oncogenic types, 16 and 18 and the quadrivalent form is directed against HPV 6,11,16,18. It is estimated that targeted HPV protection with the bivalent or quadrivalent vaccine would prevent half of the high-grade precancerous lesions (CIN 2 or 3) and two thirds of the invasive cancers. The quadrivalent vaccine would also prevent most genital warts.

Recommendations (USA/Canada):

- quadrivalent HPV 6/11/16/18 L1 vaccine should be administered in girls and women 9 to 26 years of age
- the vaccine has been introduced into Ontario schools and is offered to students in grade 8.

Prostate Cancer

Prostate cancer often grows so slowly that most men die of other causes before the disease becomes clinically advanced. These individuals would therefore not benefit from screening. However, those with aggressive localized disease may benefit from early treatment and thus, a screening program that could identify asymptomatic men with aggressive localized tumors might be expected to reduce morbidity and mortality.

PSA testing has revolutionized prostate cancer screening. Although it was originally introduced as a tumor marker to detect cancer recurrence or progression it became adopted for screening in the early 1990's. Although it led to a dramatic increase in incidence of prostate cancer, there is no evidence that screening in symptomatic men leads to decreased mortality. 2 Large studies published in 2009 compared men who had regular screening vs. men who did not. The European study found that screening reduced prostate cancer death by 20% but the US Study did not detect any decrease in mortality with screening. Nevertheless, most physicians advocate for screening with PSA.

Methods of screening include:

PSA (prostate specific antigen)

- sensitivity 80-90% ; specificity 50%
- elevated in benign disease also i.e. BPH
- the reference range depends on age of the patient i.e. <or = 49, the normal range is 0-2.5 but patients <or = 79 have a normal range of 0-6.
- PSA can be elevated with TRUS or TURP, infection or prostatic massage
- not recommended for screening by the Canadian Task Force in the periodic health exam.

DRE (digital rectal exam)

- sensitivity 70% ; specificity 50%
- due to the cost effectiveness of this procedure, it would be useful to include it in the annual exam in men over 40-50.

<u>Recommendations</u>:

- The European Union, World Health Organization, Canadian Task Force and US Preventative Services Task Force all conclude that there is insufficient evidence to recommend for or against routine screening using PSA or DRE
- The American Cancer Society does not recommend routine PSA testing but believes that it should be offered along with DRE annually to men 50 yrs of age and older with a life expectancy greater than 10 yrs. High risk patients should be screening beginning at age 45.

Lung Cancer

75% of patients with lung cancer present with symptoms due to advanced local or metastatic disease that is not amenable to cure therefore prevention, rather than screening is the most effective strategy to reduce the burden of lung cancer.

Because of the high mortality and morbidity from lung cancer, screening of asymptomatic individuals has been the focus of many trials. Some of the tools used for screening include:

- Chest X-ray
- Sputum cytology plus chest X-ray
- Chest CT

Taken all together, these trials have shown the following:

- CXR and CT do detect early stage asymptomatic lung cancers
- There are high rates of false positive findings leading to additional, usually invasive procedures
- Long-term follow-up has failed to demonstrate a reduction in mortality with screening using CXR or CT

<u>Recommendations:</u>

- Screening with CT or CXR is not recommended by any professional organization

Colorectal cancer

Although screening has been shown to reduce mortality from colorectal cancer, screening rates are low. This is likely due to several factors:

- Embarrassment on the part of the patient
- Discomfort of the colonoscopy
- Limited accessibility of the equipment and specialists

It is important to look at risk factors when deciding on who is a good candidate for testing. Some of these risk factors include:

- Family history of colorectal cancer or polyps
- Personal history of inflammatory bowel disease
- Personal history of polyps

The appropriate choice of screening modality, age to initiate screening and frequency of screening is dependent on individual patient factors and risk

Screening tests include

- Fecal occult blood testing
  - Low sensitivity and specificity
  - Has been shown to reduce cancer specific mortality in some studies
- Sigmoidoscopy
  - Patient sedation is not required and it can be performed by trained GP's
  - It can only reach to the splenic flexure so may miss some cancers
  - Studies have shown that it can reduce cancer specific mortality by 1/3
  - A 5 year screening interval is recommended with a negative initial sigmoidoscopy
  - Positive sigmoidoscopies should be followed by colonoscopy and biopsy
- Colonoscopy
  - has been shown to prevent colorectal cancer and decrease cancer specific mortality
  - risk of major complications is 1-2/1000 procedures.
  - Patients require sedation and careful bowel preparation
- New technologies-virtual colonoscopy
  - Computer enhanced spiral CT scan after bowel prep and air insufflation
  - Sensitivity is 55-90%
  - Very expensive and availability is limited

<u>Recommendations (USA)</u>

- AGA recommends screening for all patients
- Patients who are at average risk should be screened starting at age 50 with annual fecal occult blood testing and flexible sigmoidoscopy every 5 years or colonoscopy every 10 years
- Those at high risk should start screening approximately 10 years earlier

<u>Recommendations (Canada)</u>

- The Canadian Cancer Society recommends that average risk patients age 50 and over have a fecal occult blood test at least every 2 years
  - Sigmoidoscopy and colonoscopy are only recommended for follow-up of a positive fecal occult blood test
- Patients at high risk should discuss surveillance with their doctor. Surveillence may include fecal occult blood testing with or without sigmoidoscopy or colonoscopy
  - There are *no* specific recommendations for or against screening in higher risk patients in Canada