Cancer Screening: An Evidence Based Approach

Practical Management Guidelines for Primary Screening

Timothy Munzing, MD

2011

Objectives

- **After the lecture participants will:**
  - Understand general principles of screening
  - List criteria needed to justify screening
  - Be familiar with lead time, length time, and screening biases as they relate to cancer screening
  - Understand evidence based guidelines, including related controversies, for cancer screening numerous cancers

General Principles

- Great variation in recommendations
- Consider source of recommendations
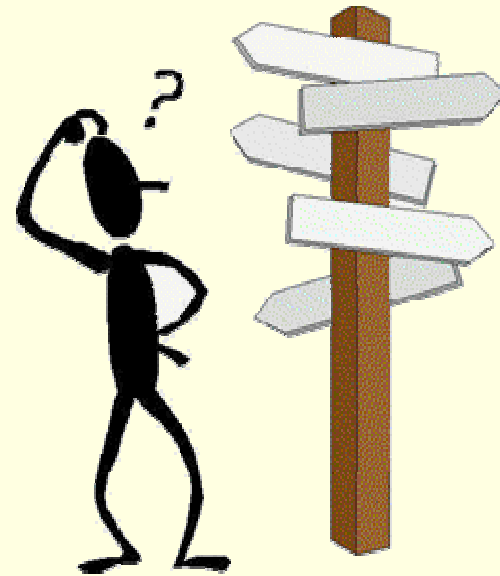
Screening - definition

- Diagnostic procedures applied to asymptomatic people in hope of identifying subgroup that may benefit form early intervention

Why Do Screening

- Detect asymptomatic disease when it is more amenable to treatment
- Decrease morbidity and mortality
- Philosophy of Family Medicine

Why Not to Screen

- Unable to make asymptomatic patients feel better (benefit must outweigh risks)
- False-positives (as high as 70%+)
- False-negatives - false reassurance
- Labeling - Diagnose at incurable stage
- Unnecessary anxiety
- Additional screening w/o effective tx

Criteria to Justify Screening

- Disease has serious consequences and substantial public health impact
- For cancer: detectable, prevalent, asymp. Non-metastatic phase present
- Natural history of disease understood
- Agreed upon policy exists regarding whom to screen and treat
  - The Permanente Journal

Criteria to Justify Screening

- Screening test is simple to perform, available, low cost, adequate sensitivity and specificity, acceptable to pt. and MD

- Test improves outcomes - measured by cause specific mortality rate

- Improvement in prognosis justifies cost, effort, risks and discomfort
  - The Permanente Journal

Screening Biases

- Lead Time Bias - Diagnosing a cancer at an earlier time without changing the ultimate time of death

- Length Time Bias - Screening tends to diagnose less aggressive / advanced cancers.
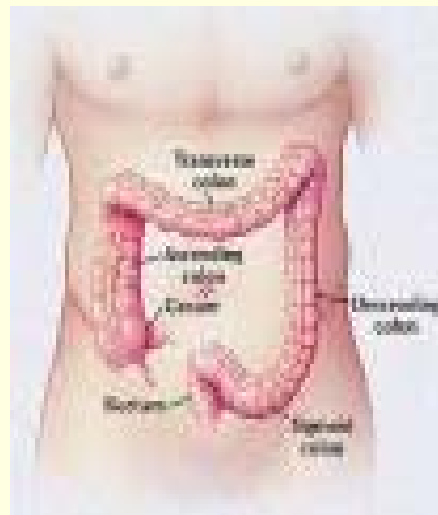
- Screening Bias

Lead Time Bias
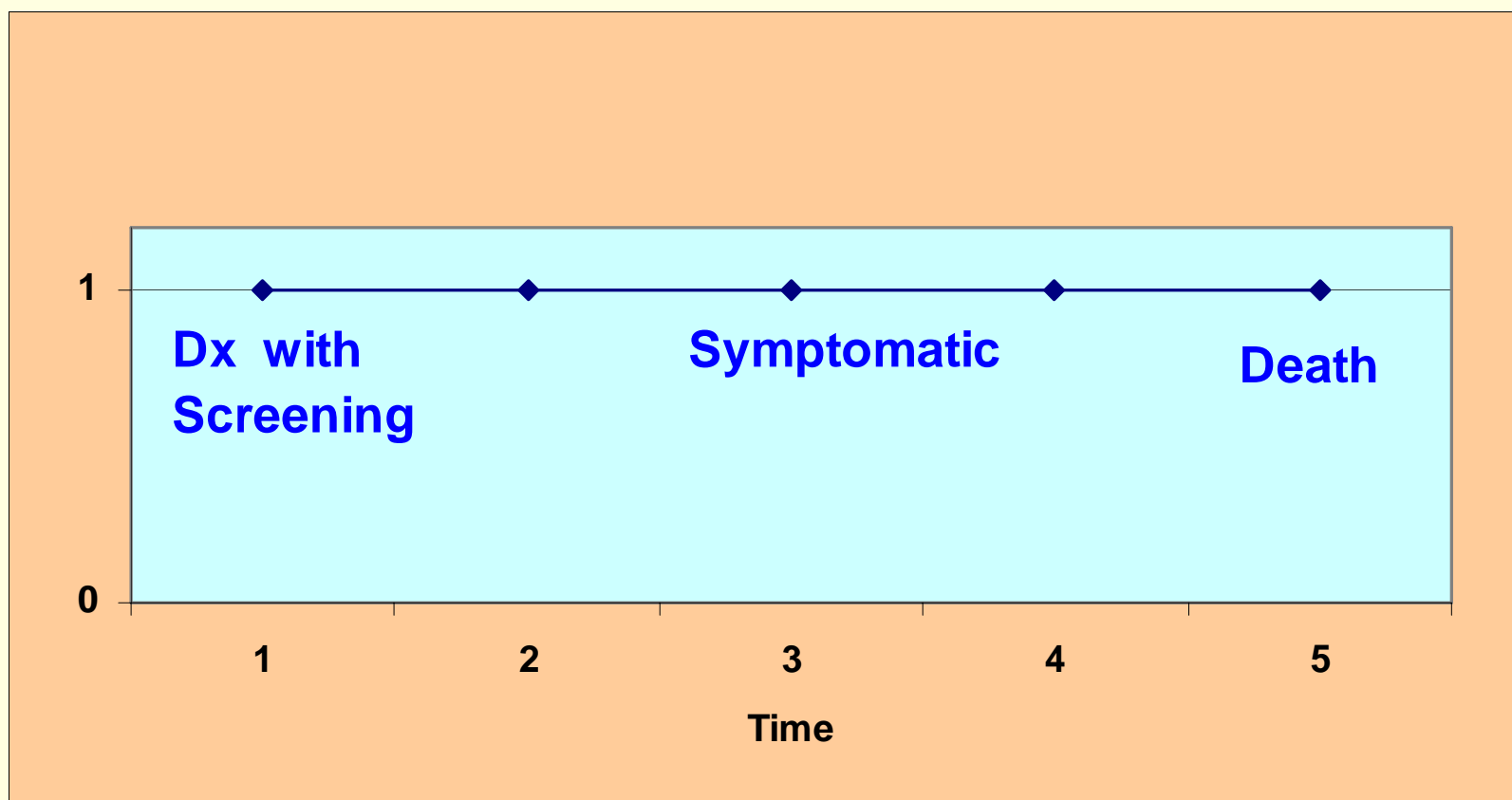
Screening Recommendations - Where to Find Them

- US Preventive Services Task Force (USPSTF)
- AAFP
- American Cancer Society
- American College of OB/Gyn (ACOG)
- Kaiser Permanente
- Other Organizations and Societies

Colorectal Cancer

- This will be the topic of the rest of the conference so this will not be examined here

Breast Cancer - Burden

- 210,00 new cases (U.S. – 2010 est)
- 40,000 deaths (U.S. – 2010 est)
- 32% of new cancers in women
- Lifetime risk of dying for women - 3.6% (CAD - 43%)
- 48% of new breast cancers occur in women <65 yrs old
  - USPSTF, Swedish trials, Canadian Nat. Breast Ca Screening Study

Breast Cancer Risks

- Menarche <12, Menopause >55
- Nullip or 1st child after 30
- H/O Benign breast dz, atypical hyperplasia or mult. breast bx
- Family H/O breast ca
- Thoracic radiation treatment
- Obesity, Heavy ETOH use
- ERT - small increase (weigh w/ benefits)
  - Tobin - Fam Med: Prin. & Practice

Breast CA Screening/Detection Methods

- Mammography
- Clinical Breast Exam (CBE)
- Self Breast Exam (SBE) – no conclusive date to support
- Ultrasound - <u>not</u> recommended for screening

Screening Accuracy

- Ages 50 - 59
  - Mammography sensitivity - 75%
  - Mammography + CBE sensitivity - 75% to 88%
  - Mammography specificity - 83 to 98.5%
- Ages 40 - 49
  - Mammography or mammo + CBE - 10-15% lower
    - HIP and Canadian NBSS

Effectiveness of Early Detection

- Six randomized controlled trials –
- Patients ages 50 to 74
  - 20 - 30% reductions in breast ca mortality
    - USPSTF

Screening Interval

- Swedish two county trial
  - Little evidence of q. 1 vs 2 yrs screening
- Meta-analysis women aged 50 - 74
  - Screening interval of 12 mos vs 18-33 mos – no difference in outcomes

Potential Harms of Screening

- False Positives - 80 - 90%
- Follow-up testing required
- Risk of false-positive after 10 mammograms - up to 49%
- Over-dx and treatment of Ductal CA-in-situ
  - Natural hx variable - treated aggressively
  - 750% increase in 2 decades
- Radiation Induced Breast CA - minimal
  - USPSTF

The Media Controversy – USPSTF's Guidelines - 2009

- No mammogram screening age 40 – 49 unless physician feels it is needed
- Ages 50 – 74 – biennial screening
- Age >75 – insufficient evidence of benefit
- Recommends against teaching SBE
- Says evidence of CBE benefits lacking
- Insufficient evidence regarding digital mammography or breast MRI
    - USPSTF - 2009

Mammography - Low Risk Women - When to Start?

- Age 40 with or w/o CBE - USPSTF, AMA, ACOG, Am. Cancer Soc., Am Soc. Of Radiol. Kaiser Permanente

- Age 50 - AAFP, Canadian Task Force on Preventive Health Care, Am. Col. Of Preventive Med.

Mammography - Low Risk Women - How Often?

- Annual - AMA, ACR, NCCN and ACS
- 1-2 Years - AAFP, ACPM, KP-Scal, and CTFPHC
- 1-2 yrs ages 40 - 49, and q yr after age 50 - ACOG

Breast Cancer - Mammography

- Asymptomatic women w/ risk factors - annual mammography screening – high risk (MRI?)

- Risks:
  - Personal hx of breast ca - screening starts with diagnosis
  - Breast biopsy with atypical hyperplasia or histology unknown - start screening
    - KP-SCAL

Screening with Risk Factors

- Risks - cont.
    - Mother or sister with breast ca >50 yrs old - start screening at 40 yrs
    - Mother, sister, or daughter with breast ca < 50 yrs old, start screening at age 35 yrs
    - H/O Thoracic radiation treatment
- Woman any age with a dominant mass in the breast or skin changes - need clinical breast exam (CBE) and surgery eval.
    - KP-SCAL

Screening Caveats

- Uncertainty of mammography screening women of 40 - 49, however national effort to recommend screening - leading cause of death in this age group

- HRT or hormone contraception - some affect on breast ca risk (WHI study)

- Silicone breast implants - no evidence of increased risk
  - KP-SCAL

Screening Caveats

- No evidence of mammography benefit >75 yrs - personal decision with patient/MD
- SBE - no direct evidence of reduction in mortality - however encouraged to engage patients in their own health care
  - KP-SCAL

Cervical Cancer

- 11,000 new cases – invasive - yearly
- 4,000 women die annually
- Higher incidence – Hispanics and African Americans
- Lifetime risk of dying of cervical ca - 0.3%
- 5-year survival rate
 - 90% for localized ca
  - 14% for Stage IV

Cervical Cancer Risk Factors

- Low socioeconomic status
- Multiple sexual partners
- Early onset of sexual intercourse
- Smokers
- HPV infection
- HIV infection

Accuracy of Tests

- **Pap Smear**
  - False negative rates - 20 - 45%
    - Poor specimen collection
    - Cytopathologic lab interpretation
  - Specificity - >90%
  - Improved accuracy of interpretation of results with HPV testing

Cells are removed from the cervix.
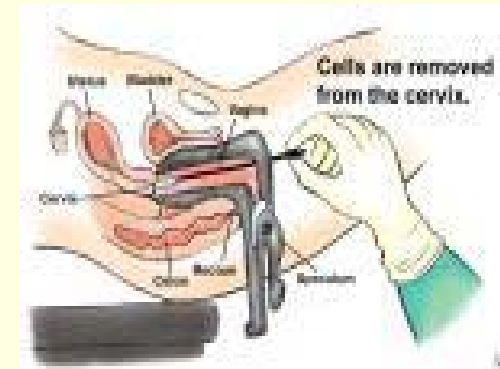
Accuracy of Tests

- Colposcopy - Poor for screening
  - Sensitivity - 34 - 43%
  - Specificity - 68%
  - PPV - 4 - 13%
  - Cost and discomfort issues
    - USPSTF

ACOG PAP Revisions - 2009

- Start screening at age 21 – regardless of hx
- Ages 21 – 29 – pap every 2 yrs
- Low risk women - >30 yrs and negative past screenings – pap every 3 yrs
- H/O hysterectomy for benign cause – stop pap
- Women w/o abnl paps in last 10 yrs including last 3 paps – stop paps at age 65 – 70

  - ACOG

Effectiveness of Early Detection

- Multiple studies in US, Europe and Canada - reductions of invasive and mortality (20 - 60%) in patients undergoing pap smear screening

- Little evidence of increased benefit of screening annually vs q. 3-5 yrs

- Women who never engaged in sexual intercourse don't need screening, no risk
  - USPSTF

Cervical Cancer Screening - USPSTF Recommendations

- Pap smear at least q. 3 yrs starting with onset of sexual activity
- Insufficient evidence of upper limit - consider stopping at age 65 if normal in past
- Insufficient evidence to recommend screening with colposcopy, cervicography or HPV testing
  - USPSTF

Prostate Cancer - Burden

- Most common non-cutaneous cancer in American men
- 2nd most cancer deaths in men - 14%
- 222,000 new cases annually (2010 est)
- 32,000 deaths annually (2010 est)
- Lifetime risk of prostate ca – 17% and dying from prostate ca - 3.4%
  - USPSTF

Prostate Cancer - Burden

- Only 1/3 to 1/4 of men with prostate cancer die from the cancer

- 61% occurs in men >75 yrs old

- 58% localized when diagnosed
  - Permanente Journal

Prostate Cancer - Risk Factors

- Age > 50
- African-American
- Family history of prostate cancer

Prostate Cancer - Accuracy of Tests

- DRE
  - Poor sensitivity – 72 – 82% of biopsies due to DRE show no cancer
  - DRE not shown to improve survival as most spread beyond the gland at diagnosis
- Transurethral Ultz - no evidence of benefit for screening

Prostate Cancer - Accuracy of Tests

- PSA - using value of 4 ng/dl as "normal"
    - Reported sensitivities - 29% to 80%
    - Specificity - 38 - 59%, PPV - 20 - 30%
    - Incr. Ca risk if >0.75 ng/ml annual increase
    - Up to 75% false positives (BPH, etc.)
    - May consider age adjusted "normal" values
    - PSA detects 33% missed by DRE and DRE detects 20% missed by PSA
    - PSA < 4 in 15 – 38% of new prostate ca patients

Effectiveness of Early Detection

- Indirect evidence that early detection of prostate cancer improves outcomes is limited
- 5-year survival for Stage A (87%) vs B (81%) vs C (64%) vs D (30%)
- Uncertainties regarding tx and related complications

Normal prostate
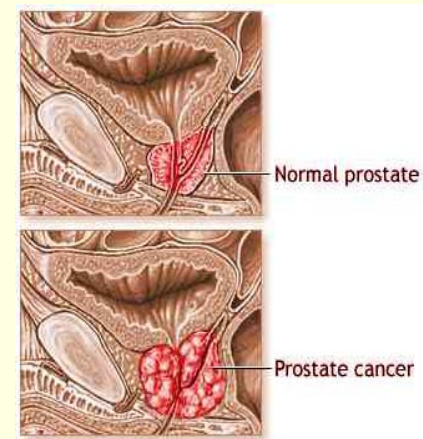
Prostate cancer

Prostate Cancer Treatment & Potential Side Effects

- Radical Prostatectomy
- Radiation treatment
- Hormonal therapy
- Watch and monitor

- Sexual dysfunction
- Urinary incontinence
- Bowel dysfuntion

Prostate Screening Estimate of Risks/Costs/Benefits

- One time DRE and PSA - increase life expectancy by 2 weeks, with considerable iatrogenic illness (favorable assumptions)
- Using less favorable assumptions - benefit decreases and cost increases
- Screening may be reasonable for younger men, clinician-patient discussion needed
  - Coley, et. al., Ann. Intern. Med., March, 1997

PSA Testing

- Medicare population - 11 years of follow-up
- Seattle –
  - Intensive screening and treatment
- Connecticut –
  - Less intensive screening
- No significant affect on prostate cancer specific mortality

  - BMJ Oct. 2002

Prostate Cancer Screening - Others

- USPSTF and CDC - No DRE or PSA is recommended

- AAFP - Men 50 - 65 yrs should be counseled about the risks and uncertain benefits of screening

- Am. Col. Of Physicians - No routine screening, discuss with patients and recommends enrolling patients in ongoing clinical studies

Prostate Cancer Screening - Others

- ACS, AUA, Am Col of Surgeons - Offer PSA and DRE to men starting at 50 yrs if life expectancy is >10 yrs

- NCI - Insufficient evidence to establish whether screening decreases mortality

- Canadian Task Force on Periodic Health Exam - Not recommend PSA or DRE

Lung Cancer

- 222,000 new cases (U.S. – 2010 est)
- 157,900 deaths (U.S. – 2010 est)
- 5 year survival <13%
- 85% attributable to smoking
- Other causes: 2nd hand smoking, exposure to carcinogens

  - NCCN 2000

Lung Cancer

- 1960's - annual CXR's of all smokers >45
  - Apparent success - due to length and lead time biases
  - RCT's - no benefit from screening
  - Cochrane review - standard to intensive screening - higher mortality in intensive group

Lung Cancer

- Low Risk
  - No evidence that screening is useful
  - USPSTF counsels against screening sputum cytologies, CXR's
  - Advise against smoking and exposure

Lung Cancer

- **Spiral CT**
  - **Japanese study - Spiral CT has higher detection rate than CXR for stage 1 lung cancer.**
  - **No data available on mortality rates**
  - **RCT's are needed**
- **USPSTF and CTFPHC - periodic screening with sputums and CXR's does not reduce mortality**