Evidence-based Cancer Screening & Surveillance

Martin C. Mahoney, MD, PhD, FAAFP
Departments of Medicine & Health Behavior

/Oncology_Feb 2014.ppt
Objectives:

- Principles of screening
- Assessing accuracy of screening tests; sources of bias
- Review current cancer screening guidelines
- Highlight current rates of cancer screening
- Community based screening
Prevention:

- **Primary**
  - reduce/eliminate exposure
  - Examples: vaccination, tobacco control

- **Secondary**
  - screening and early detection
  - Example: mammography, Fecal Occult Blood Testing (FOBT)

- **Tertiary**
  - prompt diagnosis & treatment
  - Example: blood sugar control in diabetics, BP control among hypertensive patients
Medical Screening:

“The presumptive identification of unrecognized disease or defect by the application of tests, examinations, or other procedures that can be applied rapidly.”

United States Commission on Health (1957)
Screening vs. Surveillance

- **Screening** = “general population risk”
- **Surveillance** = “increased risk”
Screening vs. Surveillance

- Screening = “general population risk”
  - persons not known to have a medical condition(s), family history or specific exposure(s) that would increase disease risk above that of the general population.
  - used for the early diagnosis of disease in otherwise healthy persons at general population risk; e.g., mammography to identify breast cancers among women 40+ years of age in the general population not known to be at increased risk of developing breast cancer.
Screening vs. Surveillance

**Surveillance** = “increased risk”

- persons known/suspected to be at increased risk due to personal and/or family history of medical condition(s) or exposure(s); e.g., woman with relative(s) diagnosed with breast cancer <age 60 may warrant surveillance using more frequent or other imaging studies at specific intervals; cancer survivors; precancerous lesions

- explicit strategies for assessment and/or examination at precise time intervals *among persons at increased disease risk*.

- levels of increased risk are variable and surveillance plans are often individualized
Rationale for Screening:

- Detection of disease at a stage where intervention can impact natural history and/or outcome

Natural history:
- Biological onset of disease
- Preclinical interval (unrecognized)
- Clinical symptoms
- Disease outcome
Criteria for Screening:

- Condition/risk factor is important
- Recognizable pre-clinical phase
- Accurate/reliable method of detection
  » Sensitivity, specificity, PPV
- Modification of risk factor or treatment in preclinical phase makes a difference
- Capacity for implementation
- Cost/benefit
- Patient acceptability

Wilson and Junger (1968); Smith R (1999)
Validity of screening:

- **Sensitivity** = “positive in disease”
  - Test yield of positives; % of (+) screens with disease

- **Specificity** = “negative in health”
  - % of (-) screens without disease
  - Poor specificity leads to harms and/or added costs of work-up

- Summary measures of screening program effectiveness
- Measures are inversely related for the same test
- Thresholds are value judgments
Assessing screening accuracy – sensitivity and specificity:

<table>
<thead>
<tr>
<th>Test:</th>
<th>Condition:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>positive</td>
<td>present</td>
<td>TP</td>
</tr>
<tr>
<td></td>
<td>absent</td>
<td>FP</td>
</tr>
<tr>
<td>negative</td>
<td></td>
<td>FN</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TN</td>
</tr>
</tbody>
</table>

Sensitivity = \( \frac{TP}{TP+FN} \)
Specificity = \( \frac{TN}{TN+FP} \)

TP-true positive
FP-false positive
FN-false negative
TN-true negative
Predictive value of screening:

- Positive predictive value = “% with disease among those testing positive”
- Positive predictive value = “% healthy among those testing negative”

(values depend on test accuracy & disease prevalence)

<table>
<thead>
<tr>
<th>Prevalence</th>
<th>(+) PV</th>
<th>(-) PV</th>
</tr>
</thead>
<tbody>
<tr>
<td>10%</td>
<td>68%</td>
<td>99.4%</td>
</tr>
<tr>
<td>1%</td>
<td>16%</td>
<td>99.9%</td>
</tr>
<tr>
<td>0.1%</td>
<td>2%</td>
<td>99.99%</td>
</tr>
</tbody>
</table>
Assessing screening accuracy – Positive & Negative Predictive Value:

<table>
<thead>
<tr>
<th>Test:</th>
<th>Condition:</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>present</td>
<td>positive</td>
<td>TP</td>
<td>FP</td>
</tr>
<tr>
<td>absent</td>
<td>negative</td>
<td>FN</td>
<td>TN</td>
</tr>
</tbody>
</table>

Positive Predictive Value = TP / (TP + FP)
Negative Predictive Value = TN / (FN + TN)
Assessing screening accuracy – an example:

<table>
<thead>
<tr>
<th>Test:</th>
<th>Condition:</th>
<th>present</th>
<th>absent</th>
</tr>
</thead>
<tbody>
<tr>
<td>positive</td>
<td>80</td>
<td>15</td>
<td>95</td>
</tr>
<tr>
<td>negative</td>
<td>40</td>
<td>90</td>
<td>130</td>
</tr>
</tbody>
</table>

- 225 persons screened; 120 with condition
- 95 tested positive; 130 tested negative

Sensitivity = TP/ (TP+FN) = 80/(80+40) = 67%
Specificity = TN/(TN+FP) = 90/(90+15) = 86%
Positive predictive value = TP/(TP+FP) = 80/(80+15) = 84%
Negative predictive value = TN/(FN+TN) = 90/(40+90) = 69%
Screening biases:

- **Lead-time bias:** diagnosis at an earlier point; survival appears increased
  - Preclinical phase shortened
  - Clinical phase lengthened
Lead Time Bias:

Asymptomatic (unrecognized) Disease onset

screen detected (age 45)
clinical disease
clinically detected (age 50)

Death (age 60)

Lead time
Screening biases: (con’t)

- **Length bias:** persons diagnosed via screening appear to have improved survival
  - Slow growing tumors more likely to be detected with screening
  - Fast-growing tumors more likely to manifest symptoms between screening intervals
Length Bias:

Rapidly progressive cases:

- onset of disease
- Dx – clinical diagnosis

Slowly progressive cases:

- test
- retest

Screen detected
Interval case
Screening biases: (con’t)

- **Overdiagnosis bias**: overestimation of survival among screen-detected cases due to inclusion of subclinical disease.
Potential pitfalls of screening:

- Some screening tests involve risk of complications
- False positive results may lead to anxiety and invasive diagnostic procedures
- Risk overdiagnosis, more common as screening tests detect smaller tumors
- False negatives may inappropriately reassure and delay diagnosis
Rationale for Screening

Asymptomatic

Symptomatic

Preclinical detectable phase

Disease process begins

Disease detectable by screening

Disease actually detected by screening

Lead time

Symptoms of condition

Time of recovery or death
Sites potentially amenable to Cancer Screening:

- Breast
- Cervix
- Colon & rectum
- Prostate
- Skin
- Endometrium
- Testes
Cancer Screening
Recommendations:

- ACS
- NCI
- USPSTF
- Specialty societies: Gastroenterology, Urology, NCCN, others

Evidence Consensus
Screening & Evidence-based Medicine:

- ↑ emphasis on scientific rigor
- US Preventive Service Task Force
  - Grading of recommendations
  - Certainty of net benefit

USPSTF - an independent panel of non-Federal experts in prevention and evidence-based medicine and is composed of primary care providers, nurses, and health behavior specialists.

USPSTF conducts scientific evidence reviews of a broad range of clinical preventive health care services (such as screening, counseling, and preventive medications) and develops recommendations for primary care clinicians and health systems.
<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
<th>Suggestions for Practice</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A</strong></td>
<td>USPSTF recommends the service. There is high certainty that the net benefit is substantial.</td>
<td>Offer or provide this service.</td>
</tr>
<tr>
<td><strong>B</strong></td>
<td>USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.</td>
<td>Offer or provide this service.</td>
</tr>
<tr>
<td><strong>C</strong></td>
<td>Clinicians may provide this service to selected patients depending on individual circumstances. However, for most individuals without signs or symptoms there is likely to be only a small benefit from this service.</td>
<td>Offer or provide this service only if other considerations support the offering or providing the service in an individual patient.</td>
</tr>
</tbody>
</table>

Continued on next panel: [http://www.uspreventiveservicestaskforce.org/uspstf/gradespost.htm](http://www.uspreventiveservicestaskforce.org/uspstf/gradespost.htm)
### USPSTF Grade Definitions (2007)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
<th>Suggestions for Practice</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>D</strong></td>
<td>USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.</td>
<td>Discourage the use of this service.</td>
</tr>
<tr>
<td><strong>I</strong></td>
<td>USPSTF concludes that the current evidence is insufficient to assess the balance of benefits &amp; harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.</td>
<td>Read the clinical considerations section of USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.</td>
</tr>
</tbody>
</table>

## USPSTF-Levels of Certainty Regarding Net Benefit

<table>
<thead>
<tr>
<th>Level of Certainty</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High</strong></td>
<td>• available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.</td>
</tr>
</tbody>
</table>
| **Moderate**       | • The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by such factors as: The number, size, or quality of individual studies.  
  - Inconsistency of findings across individual studies.  
  - Limited generalizability of findings to routine primary care practice.  
  - Lack of coherence in the chain of evidence. As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion. |
## USPSTF-Levels of Certainty Regarding Net Benefit

<table>
<thead>
<tr>
<th>Level of Certainty</th>
<th>Description</th>
</tr>
</thead>
</table>
| **Low**            | • The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of:  
- limited number or size of studies.  
- Important flaws in study design or methods.  
- Inconsistency of findings across individual studies.  
- Gaps in the chain of evidence.  
- Findings not generalizable to routine primary care practice.  
- Lack of information on important health outcomes. More information may allow estimation of effects on health outcomes. |

Screening & Evidence-based Medicine:

- Screening recommendations from most other organizations use a less rigorous approach
- Less reliant upon evidence base
- Illustration:
  - Breast cancer screening – USPSTF vs ACS
The USPSTF recommends biennial screening mammography for women aged 50 to 74 years. Grade: **B recommendation**.

The decision to start regular, biennial screening mammography before the age of 50 years should be an individual one and take patient context into account, including the patient's values regarding specific benefits and harms. Grade: **C recommendation**.

The USPSTF concludes that the current evidence is insufficient to assess the additional benefits and harms of screening mammography in women 75 years or older. Grade: **I Statement**.

*Continued*…. 
The USPSTF recommends against teaching breast self-examination (BSE). Grade: **D recommendation**.

The USPSTF concludes that the current evidence is insufficient to assess the additional benefits and harms of clinical breast examination (CBE) beyond screening mammography in women 40 years or older. Grade: **I Statement**.

The USPSTF concludes that the current evidence is insufficient to assess the additional benefits and harms of either digital mammography or magnetic resonance imaging (MRI) instead of film mammography as screening modalities for breast cancer. Grade: **I Statement**.
Screening for Breast Cancer (Am Cancer Society)

- Yearly mammograms are recommended starting at age 40 and continuing for as long as a woman is in good health.
- Clinical breast exam (CBE) about every 3 years for women in their 20s and 30s and every year for women 40 and over.
- Breast self-exam (BSE) is an option for women starting in their 20s.
Updated ACS Colorectal Cancer Screening Guidelines, Adults ages 50+

**Tests That Detect Adenomatous Polyps & Cancer:**

- Flexible sigmoidoscopy (FSIG) every 5 years, or
- Colonoscopy every 10 years, or
- Double contrast barium enema (DCBE) every 5 years, or
- CT colonography (CTC) every 5 years

**Tests That Primarily Detect Cancer:**

- Annual guaiac-based fecal occult blood test (gFOBT), or
- Annual fecal immunochemical test (FIT), or
- Stool DNA test (sDNA), *[interval uncertain]*

*with high sensitivity for cancer; newly recommended tests.*
ACS recommendations – Prostate Cancer Screening:

- Starting at age 50, men should talk to a doctor about the pros and cons of testing so they can decide if testing is the right choice for them.

- If they are African American or have a father or brother who had prostate cancer before age 65, men should have this talk with a doctor starting at age 45.

- If men decide to be tested, they should have the PSA blood test with or without a rectal exam. How often they are tested will depend on their PSA level.
PSA testing?

**PROS:**
- No other screening test for prostate CA (except for “complexed PSA”, which is still only offered as follow up for ambiguous PSA result in the 4-10 range)
- Complements DRE
- ? correlation of ↑ incidence, ↓ mortality

**CONS:**
- No randomized clinical trials confirming mortality benefit
- PSA associated with risks (psychological distress, cost, risk of work-up/treatment)
- PSA is not prostate cancer specific
ACS recommendations – Cervical Cancer Screening (2012)

- begin at age 21; women under age 21 should not be tested.
- Women ages 21 - 29 yrs should have a Pap test every 3 years. HPV testing should not be used unless it is needed after an abnormal Pap test result.
- Women ages 30 - 65 should have a Pap test plus an HPV test (called “co-testing”) every 5 years. This is the preferred approach, but it is also OK to have a Pap test alone every 3 years.
- Discontinue testing in women >65 yrs who have had regular testing with normal results. Women with a history of a serious cervical pre-cancer should continue to be tested for at least 20 years after that diagnosis, even if testing continues past age 65.
- Pap screening not needed after total hysterectomy for benign conditions
Screening for Lung Cancer:

- **USPSTF**: Not recommended

- **HOWEVER, NLST report Nov 2010** –
  - 20% fewer lung cancer deaths among trial participants screened with spiral CT vs chest X-ray screening.
  - Ancillary finding, not a main endpoint of the trial, showed 7% ↓ for all-cause mortality (deaths due to any factor, including lung cancer) in spiral CT group. A substantial portion of this lower rate was attributable to lung cancer.

Lung Cancer “Screening” (2014) – with annual low-dose chest CT

American Cancer Society: CA Cancer J Clin 2013
- healthy patients ages 55 years to 74 years with 30+ pack-year smoking history and who currently smoke or have quit within the past 15 years.
- informed & shared decision-making with a clinician related to the potential benefits, limitations, and harms associated with screening for lung cancer with low-dose computed tomography
- cessation counseling remains a high priority

- age 55-74, 30+ pk-yr smoker or quit <15 yrs; or >50 yrs, 20+ pk-yr smoker with other risk factors (COPD, family hx, occupation exposure, radon).

USPSTF:  http://www.uspreventiveservicestaskforce.org/uspstf13/lungcan/lungcanfinalrs.htm
- age 55-80, 30+ pk-yr smoker or quit <15 yrs; stop once a person has not smoked for 15 years or develops a significant health problem (B recommendation)
Trends in Annual Mammography Use by Health Insurance Status, US, 2000-2010

A mammogram within the past year among women ≥ 40 years; estimates are age-adjusted to the 2000 US standard population.
Source: National Health Interview Survey, National Center for Health Statistics, Centers for Disease Control and Prevention.
Trends in Pap Test Prevalence* by Health Insurance Status, US, 2000-2010

*A Pap test within the past three years among women age 21-65; estimates age-adjusted to the 2000 US standard population. Source: National Health Interview Survey, National Center for Health Statistics, Centers for Disease Control and Prevention.
Trends in the Prevalence of Fecal Occult Blood Test* by Health Insurance Status, US, 2000-2010

*A fecal occult blood test in the past year among adults ≥ 50 years; estimates age-adjusted to the 2000 US standard population.
Source: National Health Interview Survey, National Center for Health Statistics, Centers for Disease Control and Prevention.
Flexible Sigmoidoscopy or Colonoscopy Prevalence* by Race/Ethnicity and Health Insurance Status, US, 2010

* A sigmoidoscopy within five years or a colonoscopy within 10 years among adults ≥ 50; estimates age-adjusted to the 2000 US standard population. Source: National Health Interview Survey, National Center for Health Statistics, Centers for Disease Control and Prevention.
Interfacing Cancer Early Detection & Evidence-based Medicine:

- ↑ emphasis on scientific rigor
- US Preventive Service Task Force
  - Grading of recommendations
  - Certainty of net benefits
  - ↑ emphasis on scientific rigor
- Guidelines by American Cancer Society & other organizations
Next Steps:

- Enhancing compliance:
  - patients: motivation, clarity of message, value
  - clinicians: priority, clarity of recommendations, value
  - system: capacity, value, access

- Examination of new technologies

- Evaluation of community-based screening programs
  - Strategies/best practices
  - evidence-based guidelines
Next Steps: (con’t)

● Clear and concise messages to
  » General public
  » Clinicians

average risk = screening;
high-risk = surveillance
Key points:

- Understand sensitivity, specificity, (+) & (-) predictive value; sources of bias in screening
- Screening vs. surveillance
- ACS screening recommendations
- Trends in screening rates
- Lung cancer early detection