Burden of Cancer in U.S., 2008
(ACS Cancer Facts and Figures, 2008)

- 1.4 million cancers diagnosed
- 560,000 cancer deaths
- 1 in 4 deaths in the US
- $220 billion
  - $90 billion in medical costs
  - $20 billion in lost productivity
  - $110 billion in premature death

2008 Estimated US Cancer Deaths*

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>Men</th>
<th>Women</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung &amp; bronchus</td>
<td>31%</td>
<td></td>
<td>26%</td>
</tr>
<tr>
<td>Prostate</td>
<td>10%</td>
<td></td>
<td>15%</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>8%</td>
<td></td>
<td>9%</td>
</tr>
<tr>
<td>Pancreas</td>
<td>6%</td>
<td></td>
<td>6%</td>
</tr>
<tr>
<td>Leukemia</td>
<td>4%</td>
<td></td>
<td>3%</td>
</tr>
<tr>
<td>Liver/Bile Duct</td>
<td>4%</td>
<td></td>
<td>3%</td>
</tr>
<tr>
<td>Esophagus</td>
<td>4%</td>
<td></td>
<td>3%</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>3%</td>
<td></td>
<td>3%</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>3%</td>
<td></td>
<td>2%</td>
</tr>
<tr>
<td>Kidney</td>
<td>3%</td>
<td></td>
<td>2%</td>
</tr>
<tr>
<td>All other sites</td>
<td>24%</td>
<td></td>
<td>25%</td>
</tr>
</tbody>
</table>

*Excludes basal and squamous cell skin cancers and in situ carcinomas except urinary bladder.

Objectives

- Brief Overview of Cancer Burden in 2009
- Screening Guidelines for the Top 4 Cancers
- New Tests and Emerging Technologies
Cancer Death Rates* by Sex, US, 1975-2004

*Age-adjusted to the 2000 U.S. standard population.

Reasons for Drop in the Cancer Death Rate
- Healthier Lifestyles?
- Better Screening and Early Detection?
- Better Treatments for Cancers Detected?
- Other Reasons?

What Makes a Good Screening Test?
- Easy
- Safe
- Accurate
  - Sensitive (few false negatives)
  - Specific (few false positives)
- Inexpensive
- Widely Available

Breast Cancer Screening
Self and Clinical Breast Exam

- Self-Breast Exam (SBE)
  - 3 large studies (none in US) -- no mortality benefit

- Clinician Breast Exam (CBE)
  - Mortality benefit is not well-established
  - May help guide the radiologist if abnormalities found
  - Many patients expect it
  - A "good CBE" takes at least 5 minutes

- USPSTF: insufficient evidence for SBE or CBE
- ACS: recommends CBE, and suggests teaching SBE so women can decide for themselves

Mammography

- Mortality Benefit
  - Age 40-49: 17% mortality risk reduction
  - Baseline risk of breast cancer death: 1/500
  - Age 50-69: 30% mortality risk reduction
  - Baseline risk of breast cancer death: 1/100
  - Continued benefit for healthy women 70+

- USPSTF and ACS
  - Mammography every 1-2 years after age 40 and continuing as long as the woman is healthy

Breast Cancer Screening: What’s New?

- Digital Mammography
  - Separates image acquisition, presentation, and storage
  - Allows for image manipulation to enhance contrast
  - Costs about twice as much as film mammography

- DMIST study
  - 42,760 women in 33 centers in the US underwent both tests and followed up 10-15 months later
  - More sensitive than conventional mammography for 3 subgroups

Digital Mammography – DMIST data

<table>
<thead>
<tr>
<th>Group</th>
<th>Sensitivity Digital</th>
<th>Sensitivity Film</th>
<th>Specificity Digital</th>
<th>Specificity Film</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>70%</td>
<td>66%</td>
<td>92%</td>
<td>92%</td>
</tr>
<tr>
<td>&lt;50*</td>
<td>78%</td>
<td>51%</td>
<td>90%</td>
<td>90%</td>
</tr>
<tr>
<td>Dense Breasts*</td>
<td>70%</td>
<td>55%</td>
<td>91%</td>
<td>90%</td>
</tr>
<tr>
<td>Pre or Peri Menopause*</td>
<td>72%</td>
<td>51%</td>
<td>90%</td>
<td>90%</td>
</tr>
</tbody>
</table>

*Statistically Significant Difference
Breast MRI

- 80%+ sensitive
- Many false positives; Risk of overdiagnosis
- Recommended yearly by ACS when lifetime risk is greater than 20-25% defined with risk tools. (Saslow, CA Cancer J Clin 2007; 57:75-89)
- Usually not recommended for follow-up of breast cancer
- Unclear when to start or stop

The Future: Breast Thermography?

- An old technology making a comeback
- Detects infrared energy and heat emitted disproportionately by breast tumors
- Potentially less expensive and less invasive than mammography
- Might become adjunct or replacement for mammography

Colorectal Cancer Screening

- It used to be so simple...
  - Home Fecal Occult Blood Tests yearly, or
  - Flexible Sigmoidoscopy q5yrs, or
  - FOBT yearly or FSIG q5yrs, or
  - Double Contrast Barium Enema q5yrs
  - Colonoscopy q10yrs

Current strategies based on premise that most colorectal cancers develop from adenomas over many years
Colorectal Cancer Screening: What’s New?

- Newer Tests Coming to the Forefront:
  - High Sensitivity guaiac FOBT (HSgFOBT)
  - Fecal Immunochemical Tests (FIT)
  - Stool DNA Tests (sDNA)
  - CT Colonography (CTC)

High Sensitivity guaiac FOBT (HSgFOBT)

- Compared to regular gFOBT:
  - Higher Sensitivity (up to 70%) for cancer;
  - Higher False Positive rate – results in more colonoscopies;
  - Similar Cost to Hemoccult II. (<$5 per test)

Fecal Immunochemical Tests (FIT)

- Compared to gFOBT and HSgFOBT:
  - Sensitivity up to 70% for cancer;
  - 2 samples probably more sensitive than 1 sample;
  - No dietary changes – specific for human globin;
  - A little more expensive (e.g. $12-25);
  - Better patient adherence.

Stool DNA Tests (sDNA)

- DNA from abnormal cells shed into the stool and potentially detected on testing
- No more sensitive than HSgFOBT or FIT. Much more expensive ($300-500 per test)
- Major Uncertainties: Optimal frequency and follow-up of abnormal tests.
CT Colonography (CTC)

CT Image

Requires bowel prep/colonic distention; “Prep-less” scans under development. Lower risk of perforation than colonoscopy.

Sensitivity similar to colonoscopy (90% for cancers and 1cm polyps);

About 20% will require colonoscopy follow-up when using 6mm as the detection threshold for polyps. May add costs to screening.

Other Questions: frequency; training; extracolonic findings; costs; and radiation risks

CT’s for Cancer Screening: A Popular Idea with the General Public

- 74% agreed “finding cancer early saves lives most or all of the time.”
- 73% “would rather have a Total Body CT Scan than $1000 in cash.”


But there are risks from the radiation!

Approximately 60 million CT scans per year in the US.

1/10,000 Risk of cancer from 1 Abdominal CT if over 50 at time of CT. What if healthy people get 6 CTC’s between the ages of 50 and 75?

Colorectal Cancer Screening: What’s do the New Guidelines say?

- ACS/ACR/USMSTF (Spring 2008)

- USPSTF (Fall 2008)
USPSTF Guidelines

- **3 Preferred Choices:**
  - Colonoscopy every 10 years, or
  - Flexible Sigmoidoscopy every 5 years plus FIT or HSGFOBT every 3 years, or
  - HSGFOBT or FIT every year
- Use clinical judgment for screening after age 75
- Don’t screen after age 85
- CTC and sDNA not recommended
- DCBE not evaluated

ACS/ACR/USMSTF Guidelines

- “Preferred because they are good at finding small polyps”
  - Colonoscopy every 10 years, or
  - Flexible Sigmoidoscopy every 5 years with or without HSGFOBT/FIT, or
  - DCBE or CTC every 5 years
- “Acceptable”
  - HSGFOBT or FIT every year, or
  - Stool DNA, interval uncertain
- Don’t screen those who can’t tolerate treatment or benefit clinically from early detection.

USPSTF Decision Analysis

- **Potential Mortality Reduction for Average Risk Screening:**
  - Colonoscopy q10 years 64.6%
  - FIT qyr 64.6%
  - HSGFOBT qyr 66.0%
  - Flex Sig q5yr/HSGFOBT q3yr 65.7%
  - Hemoccult II qyr 55.3%
  - Flex Sig alone q5yr 58.5%

This challenges the ACS/ACR/USMSTF assumption that direct visualization is always best.


USPSTF Decision Analysis

- **Caveats:**
  - Did not include procedure costs or risks
  - Did not evaluate CTC, DCBE, or sDNA
  - Assumed all FIT and HSGFOBT are the same
  - Assumed all tests are followed up thoroughly and appropriately
The Future: Colonoscopy Enhancements?

- Colonoscopy has its limitations!
  - Are right sided lesions harder to see, grow faster, or both?

- Magnification Endoscopy, Narrow Band Imaging Endoscopy, Confocal Microscopy Endoscopy –
  - New technologies to look at vascular abnormalities, tissue density, and even cell structure in real time without biopsies.

Prostate Cancer Screening

- 4% drop in mortality per year in US since 1992: Is it due to screening, treatment, or something else?

- Digital Rectal Examination (DRE)
  - Low sensitivity and specificity

- Prostate Specific Antigen (PSA)
  - PSA > 4ng/ml; misses some aggressive cancers but detects many non-aggressive cancers

Prostate Cancer Screening: What’s New?

- US Study – 77,000 men (55-74); 7-10yrs of data
  - Annual PSA and DRE; Biopsy if PSA > 4ng/ml
  - No difference in mortality detected yet, but power limited by contamination between control and intervention groups

- European Study – 180,000 men (mostly 55-69)
  - PSA every 4 years; Biopsy if PSA >3ng/ml
  - “Number Needed to Screen” to prevent 1 death in 10 years: 1410
  - “Number Needed to Treat” to prevent 1 death in 10 years: 48

The controversy is not over!

- Benefits similar to mammography, but harms are greater.
- Little information yet on risk/benefit ratio for high risk groups

(NEJM, March 2009 – 2 studies – results simplified for this slide)
Ways to reduce overdiagnosis/overtreatment

- Informed Decision-Making
- Age-specific PSA cut points:
  - 3.0 for men in their 50’s
  - 4.0 for men in their 60’s
  - 5.0 for men in their 70’s
- PSA velocity:
  - Biopsy if PSA increases by >1ng/dl per year
- Free PSA before biopsy if PSA between 4-10
  - Biopsy if Free PSA < 20%
- Don’t screen men over 75 (USPSTF new recommendation)
- Consider “Active Surveillance” for tumors with low Gleason scores
  - e.g. Gleason 3+3 or less

The Future: Proteomics for Prostate Cancer Screening?

- “Serum Protein Fingerprinting” to create serum biomarkers with greater specificity than PSA
  - 83% sensitive and 97% specific for prostate cancer
  - Better specificity may mean fewer biopsies
  - May become cheaper and widely available in a few years
- The “holy grail”:
  - Tests that correlate with aggressive disease
- A new paradigm for cancer screening in general
  - Expect to see proteomic tests for other cancers in the future

Lung Cancer Screening

Randomized Trials in 1970’s of Chest X-Ray/Sputum Cytology in Smokers

- Screening found more cancers earlier, but did not lead to better outcomes
- Since then, screening not recommended even for high risk groups
Lung Cancer Screening: What’s New?

- Some Observations:
  - If everyone quit smoking today, there would be 1 million US lung cancer deaths over the next 10 years
  - 10% of lung cancer is not smoking related
  - Left untreated, stage 1 disease is often fatal
  - Growing number of stage 1 lung cancer surgery survivors

- The Question:
  - If we detect more stage 1 lung cancer, will we save more lives?

Low Dose CT Scans (LDCT)

- 6 ongoing RCT’s in smokers
  - LDCT finds many more stage 1 cancers and leads to many more resections for stage 1 disease
  - Modeling studies suggest that LDCT might reduce lung cancer mortality by 10-20% for smokers
  - Costs, Frequency, and Risks not defined yet

- Results Coming in 2010
2009 Best Evidence – Simplified Approach

**Breast Cancer Screening**
- Mammography q1-2 yrs after 40 if healthy, +/- CBE
- Digital Mammogram if under 50, dense breasts, or premenopause
- MRI may be useful in high risk/special circumstances

**Colorectal Cancer Screening**
- Annual FIT or Colonoscopy q10 years, 50-75, +/- other choices
- No test is clearly superior, and patient test preferences vary, so offer more than one choice
- If they choose FIT, find a system to get people to do it YEARLY, and follow-up all abnormals with colonoscopy.

**Prostate Cancer Screening**
- Informed Decision-Making for PSA. Age 50-75, +/- DRE
- Consider free PSA and PSA velocity before rushing to biopsy.
- Consider active surveillance in low risk disease
- There are now more numbers you can give to help patients decide

**Lung Cancer Screening for Smokers**
- Not recommended
- Results coming in 2010 and likely to continue to be controversial