Cancer Screening
High value care

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Disclosures

- Member of ACP guidelines and high value care committees
Objectives

- Review current guidelines for cancer screening for average risk person
  - Cervical
  - Colon
  - Breast
  - Lung
- Discuss when to stop screening

Not covered: high risk populations
Screening criteria for cancers

- Detect cancer in preclinical phase
  - Cancers that are destined to cause death
- Early treatment more beneficial than waiting until CA is clinically apparent
- Mortality benefit: 10 yr survival impact
- Benefit outweighs harm
- Cost Effective
Cervical cancer

- In 2013, approx 12,000 diagnosed with cervical CA, 4200 died
- Most common occurs in age 35–55
- Population-wide PAP testing has reduced cervical mortality by 80% (Am J Clin Pathol 2012,137:516)
- From 2001–2010
  - Cervical CA incidence decreased by 1.5%–4.2% per yr
  - Mortality decreased by 1.3%–4.6% per yr

Prevention: HPV vaccination of girls and boys
Case 1: cervical

- 33 yo female comes in for routine annual exam. Her last PAP was 3 yrs ago and was normal. When should her next PAP test be?
  - A. Today
  - B. 2 years
  - C. 3 years
  - D. 5 years
Case 2: cervical

- 68 yo female originally from Somalia presents for routine health care. She has no records and cannot recall her screening previously.
- She is otherwise healthy
- What is the recommendation for cervical cancer screening?
  - A. she no longer needs screening due to age
  - B. she should get PAP test today
  - C. she should go for colposcopy
  - D. do HIV testing and then decide
Case 3: cervical

19 yo sexually active female comes in for her annual exam and contraception. Which of the following should be done?

A. PAP w/o HPV test, chlamydia screening and HIV ab test, HPV vaccination
B. PAP w HPV test, chlamydia screening and HIV ab test, HPV vaccination
C. PAP w/o HPV test and chlamydia screening, HPV vaccination
D. Chlamydia screening, HIV ab test and HPV vaccination
Cervical CA screening

- Age 21-65 every 3 yrs with NL PAP (no HPV done)
- Age 30-65 every 5 yrs with NL PAP and Neg HPV
- No benefit for PAP in age < 21
- No benefit and potential harm for HPV testing in ages 21-30
- Not needed for birth control

Stop screening (for avg risk)
- Age 65 if normal screening PAPs previously- need at least 3 negative PAP (or 2 neg PAP w/ neg HPV) within 10 yrs
- Hysterectomy for benign pathology
- Potential harm of screening higher than benefit
  - No mortality benefit for patient

Recommendations are for average risk women (not HIV+, prior CIN/CA )
Updated guidelines if abnormal PAP [http://www.asccp.org/Guidelines](http://www.asccp.org/Guidelines)

Sources:
Screening: off-target? Cervical CA

FIGURE. Percentage of women who had a recent Papanicolaou (Pap) test (within 3 years), by hysterectomy status and age group — Behavioral Risk Factor Surveillance System, United States, 2000–2010*

[Graph showing the percentage of women who had a recent Pap test, categorized by age group and hysterectomy status, with a comparison to the 2002/2003 guidelines.]

MMWR 2013;61:1043-1047
Stopping Cervical CA screening

- < 0.1% of women > 60yo w/ normal baseline PAP will develop HGSIL or cervical CA

- > 80% of women w/ HGSIL or cervical CA have had either no PAP or abnormal PAPs

- 9610 vaginal PAP smears (s/p benign TAH)
  → 1.1% abnormal PAP smears
  → Zero vaginal CAs
Colorectal cancer

- Second leading cause of cancer-related death in men and women

- Incidence 134,000 (2016, approx)
  - Declining by 2–3% over past 15 yrs

- Death approx 51,370 per year
  - Declining by 1.4–3% per year

5% lifetime risk of colorectal CA in US
- 93% occur in pts >50 yo
  - Sources: CDC statistics
50 yo male comes in for annual exam. Which of the following is appropriate for colorectal cancer screening

- A. FOBT or FIT annually
- B. Flexible sigmoidoscopy now & every 5 yrs
- C. Colonoscopy now and every 10 yrs
- D. All of the above
Case 2: colorectal

- 75 yo male with h/o CHF and CAD comes in for his Medicare wellness visit. He asks about colon ca screening (his previous colonoscopy was normal 10 yrs ago). What is the current recommendation?
  - A. repeat colonoscopy now
  - B. no longer needs colon ca screening
  - C. discuss risk vs benefit before deciding
  - D. depends on his overall health and prognosis
Colon CA screening

- Start age 50 for avg risk
- Start age 40 or 10 yrs before age of dx of 1st degree family member with colon CA
- Screening tool
  - Optimal colonoscopy for higher risk
  - Annual FOBT/FIT (fecal immunochemical test)
  - FIT-DNA - few studies, higher cost, ↑ sens, ↓ spec
  - Flex-sigmoidoscopy q 5 yrs (debate exists)
- Colonoscopy every 10 yrs if nl colonoscopy
  - Every 5 yrs if adenomatous polyps

Source: USPSTF, ACP, ACS
Screening measures

- Annual FOBT– RCTs show approx 33% lower mortality
- Annual FIT testing – may replace FOBT–1 stool, higher sensitivity, French study showed FIT detected 2x more cases of neoplasia than FOBT
- Sens: 62–79%  Spec: 87–96%
- Any positive test for either FOBT or FIT warrants colonoscopy
- Flex–sig: large prospective trials show reduction of incidence by 18–23% and mortality 22–31%, better for distal colon ca than proximal
  - NNS to prevent 1 colon CA death: 850
    - NEJM 1993;328:1365
    - Gut 2006:56
    - PLoS Med 2013;9e1001352
Screening methods

- Colonoscopy
- No RCTs evaluating reducing morbidity/mortality
- Several case-control studies, population-based study show benefit
  - 61% reduction in distal colon, 22% in proximal
- Adv: every 10 yrs, can detect and remove polyps, visualize entire colon (if good prep)
- Disadv: 2 days off work, perforation, cost, bleeding, bowel prep, sedation. Operator dependent
- Risks: 4 perf and 8 bleed per 10,000 screened,

New screening techniques

- Fecal DNA testing
  - Studies have shown good sensitivity and specificity for detection of CRC and adenoma
    - Studies cite 84–97% sens—lower for adenoma
    - spec 84–85%
  - Expensive (compared to FOBT/FIT)—approx $700
  - Included on ACS, MSTFCC, and ACR guidelines
  - Not clear yet on interval testing
  - If positive still need colonoscopy

Sources: Ann Intern Med 2014 ITC
              NEJM 2014:370:1287
              Clin Castroenterol Hepatol 2013;11:1313
Prospective observational study: age 70–79
Medicare data: random sample—no h/o CRC and no screening within 5 yrs to be included compared screening (colonoscopy) vs no screening
Outcomes: colon CA incidence, severe adverse events within 30 days of procedure
Standardized 8 yr risk for CRC
Age 70–74: 2.19% vs 2.62% screen vs no screen
Age 75–79: 2.84% vs 2.97% screen vs no screen

Ann Intern Med 2016, sept 27
Result for age 70–79

- Standardized 8 yr risk for CRC
  - Age 70–74: 2.19% vs 2.62% screen vs no screen
  - Age 75–79: 2.84% vs 2.97% screen vs no screen

- Adverse events
  - Age 70–74: 5.6 events per 1000 persons
  - Age 75–79: 10.3 events per 1000 persons

- Conclusion: colonoscopy reduced 8 yr risk for CRC from 2.6% to 2.2% age 70–74 and from 3.0% to 2.8% age 75–79

- Mortality data for CRC not available
Benefits and Harms: colorectal

Model estimates per 1000 screened

- Life years gained: 181–270
- Colon ca deaths averted: 17–24
- Complications (GI/cardiac): 9–15

- CA screening strategies comparable

- JAMA 2016;315:2564–90
- Outcomes from CISNET
Colon CA screening: caveats

But… diminishing returns with age?

- Cross-sectional study:

<table>
<thead>
<tr>
<th></th>
<th>Age 50-54</th>
<th>Age 75-79</th>
<th>Age ≥ 80</th>
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<tbody>
<tr>
<td>% with advanced neoplasia</td>
<td>3.2%</td>
<td>4.7%</td>
<td>14%</td>
</tr>
<tr>
<td>Years of life expectancy gained</td>
<td>0.85</td>
<td>0.17</td>
<td>0.13</td>
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JAMA 2006;295:2357-2365
When to stop?

Colon CA screening:
- USPSTF:
  - 76–85yo: against routine screening, consider in individual patients (C)
  - >85 yo: against screening (D)
- ACS, ACG: no stop recommendation
- AGS: Life expectancy < 3–5y
- ACP: Age 75, or if life expectancy < 10y
- AAFP: same as USPSTF
High Value Care: Colon

- Start screening with any option at age 50
  - Lower cost for FIT/FOBT
- Consider colonoscopy for higher risk pts
- Follow screening timing per method chosen
- Stop screening by age 75—sooner if <5–10 prognosis
- Pts with bleeding should have colonoscopy (diagnostic)
- FOBT/FIT testing is not an inpt exam
Breast Cancer Screening

- Accounts for 23% of all CA in women, cumulative life risk in US 12%
- Mammography remains the primary screening tool
  - Meta-analysis: 15–20% reduction in risk of mortality—all ages but less significant for younger age (ranges 8%–32%)
- Incidence of breast CA in 2015 (US)
  - 231,840 women
- Death from breast CA in 2015 (US)
  - Approx 40,290
- From 2001–2010
  - Incidence is level
  - Mortality decreased by 1.5–2% per year
- Risk Factors: FH, BRCA, alcohol, HRT, obesity, ? breast density, chest radiation

JAMA 2015;314
Ann Intern Med 2016;164
NEJM 2007: 356
Case: breast ca screening

- 45 yo woman comes in for routine health maintenance exam. No FH of breast CA. she is confused about whether she should get mammogram screening. What is the recommendation?
- A. Screen now and then annually
- B. Delay screening to age 50 and do q 1 yr
- C. Screen now and then delay to age 50
- D. Delay screening to age 50 and q 2 yrs
Breast CA screening

- ACS: variable
  - 40-44 discuss, 45-54 annual, 55+ q 1-2 yrs
- USPSTF: age 50-74; every 2 yrs
  - Age 40-49-individual decision- every 2 yr
  - Consider stopping age 75
- ACOG: age 40+ annual
  - Consider stopping or discussion age 75
- Canadian PSTF: age 50-74- annual
- ACR: age 40+ annual
  - JAMA 2014;311:1327
  - JAMA 2015; 314:1599-1614
Why the controversy?

- 40–49: RRR 15%: approx 2400 women screened to prevent 1 death
  - Higher rate of false positive (60%)
- 50–59: RRR 15%: 1500 screened to prevent 1 death
- 60–69: RRR 32%: 377 screened to prevent 1 death
- Over 10 yrs of mammogram at least 50% will have one false alarm
  - Source: Ann Intern Med apr 2010 ITC (USPSTF)
  - JAMA 2015; 314:1615–31 (USFSTF/CISNET)
Why every 2 yrs and age 50?

- 2009 USPSTF update on breast ca screening
- Gain for screening age 40–49 is small (C rec)
- New data shows little difference in mortality with biennial screening vs annual for age 50–74 (B rec)
- Insufficient evidence for screening > 75yo

Why every 2 yrs and age 50?

- Mandelblatt et al: Mammogram screening: model estimates of potential benefits and harms
- Evaluate screening strategies using 6 models
- Results:
  - Biennial screening maintained avg 81% (67–99) of annual screening benefit
  - 50% reduction of false-positive results
  - Mortality reduction (age 50–69) 16.5%, age 40–49 additional 3% reduction but more false positives
- Take home: Biennial screening achieves most of benefit with less harm than annual

Canadian study (CNBSS)

BMJ 2014;348

- 25 yo follow up for breast ca incidence & mortality
- Randomized screening trial
- Results: 89835 women followed
- 1190 breast ca found (666 in mammo/524 control
- 351 deaths (of 1190 during screening period)
- Conclusion: similar cumulative mortality between screened and control in both age groups (40–49 and 50–59)
- Controversial study–not randomized, many Ca was palpable at baseline, not state of art mammogram at time of study

- SEER data 1976–2008
- Results: increase number of cases of early breast ca (112 to 234/100,000)
- Decrease of late stage presentation (102 to 94)
- Only 8 of the 122 early ca were predicted to progress to advance disease
- Estimate that in 2008–overdx of breast ca in 70,000 women (31% of all breast ca dx)
- Decrease in death–28% (ages 40+)–study claims this is more from improved RX than screening
Analysis of Swedish two–county randomized trial and UK breast screening program

Ages: 50–69, screening every 24–33 mo

Result of Swedish study: 8.8 breast ca deaths prevented per 1000 screened
  ◦ Overdx: 4.3 per 1000

Result of UK study: 5.7 deaths prevented per 1000 screened
  ◦ Overdx 2.3 per 1000

Conclusion: for every 2 ca deaths prevented, 1 overdx
Risks of mammogram

- Overdiagnosis of breast cancer (ca that will not become clinically problematic or cause death)
- False positive – leading to biopsy, scarring, anxiety
- Radiation risks over time
What about dense breasts?

- Friedewald et al: retrospective study
- Compared digital mammogram vs digital mammogram with tomosynthesis
- Main outcomes:
  - 1207 CA in mammogram
  - 950 CA in mammo plus tomo
  - Overall increase in CA detection of 1.2 (0.8–1.6) in mammo/tomo
  - PPV 4.3% (mammo) vs 6.4% mammo/tomo
- Take home: mammo/tomo less recall and slight increase CA detection. Did not have data on harm or mortality benefit
- Risks: mammo/tomo – 2x radiation of digital mammogram

JAMA 2014;311:2499-2507
JAMA Intern Med 2013:173:807-16
So what do I do?

- Highest value is for women age 50–69
- Discuss screening for ages 40–49 (shared decision making)
- Reasonable to start age 50+ with 1–2 yr screening—no change in mortality and less false positive
- Dense breasts—? Unknown if annual vs biennial better or mammo/tomo vs mammo
- No benefit after age 80
- If healthy female—likely benefit ages 70–79
Leading cause of CA death in the US
Most impt risk factor: smoking–contributes to 85% of lung CA cases
In 2010: 201,144 dxed with lung CA
  ◦ 158,248 died from disease
  ◦ From 2001–2010
  ◦ Incidence in men decreased 2.3–2.7% per yr (women 0.6–1%)…..stable for AA, Al, NA, Asian
  ◦ Mortality in men decreased 1.6–3.3% per yr) women 0.9–1.1%)….level for Al, Asian
Case 1: Lung ca

- 60 yo male former smoker. 15pk yrs. Quit 10 yrs ago. FH + for CAD but no CA.
- What is the appropriate screening?
- A. PSA for prostate CA
- B. Colon CA
- C. CT chest for lung CA
- D. Abdominal Aortic Aneurysm
Case 2: lung ca

- 65 yo current smoker with 35 pk yrs. Has no desire to quit. Just heard about lung cancer screening and wants your opinion. What do the guidelines say?
  A. He should not have screening as he still smokes
  B. Lung CA screening may be beneficial for him
  C. He should have CXR instead
  D. Screening reduced lung ca mortality by 50%
LUNG CA Screening

- USPSTF guidelines
- Annual screening with low-dose CT
- Criteria: min 30 pk yr smoking hx
- Current smoker or quit within 15 yrs
- Age 55–80
- Life expectancy > 10 yrs
- Willing to undergo lung surgery

What’s the data

- DANTE trial: Am J Respir Crit Care Med 2009;180:445
- Men age 60–75, 20 pk yr smokers
- Compared annual LDCT x 4 yr vs control (one cxr)
- 1276 in LDCT vs 1196 in control

Results
- 60 lung ca in LDCT vs 34 in control
- More stage 1 in LDCT
- No difference in death rates (20 in each grp)
- Harm more invasive procedures for benign disease in LDCT
What’s the data

- Nat’l Lung Screening Trial (NLST)
- Randomized to annual LDCT vs CXR
- Age 55–74, 30 pk yr smoking, quit <15yr or current smoker
- Incidence of lung ca 645/100,000 person yrs (LDCT) vs 572/100,000 (CXR)
- Death 247/100,000 vs 309/100,000
- Outcome: 20% relative reduction of mortality
- 18% overdiagnosis
- NNS to prevent one lung ca death: 320
- Higher complications in LDCT screening
- Conclusions: LDCT might be beneficial but have to weigh risks/benefits

Source: NEJM 2011;365:395–409
What’s the data

source: NEJM 2011;365:395–409

B  Death from Lung Cancer

Cumulative No. of Lung-Cancer Deaths

Years since Randomization

Chest radiography
Low-dose CT
What’s the data

- 3 reviews (incl NLST )
- Findings: only NLST showed benefit, the other 2 smaller studies showed no benefit (DANTE/DLST)
- Harms: 20% of LDCT in each round had positive results requiring some f/u. only 1% had lung ca
- Conclusions: one RCT showed benefit, consider screening high risk pts but need to do risk/benefit discussion
Lung CA screening

- New study showing relative risk reduction of 20%
- Annual screen ages 55-74 with
  - 30+ pk yr smoking hx
  - Still smoking or quit within 15 yrs
- Use low dose chest CT scan with no contrast

Potential harms
  - High false positive rate-leading to procedure risk
  - Radiation exposure
  - Does not address root cause….TOBACCO

NEJM 2011;365:295-409
So what do I do?

- **Smoking cessation first line prevention**
- Consider annual LDCT if meets criteria
- Need to document in note for coverage
  - Age 55–80
  - ≥ 30 pk yr smoker
  - Current smoker or quit <15 yrs
  - >10 yr life expectancy
  - Counseled on risks/benefits of screening
What about prognosis?
Estimating life expectancy

- Health and Retirement Study
- 20,000 community-dwelling adults >50 yo
- 4-year mortality of group
- Based on pt report of following:
  - Age
  - Sex
  - Low BMI
  - Hx DM
  - Hx Cancer
  - Hx chronic lung disease
  - Hx CHF
  - Smoking
  - Difficulty w/ bathing
  - Difficulty managing money
  - Difficulty walking several blocks
  - Difficulty pushing or pulling large objects
Estimating life expectancy
Health and retirement study

82 yo woman, BMI 27, no major co-morbidities, non-smoker, active and independent
→ 4-year mortality: 5%

73 yo man, BMI 22, COPD, DM, smokes, walking and pulling/pushing is limited
→ 4-year mortality: 67%
Estimating life expectancy

- National Health Interview Survey
- 24,000 community dwelling adults age > 65yo
- 5-year mortality
- Based solely on patient report of following:

  - Age
  - Sex
  - Low BMI
  - Health self-assessment
  - Hx COPD
  - Hx Cancer
  - Hx DM
  - Smoking
  - Able to walk 3 blocks?
  - Need help w/ everyday activities?
  - Hospitalized in the last year?
82 yo woman, BMI 27, no major co-morbidities, non-smoker, active and independent
→ 5-year mortality: 8%

73 yo man, BMI 22, COPD, DM, smokes, walking and pulling/pushing is limited
→ 5-year mortality: 71%
Estimating life expectancy

Lee Schonberg Index
- Population: Community dwelling adults aged 50 and older
- Outcome: All cause 4 and 10 year mortality
- Scroll to the bottom for more detailed information

Are you a healthcare professional?  No  Yes

Risk Calculator
1. How old is your patient?  75-79
2. What is the sex of your patient?  Female  Male
3. What is your patient’s BMI?  <25
4. Which best describes your patient’s health in general?  Good
5. Does your patient have chronic lung disease, such as emphysema or chronic bronchitis?  Yes  No
6. Has your patient ever had cancer (excluding minor skin cancers)?  Yes  No
7. Does your patient have congestive heart failure?  Yes  No
8. Does your patient have diabetes or high blood sugar?  Yes  No
9. Which best describes your patient’s cigarette use?  Former smoker
10. Does your patient have difficulty walking 1/4 mile (several city blocks) without help from other people or special equipment?
Estimating life expectancy

Is there a simpler way?

Gait Speed and Survival in Older Adults

Stephanie Studenski, MD, MPH
Subashan Perera, PhD
Kushang Patel, PhD
Caterina Rosano, MD, PhD
Kimberly Faulkner, PhD
Marco Inzitari, MD, PhD
Jennifer Brach, PhD
Julie Chandler, PhD
Peggy Cawthon, PhD

Context  Survival estimates help individualize goals of care for geriatric patients, but life tables fail to account for the great variability in survival. Physical performance measures, such as gait speed, might help account for variability, allowing clinicians to make more individualized estimates.

Objective  To evaluate the relationship between gait speed and survival.

Design, Setting, and Participants  Pooled analysis of 9 cohort studies (collected between 1986 and 2000), using individual data from 34,485 community-dwelling older adults aged 65 years or older with baseline gait speed data, followed up for 6 to 21 years. Participants were a mean (SD) age of 73.5 (5.9) years; 59.6%, women; and 79.8%, white; and had a mean (SD) gait speed of 0.92 (0.27) m/s.

Main Outcome Measures  Survival rates and life expectancy.

JAMA 2011;305:50-58
Estimating life expectancy

- 34,000 community-dwelling adults ≥ 65 yo
- Gait speed: 4-meter (12ft) walk at usual pace
- Has been correlated with:
  - Comorbidities
  - Atherosclerosis
  - Cognitive impairment
  - Hospitalization
  - Institutionalization

JAMA 2011;305:50-58
JAMA 2001;305:93-94
Estimating life expectancy

Median Life Expectancy

Gait Speed of 0.8 m/s (= 4 meters in 5 sec)
Take Home Points

- Cancer screening can save lives if used appropriately
  - Cervical ages 21–65 (q3–5yrs)
  - Colon ages 50–75 (consider older if healthy)
  - Breast ages 45ish–75 (consider older if healthy)
  - Lung– ages 55–80 (only at risk)

- Know when to stop screening for elderly, co-morbid or when necessity is gone (ie TAH)

- Screenings not recommended as greater harm than benefit (PSA, ovarian)