AN OUNCE OF PREVENTION IS WORTH A POUND OF CONTROVERSY

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SCREENING TESTS

- Benefit outweighs risk
  - Detect disease early
  - Effective treatments are available
  - Cost effective
  - Widely available
  - Safe to use
  - Leads to improved outcomes

GUIDELINES

- Choose your loyalty
- USPSTF
- ACP
- Organizations are not infallible
- Guidelines not mandates
- Insurance follows

USPSTF (U.S. PREVENTATIVE SERVICES TASKFORCE)

- Independent panel of non-Federal experts
  - Expert in prevention and evidence-based medicine
  - Varied members
- Scientific evidence reviews
  - Screening
  - Counseling
  - Preventive medications
  - Recommendations for primary care clinicians

USPSTF GRADE DEFINITIONS

Grade	Definition	Practice
A	Recommended/high certainty of substantial net benefit	Offer to patients
B	Recommended/high certainty of moderate benefit; moderate certainty of substantial benefit	Offer to patients
C	Recommend against routine use. In some patients may consider; moderate certainty net benefit small	Do not routinely recommend; offer only if other considerations suggest
D	Not recommended; harm outweighs benefit	Discourage
I	Evidence lacking; insufficient data	Discuss in individual cases

A DAY IN THE LIFE

50 year old female with well controlled diabetes complicated by obesity is in your office to discuss left shoulder pain before initiating exercise with a personal trainer. For you, this was her three month scheduled diabetes follow-up

What ambulatory screening is necessary?

- Preventative
- Disease specific

THE TOTAL

- Colorectal ca screening
- Mammogram
- Pap
- Weight loss/diabetic diet
- HgA1c
- LDL
- Ophthalmology
- Complete foot exam
- Urine microalbumin
- Pneumovax
- Hep B series
- Flu vax
- Stress Test
- …

BREAST CANCER

BREAST CANCER

- Most common cancer in women
- 1:8 lifetime risk of invasive cancer
- Connecticut
- Effective screening- before palpable
- Mortality decreasing at 2.2% each year in developed countries

BCA RISK FACTORS

- Hormone related
  - Early menarche (<12)
  - Late menopause (55)
  - Late first time birth (>30)
  - OCP exposure>5 years
  - Nulliparous
- Other
  - Obesity
  - Inactivity
  - Density of tissue
  - Past personal history
  - DES/Radiation exposure

HIGH RISK

- Refers to women with >20% lifetime risk
- Categories
  - Family history of several breast cancers with early onset
  - Breast and ovarian cancer in the family
  - Positive genetic testing
  - History of chest irradiation under 30 years of age

BREAST CANCER SCREENING

- Mammography
- Self breast exams
- Clinical Breast exams
- Recommendations are based on *average risk*
- Assess Risk: can use a risk assessment model
  - Gail model
  - National Cancer Institute
  - The models assess a population risk *not necessarily the individual*

CLINICAL BREAST EXAM

- ACOG: at 20 begin doing annually
- ACP: no
- USPSTF: insufficient evidence for use over 40
- ACS: every 3 years 20-40 and then yearly

SELF BREAST EXAM

- Large studies Shanghai and Russia:
  - Almost identical mortality
  - BSE group had more biopsies
  - 10+ years of follow up
- Ideal screening test
- Young breast tissue= “lumps” and unnecessary biopsy
- Role of the clinical breast exam

MAMMOGRAPHY

- Plain mammography
  - RR 15-20%
- Digital mammography
  - Increased cost/ decreased availability
  - >60/dense breasts has ↑sensitivity
  - Equal CA detection
- Dense breast tissue
  - Ultrasound versus MRI
    - Reimbursement
    - Suggest higher sensitivity with MRI
    - Both higher false positive rate (unnecessary biopsy) than mammogram

Ann Int Med Oct 18, 2011; 155 (8)

THE MAMMOGRAM CONTROVERSY

- USPSTF 2009- upper age limit
- USPSTF 2009 – under 50
  - Age 40-49 moves from a B to a C recommendation
  - Making it an individual, but not widely recommended test
- USPSTF 2009 – change in screening interval
  - Frequency decreased to 2 years 50+
- Payment fallout
- Women's rights
- Young lives

MAMMOGRAMS FOR THE 40'S

- ACP
  - Individualized (Q1-2)
- USPSTF
  - Discuss- insufficient evidence
  - Not more than biannual screening
- ACOG
  - Screening Q 1-2 years
  - Self breast exam
  - Clinical exam annually
- ACS
  - Annual screening starting at 40

AGE TRIAL

- Focused on women in 4th decade
- High number of screenings to prevent one cancer
- Review of 70 years at Mayo clinic under 25
  - Aggressive
  - Genetic
  - 12 cases
- Limitations
  - Lower sensitivity of mammogram
  - High false positive rates

Adjusted False-Positive Recall Probabilities at First and Subsequent Examinations, Stratified by Associated Characteristics.

False-positive recall for a single, initial screening 16.3%

Table 2. Adjusted False-Positive Recall Probabilities at First and Subsequent Examinations, Stratified by Associated Characteristics

Variable	First Examination*		Subsequent Examination†	
	False-Positive Results, %	Odds Ratio for False-Positive Recall (95% CI)‡	False-Positive Results, %	Odds Ratio for False-Positive Recall (95% CI)
Age at mammogram				
40–44 y	16.4	1.00 (reference)	8.9	1.00 (reference)
45–49 y	19.9	1.27 (1.21–1.33)	9.4	1.07 (1.01–1.12)
50–54 y	21.4	1.39 (1.31–1.47)	8.7	0.98 (0.92–1.05)
55–59 y	19.7	1.25 (1.15–1.36)	8.0	0.89 (0.82–0.97)
60–64 y	–	–	8.3	0.92 (0.83–1.03)
≥65 y	–	–	9.6	1.09 (0.89–1.33)
Family history of breast cancer				
Yes	20.5	1.21 (1.13–1.30)	8.8	0.98 (0.91–1.05)
No	17.6	1.00 (reference)	8.9	1.00 (reference)
BI-RADS breast density				
Almost entirely fat	11.8	0.62 (0.56–0.67)	3.7	0.45 (0.40–0.50)
Scattered fibroglandular densities	17.8	1.00 (reference)	7.9	1.00 (reference)
Heterogeneously dense	19.3	1.11 (1.06–1.16)	10.7	1.40 (1.33–1.46)
Extremely dense	15.5	0.85 (0.79–0.91)	9.0	1.16 (1.08–1.25)
Current hormone therapy use				
Yes	17.3	0.96 (0.90–1.03)	9.3	1.05 (0.99–1.12)
No	17.8	1.00 (reference)	8.9	1.00 (reference)
Year of first examination				
<1997	13.6	1.00 (reference)	8.6	1.00 (reference)
1997–1999	15.7	1.18 (1.07–1.31)	8.8	1.02 (0.96–1.08)
2000–2001	17.5	1.35 (1.21–1.50)	9.1	1.07 (1.00–1.14)
2002–2004	19.3	1.52 (1.37–1.69)	9.5	1.12 (1.03–1.21)
>2004	20.7	1.67 (1.49–1.86)	11.0	1.31 (1.10–1.57)
Comparison mammogram available				
Yes	–	–	8.7	0.50 (0.45–0.56)
No	–	–	15.8	1.00 (reference)
Time since last mammogram				
9–18 mo	–	–	8.3	1.00 (reference)
19–30 mo	–	–	9.3	1.13 (1.08–1.19)
>30 mo	–	–	10.7	1.33 (1.26–1.40)

BI-RADS = Breast Imaging Reporting and Data System.
* Estimates for first examinations are based on data for 81 305 women.
† Estimates for subsequent examinations are based on data for 121 662 mammograms from 57 282 women.
‡ Odds ratios are from multivariable logistic regression models, including all variables presented above as well as registry and random radiologist intercepts.

Hubbard R A et al. Ann Intern Med 2011;155:481-492

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THE HARD FACTS

- AGE trial
  - Insignificant mortality effect under 48
  - Number needed to “treat”- 2512
  - Insufficient sample
  - Test technique
- Gothenberg Breast Screening Trial
  - 1904 to save a life (45% mortality reduction)
- USPSTF - NNS is 1964
- No statistical difference in late-stage CA biennial versus annual screen in women

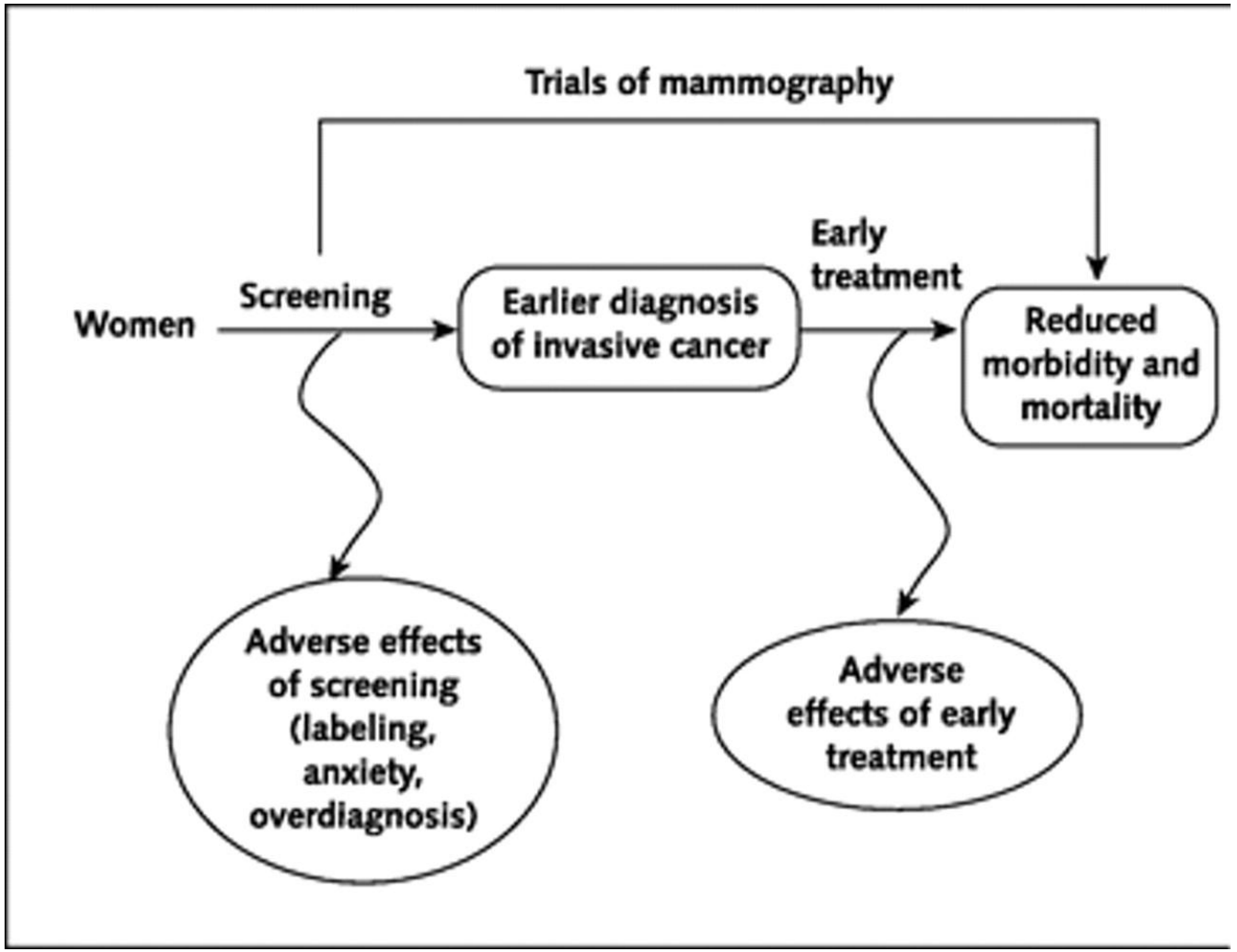
Ann Int Med Oct 18, 2011; 155 (8)

EFFECTS OF OVERSCREENING

- 42 yo female
  - Nulliparous
- RR for mortality by 15%
- *BUT* call back rate is 40%
  - Anxiety provoking
- Risk of biopsy for those are 3% for a benign lesion
- Ann Int Med Oct 2011

Statistics are for a benign lesion only

Analytic framework.



Humphrey L L et al. Ann Intern Med 2002;137:347-360

Annals of Internal Medicine

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50-74 CONSENSUS (SORT OF)

- ACOG: annual screen
- ACS: annual screen
- USPSTF: every 2 years
- ACP: every 1-2 years
- Decreases mortality in this group

UPPER LIMIT FOR SCREENING

- ACP
  - 74
- USPSTF
  - 74 If choose later, no more than every two years (I recommendation)
- ACOG
  - No limit if in good health
- ACS
  - No limit when in good health

POOLED TRIAL DATA

AGE	TRIALS	NNS to Prevent 1 Death
39-49	8	1904
50-59	6	1339
60-69	2	377
70-74	1	unknown

BREAST CANCER CONCLUSION

- Quality evidence for reduced mortality with mammography 50-74
- Arch Int Med 2011
  - Is mortality decreased by screening or awareness
- No evidence that CBE reduces death>mammo
- Evidence against SBE
  - Consider the patient
- Ages 40-49 are a long standing controversy
  - Evidence against
  - Increase in life expectancy may be worth it

CERVICAL CANCER

CERVICAL CANCER

- Goal of screening – sample the transformation zone
  - 95-100% of cervical squamous cell CA secondary to HPV

- Current issues:
  - When to start screening: 21 all women
  - Frequency of screening
  - Conventional versus liquid pap
  - To use HPV or not

EFFECTS OF SCREENING

- 1973
  - 14.2 new cases/100,000 women
- 1994
  - 7.8 new cases
- 1998
  - 3 deaths per 100,000 women
- No direct comparisons of traditional pap and newer methods
- Newer (thin prep) cost effective
  - $50G/ life year
  - Only when done every three years

BENEFIT - HARM

- Recommendations change as women age
  - Prevents ↑ false positives
- Study screened 2561 postmenopausal women
  - Normal at baseline
  - Low risk
  - 110 abnormal results over 4 years
  - Created 231 additional interventions
  - For one “mild to moderate dysplasia”

ASSESSING RISK

- High risk features
  - Young age at first sexual activity
  - 5+ lifetime partners
  - Smoking
  - HPV or other STD's
  - OCP's >5 years (reversible)
- Newer tests
  - Thin prep is more sensitive less specific than the traditional- but close enough
  - HPV test alone
    - Not useful under 30
    - Expensive
    - Requires special lab

USPSTF (2011)

- Recommends screening sexually active women with a cervix (A)
  - Exact age to start and intervals have only indirect evidence
- Best guess for benefit:
  - Start 21
  - Screen every 3 years
  - Against routine screen over 65 with previous normal results and no high risk factors (D)
  - No screening if TAH for benign reasons (D)
  - HPV as primary test (I)
  - Liquid and conventional pap equal

Ann Int Med 2011;155(10): 687-704

ACS (REVISION PENDING 2012)

- Start screening 3 years after intercourse or 21
- Under 30
  - Standard pap yearly
  - Liquid every 2
- At 30
  - *If* 3 past normals, Q2-3 years (3)
  - Or every 3 with HPV (3-5 +HPV)
- At 70 (65)
  - If past 3 paps normal
  - ***AND*** no abnormals for 10 years
    - Then stop
- After total hysterectomy
  - Can stop for low risk

ACOG (2009)

- 21-30
  - Every two years
- 30+ Rule of Threes
  - Pap + HPV neg → every 3 years
  - After 3 negatives, every 3 years
  - Stop at 65-70 if negative
- Additional risk factors
  - H/O cervical neoplasia
  - HPV, HIV, or other STDs
  - Immunosuppressed
  - High risk sexual behavior
  - DES exposure in utero

CERVICAL CANCER CONCLUSION

- 21
- Consensus for every three years
  - W/wo HPV
  - After 30
  - If all else normal
- Stopping screening
  - TAH for benign reasons
  - 65-70 with normal paps

COLORECTAL CANCER

- Controversies
  - Overuse/underuse/misuse
  - Health disparities
- Screening modalities
  - Colonoscopy
  - gFOBT
  - iFOBT
  - Sigmoidoscopy
  - Double contrast barium enema
  - Virtual colonography

Ann Int Med March 2012;156(5): 378-384

POWER OF CANCER PREVENTION

- Colonoscopy associated with decreased risk CA with unscreened controls
  - 73% lower risk for distal CRC
  - 54% for proximal
  - Retrospective data from Medicare
- Hot off the press
  - Population based case-controlled study in Germany (over 4000) 2003-2007
  - Persons with 100% negative colonoscopy may not need repeat screening for 20 years
  - Maybe even in persons with a family history
  - Smoking still a significant risk factor

Jnl Clin Onc October 1,2011; 29(28)

COST EFFECTIVE COLONOSCOPY

- Computer model
  - Hypothetical 100,000 ppl
  - Those over 50
    - Colonoscopy Q10
    - gFOBT Q1
    - Flex sig Q5
- gFOBT
  - Positive results ⇒ colonoscopy
  - Costs less but saves fewer “life-years”
- Flexible sigmoidoscopy
  - Adenomatous polyp ⇒ colonoscopy
  - Less cost effective than either two

WHAT TO SCREEN FOR

- Cancer and polyps
  - Flexible sigmoidoscopy
  - Colonoscopy
  - Barium enema
  - Virtual colonoscopy
- Just cancer
  - gFOBT (guiaic)
  - iFOBT (immunochemical)

RECOMMENDATIONS

- For *average risk patients*
  - Most cases occur in average risk patients
  - Higher risk with African Americans, male sex, and increasing age
  - AA have highest mortality
  - Family/personal history and IBD higher risk
- Some organizations with statements
  - ACP
  - USPSTF
  - ACG
  - ACS

USPSTF

- Screen 50-75
  - Flex sig - every five years
  - gFOBT - annually
  - Colonoscopy- every 10 years
  - No comment on high risk population
- 76-85 screen if life expectancy >10 years
  - Not routinely
  - Individualized
- Do not screen over 85
- Insufficient evidence
  - Fecal DNA testing
  - CT colonography (CTC)- only group

ACP

- Screening cohort 50-75
  - Flex sig/CT colonography/DCBE) - every five years
  - gFOBT or iFOBT- annually
  - Colonoscopy- every 10 years
- 76-85 screen if life expectancy >10 years
  - Not routinely
  - Individualized
- Do not screen over 85
- High risk- start at 40 or 10 years earlier
- Insufficient evidence
  - Fecal DNA testing

ACS

- ACS- screen starting at 50
  - For average risk
  - Also recommends double contrast barium enema every 5
  - Virtual colonography every 5
  - iFOBT yearly or stool DNA test (uncertain interval)
  - No upper limit

ACG

- Took a new tact- accepted disparities
  - Emphasized need to see what is available
  - And if the patient is willing
  - No discussion harm/benefit
- Types of screening
  - Flex sig every 5-10 years
  - Colonoscopy every 10 (every 5 in high risk)
  - CT colonography every 5 years
  - Annual iFOBT
- Pay special attention to risk factors
  - Obesity
  - Smoking
  - Race

SCREENING IN THE "ELDERLY"

- 65-85
- Model/estimation based on review of pertinent studies
- gFOBT $35G per life year saved
- Sigmoidoscopy $47G
- Reasonably cost effective

OVERUSE

- Article by Goodwin
  - 24,000 $\geq$ 66
  - Negative screens
  - Repeat at 5 yrs - 25%
  - Repeat at 7 – 46%
- Repeat screening in a group that least needed
  - 80+ years 33% had repeat screening within 7 years

HARMS OF OVERSCREENING

- Cost and limited availability
- Bleeding with polyp removal
- Perforation
- Cardiopulmonary complications
- Diverticulitis
- Severe abdominal pain
- False negative results/false assurance

Ann Int Med March 2012; 156 (5)

CRC SCREENING CONCLUSION

- Average risk start at 50
- Sooner increased risk start
- Screen to age 75
- Above that
  - gFOBT/sigmoidoscopy most cost effective
  - Look at life expectancy
  - Look at concurrent morbidities

PROSTATE CANCER

PROSTATE CANCER

- Most common cancer in men
- Second most diagnosed cancer
- 90% cases detected with screening
- Median age
  - Dx- 67
  - Death- 81
- Risk factors:
  - Age
  - Race
  - Family history

NEJM November, 2011; 365 (21): 2013-2020

TEST AND TREATMENT

- Faults with PSA
  - Not specific to cancer
  - Can't determine aggressive vs indolent
  - Unnecessary biopsies
  - USPSTF feels "10 yr mortality benefit small to none…moderate certainty… no net benefit"
- Adverse effects of treatment
  - Greatest with radical prostatectomy
  - Incontinence
  - Sexual dysfunction

THE IMPETUS FOR CHANGE

- PSA testing popular before data on Tx early PCA
- 70% of men 70+ have occult prostate cancer
- 2 recent large studies
  - ERSPC- found decreased mortality
    - 1410 NNS twice to prevent one death
    - Many procedures benefited only a few
  - PLCO- no effect on mortality
    - Screening outside trial in control group
- USPSTF no longer advocates testing in any patient

NEJM November, 2011; 365 (21): 2013-2020

CURRENT RECOMMENDATIONS

- AUA
  - Shared decision
  - Start at 40
  - PSA + DRE
  - Normal range for PSA
    - Age
    - Race
- ACS
  - Shared decision
  - 50 (45 for AA or family history)
  - Those tested: PSA ± DRE
  - Interval depends (Q2 years)

Table 2. Prostate-Cancer Screening Guidelines.*

Recommendation	American Urological Association	American Cancer Society	U.S. Preventive Services Task Force
Shared decision making between patient and clinician	Yes	Yes (consider use of decision aid)	Yes (when patient requests screening)
Age to begin offering screening — yr			
Average-risk patients	40	50	Not applicable
High-risk patients (black patients and those with first-degree relative with prostate cancer)	40	40–45	Not applicable
Discontinuation of screening	Life expectancy <10 yr	Life expectancy <10 yr	Not applicable
Screening tests	PSA, digital rectal examination	PSA, optional digital rectal examination	Not applicable
Frequency of screening	Annual (possibly less often for men in their 40s)†	Annual (every other year when PSA <2.5 ng/ml)	Not applicable
Criteria for biopsy referral	Age, family history, race or ethnic group, findings on digital rectal examination, total PSA, free PSA, PSA velocity, PSA density, previous biopsy findings, coexisting conditions	PSA ≥4.0 ng/ml, abnormal digital rectal examination; individualized risk assessment if PSA is 2.5–4.0 ng/ml	Not applicable

* The sources for the guidelines are as follows: the American Urological Association,[13] the American Cancer Society,[11] and draft guidelines from the U.S. Preventive Services Task Force.[48]

† The guidelines indicate that the initial PSA value at 40 years of age (relative to the median value of 0.6 to 0.7 ng per milliliter for this age group) would determine subsequent (but unspecified) screening intervals. The National Comprehensive Cancer Network recommends using a PSA cutoff level to determine whether subsequent testing should be performed annually or at 45 years of age (and then at 50 years of age).[49] However, these recommendations are not evidence-based.

NEJM November, 2011; 365 (21): 2013-2020

The NEW ENGLAND JOURNAL of MEDICINE

NOT RECOMMENDED

- AAFP
- USPSTF
  - D recommendation
  - Harm > good
- American College of Preventative Medicine

20% of men with cancer will have a normal PSA

If you do check: a different approach is surveillance of those men who test positive

serial psa, rectal exams, and biopsies

ADDITIONAL RECOMMENDATIONS

USPSTF

- AAA
  - Men 65-75
  - Current or former smokers
  - No recs for women
- Blood pressure
  - Periodically over 18
- GC/CL
  - Men and women ≤ 25
  - Typically asymptomatic and risk of harm
- Diabetes screening
  - If BP >135/80
- Depression screening
  - Only if services for Dx, Tx, and follow up

USPSTF

- HIV
  - Pregnant women
  - High risk annually
  - All patients in health care setting (optimal interval not known)
    - Encouraged for annual exam ages 13-65
- Lung CA
  - Insufficient evidence
- Lipids
  - Men ≥ 35
  - Women ≥ 45
  - Start at 20 if increased risk for CAD
  - No recommendation against accelerated schedule

USPSTF

- Ovarian CA
  - No screening recommended
- Osteoporosis
  - Post menopausal 65
  - Higher risk for fractures at 60
  - No recommendation for younger
  - Rescreening article- NEJM January 2012
  - Risk factors
    - Estrogen deficiency, skeletal abnormalities, daily steroids for >3 months, meds (dilantin), hyperparathyroid, etc

(ACP recommends assessing a man's risk and screening but no definite age to start)

SCREENING SPECIFICALLY IN THE "ELDERLY"

- "Despite Guidelines, the Elderly are Getting Cancer Tests" *Arch of Intnl Med; Jan 2012*
  - Most Americans >75 still undergo screening
  - Half of these because the doc recommended
  - USPTF >65 no paps, >75 ∅ mammo/colon/pros
- The question is:
  - If the risks and benefits are reviewed
  - One of individualization

Arch. Intern. Med. 2011;171: 2031-8

TARGET VS ELDERLY POPULATIONS

- Data From Arch. Intern. Med. and National Health Survey Interview Surveys 2005, 2008
  - Sample size 50,000
  - Mammogram: 62% 75-79; almost equal to 74% in target population
  - Pap: 53% 75-79, 38% over 80
  - Colon: highest screening rate of 57% in 75-79 exceeding target population (48%); >80 47% screened
  - Prostate: lowest in target population of 50-74 and highest 75-79 at 42%

Arch. Intern. Med. 2011;171: 2031-8