Breast cancer affects everyone

Est. new cases of cancer in US in 2017

252,710 cases of invasive breast carcinoma in women
63,410 cases of in situ breast carcinoma in women

CA Cancer J Clin 2017;67:7-30
Estimated cancer deaths in US in 2017

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung &amp; bronchus</td>
<td>64,730</td>
<td>71,299</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>27,196</td>
<td>40,648</td>
</tr>
<tr>
<td>Prostate</td>
<td>26,498</td>
<td>23,170</td>
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<tr>
<td>Breast</td>
<td>20,530</td>
<td>14,516</td>
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<tr>
<td>Colon &amp; rectum</td>
<td>27,196</td>
<td>40,648</td>
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<tr>
<td>Leukemia</td>
<td>11,430</td>
<td>11,810</td>
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<tr>
<td>Liver &amp; intrahepatic</td>
<td>12,240</td>
<td>5,411</td>
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<tr>
<td>Non-Hodgkin lymphoma</td>
<td>11,498</td>
<td>8,000</td>
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<tr>
<td>Brain &amp; other nervous</td>
<td>9,020</td>
<td>7,000</td>
</tr>
<tr>
<td>All cancers</td>
<td>315,458</td>
<td>283,288</td>
</tr>
</tbody>
</table>

CA Cancer J Clin 2017; 67:7-30

Risk Factors for Breast Cancer
- Age
- Race/ethnic group
- Age at menarche
- Nulliparity
- Age at first full-term pregnancy
- Parity - number of births
- Breastfeeding
- Age at menopause

Risk Factors for Breast Cancer
- Postmenopausal hormone replacement
  Decline in incidence in breast cancer incidence after publication of results of Women’s Health Initiative in 2002 and other trials
- Diet – controversial
- Obesity, weight gain, physical activity, alcohol
- Radiation – especially at younger age
  Atomic bomb survivors
  Therapeutic – esp after treatment for Hodgkin’s
Risk factors for breast cancer

- 5-10% of breast cancers due to inheritance of cancer susceptibility gene
- Mutations in BRCA1 and BRCA2 account for 80-90% of hereditary breast cancer
- To reduce but not eliminate risk: Prophylactic mastectomies, bilateral salpingo-oophorectomy

Hereditary Breast Cancer

- There are other mutations associated with increased risk for breast cancer, including p53 (Li-Fraumeni syndrome), CHEK2, ATM, PTEN, PALB2, CDH1, etc
- With increasing genetic testing using broader panels, we are finding more mutations of unknown significance

Risk Factors for Breast Cancer

- FEMALE GENDER
  Lifetime risk for invasive breast cancer is 1 in 8 = 12.5%
  by age 85 for American women
Men can get breast cancer too

Male Breast Cancer

- In 2017, in US, estimated that 2470 men will be diagnosed with breast cancer
  460 men will die of breast cancer
- Most are invasive ductal carcinoma
- African-American men tend to be diagnosed at earlier age and more advanced stage

Male Breast Cancer - Hereditary

- 5-10% of female breast cancer hereditary
- Lifetime risk for breast ca for women with BRCA mutation 50-85%
- 15-20% of men with breast cancer have family history of breast cancer
- Cumulative risk for breast cancer for men with BRCA2 mutation 6.5% by age 70
- NCCN guidelines: test all men with breast ca for BRCA mutations. Test all women with breast ca with Fam Hx of male breast ca for BRCA mutations
Risk reduction in the Radiology suite

- No prelabeling of containers at the beginning of the day, morning, or afternoon
- Differential colors into formalin for bilateral biopsies – e.g., red/orange for red, blue for left

Risk reduction in Pathology
Risk reduction in Pathology

Bar codes
Different color ink for each case
Verbal or mental time-outs

Risk reduction in Pathology

Bar codes
One case per tray
Verbal or mental time-outs, comparing block and slides

Breast biopsies often get it wrong

Breast Health: Breast Cancer Biopsies Often Misdiagnosed, May Require A Second Opinion
Diagnostic concordance among Pathologists Interpreting Breast Biopsy Specimens (JAMA 2015)

- One slide per case – biopsies and excisions
- No consultation with colleagues
- Case mix not representative of usual practice – weighted towards atypical cases
- Level of concordance between study pathologists and consensus diagnosis (75%) same as initial diagnostic concordance rate among the 3 experts
- No outcome data to suggest that reference dx between the 3 pathologists the correct diagnosis

Davidson NE, Rimm DL. Editorial. JAMA 2015;313:1109-10

Diagnostic Concordance among Pathologists Interpreting Breast Bx Specimens (JAMA 2015)

- Gaming the test
- Unlimited time – time for second guessing yourself
- Or less time per case since at end of day in life of exhausted pathologist and not a real patient
### Controversies in real life

- Selected lesions found on radiographically-directed biopsies – surgically excise or follow?
- Breast conserving surgery for DCIS – what’s an adequate margin?
- Are we overdiagnosing and overtreating DCIS? Should we remove the word “carcinoma” from DCIS?
- Screening: when to start, when to stop, intervals, harms and benefits

### Flat epithelial atypia (FEA)

- Part of spectrum of columnar cell alterations
- Like other columnar cell lesions, often detected during targeting of indeterminate calcifications
- Similar genetic alterations in FEA, ADH, and low grade invasive carcinoma in same tissue
- FEA may be nonobligate precursor in pathway of development of low grade breast cancer

### Flat epithelial atypia (FEA)

- Enlarged dilated acini and terminal ducts lined by monotonous cells
- Low grade cytologic atypia with rounding of nuclei, small nucleoli
- Loss of nuclear polarity
Flat epithelial atypia (FEA)

- Does having flat epithelial atypia increase the risk of subsequently developing breast cancer?

- If there is flat epithelial atypia on a core biopsy, what is the likelihood of finding a more advanced lesion on excision; i.e., DCIS and invasive cancer?

   The data guides decisions on whether patients with FEA on core biopsy need to undergo surgical excision.

Flat epithelial atypia (FEA)

- Mayo Clinic Cohort study
  - 11,591 pts who had excisional biopsy or core needle bx followed by surgical excision, 1967-2001
  - FEA in 2.4%; 1.3% before 1981, 2.4% after 1981
  - 282 patients with FEA
    - 46% with atypical hyperplasia (ADH>>ALH)
    - 54% with proliferative disease without atypia


Flat epithelial atypia not an independent risk factor (Said et al. Cancer 2015;121:1548-55)

- Expected
- PDWA – FEA
- PDWA + FEA
- AH – FEA
- AH + FEA
FEA on core biopsy. What is upgrade rate on surgical excision?

- Until recently most papers recommended surgical excision after dx of FEA on breast core biopsy
- 0-21% of pts with FEA on core biopsy found to have carcinoma in subsequent surgical excision
- Issues: lack of concordance for diagnostic threshold, sampling

Flat epithelial atypia

- 3.2% of pts with pure FEA on core biopsy had carcinoma on subsequent surgical excision
- 18.6% of pts with FEA and atypical hyperplasia on core biopsy had carcinoma on surgical excision
- 0% of those with pure FEA on core biopsy who did not have surgical excision developed carcinoma after mean follow-up of 5 years

Uzoara et al. Virchows Arch 2012; 461:419-23
FEA on core biopsy. What is upgrade rate on surgical excision?

- Carolinas Medical Center, 210 pts, 2004-2013
- 7% of pts with pure FEA on core bx (5/73) had invasive carcinoma or DCIS on excision
  - All inv ca T1a, ER positive
  - All DCIS ER positive, low to intermediate grade
- 23% had ADH or lobular neoplasia on excision
- No upgrade in 14 cases where all calcifications removed at biopsy

Calhoun et al. Modern Pathol 2015;28:670-676

FEA on core biopsy. Upgrade rate on surgical excision.

- Isolated FEA without other atypia on CNB has <7% upgrade to low grade CIS on surgical excision, mainly when residual calcifications after biopsy
- May be upgraded to ALH or ADH
- Higher rate of upgrade if FEA combined with ADH, ALH or LCIS

Dialani V et al. Breast J 2014

FEA on core biopsy. Upgrade rate on surgical excision. Houston Methodist experience

- 71 bx’s in 67 pts with FEA ± ADH on core biopsy
- All underwent surgical excision
- One pt with FEA + ADH had 1.6 mm tubular ca on resection
- No other upgrades
- Supports growing evidence that isolated FEA with removal of most radiographic calcifications can be observed

McCroskey et. al. To be presented at USCAP 2017
Intraductal papillomas without atypia on core biopsy. Do they need to be excised?

- Variable rates of upgrade in surgical excision to malignancy and atypia in published literature
- 0-29% reported upgrade rate to malignancy, average 5.4%

Intraductal papillomas without atypia on core biopsy. Do they need to be excised?

- With larger gauge needles, more of lesion removed
- Consider multidisciplinary approach
- Surgical excision of larger (>1-1.5 cm) lesions, and those with rad-path discordance

Findings on core biopsy. Do these need to be excised?

- Fibroadenomas
- Small radial scars
- Pseudoangiomatous stromal hyperplasia (PASH)
- Columnar cell change/columnar cell hyperplasia
  NO! Unless there is rad-path discordance
Findings on core biopsy
Do these need to be excised? YES!

- Phyllodes tumors
- Fibroepithelial neoplasm/lesion
- Mucocele-like lesions

Epithelial breast lesions - Relative risk of developing invasive breast cancer

<table>
<thead>
<tr>
<th>Relative risk</th>
<th>Proliferative benign breast disease e.g., Usual ductal hyperplasia Sclerosing adenosis</th>
<th>Atypical lobular hyperplasia (ALH)</th>
<th>Atypical ductal hyperplasia (ADH)</th>
<th>Lobular carcinoma in situ (LCIS)</th>
<th>Ductal carcinoma in situ (DCIS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5-2</td>
<td></td>
<td>4-5</td>
<td>4-5</td>
<td>8-10</td>
<td>8-10</td>
</tr>
</tbody>
</table>

Atypical ductal hyperplasia (ADH) on core biopsy. Does it need to be excised?

- Reported range of 0-62% upgrade from ADH on bx to DCIS + on surgical excision
- Generally 10-30% upgrade rate (18-25%)
- General consensus to excise
ADH on core biopsy. Does it need to be excised? MDACC study

- ADH without significant cytologic atypia and necrosis, and with removal of >95% targeted calcifications:
- Less than 3% risk of carcinoma in surgical excision
- Authors conclude can consider observation with mammographic follow-up for these low risk ADH


Atypical lobular hyperplasia (ALH) and LCIS on core biopsy. Do they need to be excised?

- No consensus
- Variable published data on upgrade rates, 0-67%
- UCLA: 9% for ALH, 28% for LCIS (Mooney et al. Modern Pathol 2016; 29:1471-84)
- Lower % in other studies
- Shift away from surgery in many centers

ALH/LCIS on core biopsy. Do they need to be excised? HMH multidisciplinary consensus

Surgical excision recommended for:
- Pleomorphic LCIS
- LCIS with central comedo necrosis
- LCIS variants, grade 2
- Extensive LCIS
- Rad-path discordance
What are optimal margins for DCIS treated with breast-conserving therapy?

- Breast conserving therapy (BCT) defined as surgical excision of the primary tumor with negative margins followed by whole breast irradiation (WBRT)
- Long-term cancer-specific survival rates >95% for pts with DCIS treated with BCT and WBRT
- WBRT after surgery does not improve survival
- WBRT after surgery reduces rate of ipsilateral breast tumor recurrence

What is a negative margin for DCIS treated with breast-conserving therapy?

- No consensus
- No tumor on the ink – in 3 early randomized trials, including NSABP B-17 and B-24
- Retrospective studies suggested that >1 cm margins may elim. need for WBRT, so are larger margins better for pts receiving WBRT?
What are optimal margins for DCIS treated with breast-conserving therapy?

- Up to 1 in 3 women with DCIS attempting breast conserving therapy undergo re-excision
- Downsides of re-excision: cost, time, stress
  - worse cosmetic outcome
  - potential for surgical complications
  - conversion to mastectomy
  - conversion to bilateral mastectomy

What are optimal margins for DCIS treated with breast-conserving therapy?

- Multidisciplinary panel convened by Society of Surgical Oncology (SSO)
  - American Society of Radiation Oncology (ASTRO)
  - American Society of Clinical Oncology (ASCO)
- Monica Morrow, Jay Harris, Stuart Schnitt et al
- Primary question: What margin minimizes ipsilateral breast tumor recurrence in patients with DCIS receiving breast conserving therapy?
- Meta-analysis of 20 studies

SSO-ASTRO-ASCO Guideline Recommendations for BCT for DCIS

- Positive margin, defined as ink on DCIS, associated with significant increase in ipsilateral breast tumor recurrence (IBTR)
  - Increased risk not nullified by use of whole breast radiation therapy (WBRT)
- Margins of at least 2 mm associated with reduced risk of IBTR in patients receiving WBRT
- No evidence to support negative margins > 2mm

SSO-ASTRO-ASCO Guideline
Recommendations for BCT for DCIS

- Treatment with excision alone, regardless of margin width, associated with substantially higher rates of IBTR than treatment with excision and WBRT, even in predefined low risk patients
- Insufficient evidence to address optimal margin widths for accelerated partial breast irradiation
- DCIS with microinvasion – defined as no invasive focus > 1 mm: should be considered as DCIS when considering optimal width


DCIS in the prescreening era

- Presented as large palpable mass or abnormal nipple discharge
- Often high grade with comedo necrosis
- DCIS first described in 1934 by Dr. Joseph Bloodgood, surgeon, former resident of Halsted, as precancerous tissue

DCIS in the screening era

- With introduction of widespread mammography in 1980’s, DCIS now detected mainly through mammographic screening
- Detection and incidence of DCIS have increased dramatically
- Estimated 61,000 new cases of mammary CIS in US in 2016
- Overall excellent 10 year survival rates
NIH State of the Science Conference Statement: Dx and Management of DCIS

• Convened by NIH and NCI in 2009
• Natural history of DCIS not well understood
• How does outcome vary based on pt and tumor characteristics?
• What is impact of Rx on outcome in DCIS?

Should we remove the word carcinoma from ductal carcinoma in situ (DCIS)?

“Because of the noninvasive nature of DCIS, coupled with its favorable prognosis, strong consideration should be given to remove the anxiety-producing term "carcinoma" from the description of DCIS.”

“DCIS is by definition not invasive—a classic hallmark of cancer.”

JNCI 2010; 102:161-9

Should we remove the word carcinoma from ductal carcinoma in situ (DCIS)?

... future research must focus on the accurate identification of patient subsets diagnosed with DCIS, including those persons who may be managed with less therapeutic intervention without sacrificing the excellent outcomes presently achieved.

JNCI 2010; 102:161-9
### Cancer overdiagnosis and overtreatment

- In 2012, NCI convened a meeting to assess problem of cancer overdiagnosis.
- Overdiagnosis occurs when a tumor that would otherwise not become symptomatic are identified and treated.
- When overdiagnosis not recognized, can lead to overtreatment.

### Do we overdiagnosis and overtreat cancer?

Cancer encompasses range of disorders:
- From those that always lethal if left untreated (or even if treated).
- To indolent lesions with very low potential for progression, metastasis and death.

When patients hear the word cancer, most assume they have a disease that will progress, metastasize and cause death.

Many physicians and other health care providers think the same.

### Removing the word “cancer” for low risk lesions

- Disease-based screening contributes to cancer overdiagnosis which may lead to overtreatment.
- Group of participants at the 2012 NCI meeting proposed use of term: *indolent lesion of epithelial origin* or IDLE.

Removing the word “cancer” for low risk lesions

• Molecular markers have identified group of pts with DCIS with low risk of developing invasive carcinoma
• Lowest grade DCIS has risk for invasive cancer at 10 years similar to those with atypia
• Removal of word carcinoma from dx of low grade lesions and use of IDLE term (eg atypical lesion) will encourage adoption of new approaches to management


Breast cancer mortality after diagnosis of DCIS

Narod et al. JAMA Oncol 2015:1(7):888-896
• Observational study of SEER 18 database (covers 28% of US population)
• 108,196 women diagnosed with DCIS, 1988-2011
• Women > 70 years of age excluded
• Breast cancer-specific mortality at 10 years = 1.1%
• Breast cancer-specific mortality at 20 years = 3.3%

• Higher mortality for women diagnosed before age 35 (7.8% vs 3.2% for older women, HR 2.58)
• Higher mortality for African-Americans (7.0 vs 3.0% for nonHispanic whites, HR 2.55)
• Significantly higher mortality after ipsilateral invasive breast ca (HR 18.1)

Narod et al. JAMA Oncol 2015:1(7):888-896
Breast cancer mortality after diagnosis of DCIS

- Mastectomy and radiation Rx after lumpectomy reduced risk of ipsilateral invasive recurrence, but did not reduce breast cancer-specific mortality at 10 years
- No significant difference in survival for mastectomy vs lumpectomy, after adjusting for tumor size, grade, and other factors

Narod et al. JAMA Oncol 2015:1(7):888-896

Breast cancer mortality after diagnosis of DCIS

- 54% (517 pts) of those who died of breast cancer after diagnosis of DCIS did not “experience” an in-breast invasive cancer prior to death
- No central pathology review
- Missed invasive cancer after central pathology review of DCIS ranges from 2-6%
- Sampling, interpretation

Narod et al. JAMA Oncol 2015:1(7):888-896

50 year old woman with outside dx of DCIS

- ...
Invasive ductal carcinoma mimicking DCIS

Breast cancer mortality after diagnosis of DCIS

- Often stated that DCIS is a pre-invasive neoplastic lesion that not lethal in itself
- Authors conclude that results of their study suggest revisit of this interpretation
- Conclusions: “Some cases of DCIS have an inherent potential for distant metastatic spread. It is therefore appropriate to consider these as de facto breast cancers and not as preinvasive markers predictive of a subsequent invasive cancer.”
  Narod et al. JAMA Oncol 2015:1(7):888-896

Breast cancer mortality after diagnosis of DCIS

- Less than 1% of pts died in the 20 year study
- 3.3% calculated breast ca-specific mortality at 20 years similar to Am Cancer Society statistic of chance average woman will die of breast cancer
- Therefore we should rethink our strategy for detection and treatment of DCIS
Rethinking the standard for treatment of DCIS

• Much of DCIS should be considered as risk factor for invasive breast cancer
• Should not routinely offer radiation therapy after lumpectomy for DCIS that not high risk because does not affect mortality
• Low and intermediate grade DCIS do not need to be a target for screening or early detection

Esserman L, Yau C. JAMA Oncol 2015:1(7):881-3

Rethinking the standard for treatment of DCIS

• Reassess whether clustered amorphous calcifications should be a target for screening and biopsy, especially in older women

Esserman L, Yau C. JAMA Oncol 2015:1(7):881-3

Rethinking the standard for treatment of DCIS

• Should focus on pleomorphic, linear calcifications that more often associated with invasive ca, ER/PR negative DCIS or HER2 positive DCIS

Esserman L, Yau C. JAMA Oncol 2015:1(7):881-3
Rethinking the standard for treatment of DCIS

- Need to better understand biologic characteristics of highest risk DCIS (large, high grade, ER/PR neg, HER2 positive), especially in young and African American women
- Need to develop targeted approaches to reduce death from breast cancer in those with highest risk DCIS

Esserman, Yau. JAMA Oncol 2015:1(7):881-3

Do we need to change the standard treatment of DCIS?

- Surgery vs Active Monitoring for Low-Risk DCIS (LORIS) trial: studying safety of monitoring low risk DCIS dx’d on core biopsy without excision
- Retrospective study of pts meeting LORIS trial eligibility who had surgical excision of bx-diagnosed non-high grade DCIS
- 20% had invasive carcinoma at excision. Path findings influenced adjuvant radiation, endocrine and chemotherapy; and prognosis


Do we need to change the standard treatment of DCIS?

- Observation for DCIS not ready for prime time outside of clinical trials
- Surgery for DCIS diagnosed on core biopsy warranted until additional risk stratification available to identify low risk cohort of DCIS pts
- Multigene expression assays being evaluated for risk stratification (e.g., Oncotype Dx for DCIS)
Stage at diagnosis, invasive breast cancer in women, in US, 2006-2012

5 year survival for breast ca, US, 2006-12

Breast cancer incidence and mortality rates 1975-2012
Breast cancer mortality rates, 1930-2015

Breast cancer mortality rates over time

Controversies about breast cancer screening

- Is the decreased mortality in breast cancer due to screening or to better therapy for breast cancer?
- SEER data: Large tumors (>2cm) decreased from 64 to 32% after advent screening mammography, but mainly due to increasing detection of small tumors (Welch et al. NEJM 2016 Oct 13;375:148-47)
Breast cancer screening

Controversies about breast cancer screening

• When to start screening?
• Screening interval? Annual? Biennial?
• When or if to stop screening
• What are the benefits of screening?

Potential harms:
• False positives
• Overdiagnosis – detecting cancers that if left undetected would not be clinically apparent or cause death
• Overtreatment
Breast cancer screening: False positives

- Most common false positive in screening: Recall for additional imaging for abnormality that subsequently determined to be benign/not atypical
- Probability of false positive in screening related to the model used to calculate the rate, age when screening initiated, screening interval

Breast cancer screening: False positives

- If screening initiated at age 40, unadjusted cumulative probability of at least 1 false positive recall after 10 years of screening:
  - 61.3% with annual screening
  - 41.6% with biennial screening
- 10 year cumulative probability of FP positive mammogram leading to bx recommendation:
  - 7.0% with annual screening
  - 4.8% with biennial screening


Breast cancer screening: False positives

Harms of false positives of screening:
- Patient stress, anxiety
- Cost of additional imaging
- “Invasive” biopsies which may be recommended
- Biopsy-related costs
Screening based on assumption that cancer has an orderly and gradual progression

Model of cancer progression: variable progression on the basis of biology, tumor type

Cancer screening

- For tumors that develop slowly, but likely to progress if unchecked, early detection most likely to be of benefit
  e.g., removal of cervical SIL, colonic adenomas→ decreased incidence of cervical and colon cancer
- For tumors that develop rapidly or spread early, screening less likely to improve outcome
Cancer screening

• “Screening undoubtedly detects indolent disease, best exemplified in prostate cancer, breast cancer and even lung cancer.”

• Detection of indolent disease mainly due to inherent tendency of screening tests to preferentially detect slower growing cancers

• More rapidly growing cancers more likely to present between screens


Breast cancer screening
Comparison of recommendations

<table>
<thead>
<tr>
<th>Recommended</th>
<th>ACOG</th>
<th>ACR/BR</th>
<th>ACS</th>
<th>ANA</th>
<th>NCCN</th>
<th>WPATH</th>
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</thead>
<tbody>
<tr>
<td>Age to Start Mammograms</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>Age to Stop Mammograms</td>
<td>Annual as long as woman in good health</td>
<td>When life expectancy &lt;10 years</td>
<td>When life expectancy &lt;10 years</td>
<td>When life expectancy &lt;10 years</td>
<td>When life expectancy &lt;10 years</td>
<td>Upper age first not established</td>
</tr>
</tbody>
</table>

American Cancer Society 2015 guidelines for breast cancer screening

• Strong recommendation: Women at average risk should undergo regular mammography screening starting at age 45 years

Qualified recommendations:

• Annual screening for women 45-54 years of age

• Women ≥55 years of age should transition to biennial screening or continue annual screening

• Women ages 40-44 years should have opportunity to begin annual screening
US Preventative Services Task Force (USPSTF) guidelines

- Recommend biennial screening mammography for women ages 50-74 years (grade B rec, moderate certainty of moderate net benefit)
- Women 40-49 years, screening individual choice for those who place higher value on potential benefits than potential harms (grade C recommendation, moderate certainty of benefit, but magnitude of benefit small)
- Women >75 years (grade I recommendation, evidence insufficient to assess balance of benefits and harms of screening)

Issues with decreased screening recommendations

- Focus on mortality which in breast cancer only part of the story
- Early detection can save lives
- Quality of life issues
- Early detection can mean less drastic surgery and no chemotherapy
- Early detection can find lesions amenable to chemoprevention, e.g., ALH, ADH, which can lead to decreased risk of developing carcinoma
- Many patients under the age of 50 with breast ca

Breast cancer screening

From the American Cancer Society, 2016:

“The updated ACS guideline affirms that screening mammography is the most effective way for a woman to reduce her likelihood of dying prematurely from breast cancer.”

Breast Cancer Screening

MammographySavesLives™
...one of them may be yours

Pathologists Save Lives