Current Guidelines and Controversies Associated with Breast and Cervical Cancer Screening
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Presentation Objectives
By the end of this presentation the participant will be able to demonstrate the following knowledge and/or skills:
1. Demonstrate knowledge of current evidence-based clinical guidelines and recommendations for breast and cervical cancer screening and current recommendations for HPV vaccination
2. Describe the current recommended techniques for obtaining an adequate cervical cytology specimen.
3. Examine the efficacy of the various screening methods used in breast and cervical cancer screening.
4. Analyze the benefits and harms associated with current screening recommendations.
5. Describe disparate outcomes for specific population groups with respect to access to screening and treatment.

Cervical Cancer Screening: Guidelines & Controversies

What causes cervical cancer?
hrHPV infection causes 95-100% of all cervical cancers.
- Of the 150 HPV variants, 40 are known sexually transmitted HPV types; approximately 15 are established as the most oncogenic (or high risk).
- 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 68, 73, & 82
- 70-80% caused by HPV 16 and 18
- 10% caused by HPV 31 and 45
- 90-100% of genital warts are caused by Types 6 and 11

About 25% of U.S. women test positive for one or more strains of HPV.
HPV is the most common STI worldwide according to WHO (2015).

What causes cervical cancer?
Although HPV is an STI, it can be spread by skin-to-skin contact without intercourse.
Highest prevalence of HPV is in women < 25 years with rapid decrease following due to higher use of condoms and diminished exposure.
80-90% of hrHPV infections are transient, usually becoming undetectable in 1 to 2 years. Only a small fraction of women infected will develop significant cervical abnormalities and cancer.
A persistent hrHPV infection is the most significant risk factor for development of cervical cancer.
Risk Factors Associated with Acquiring HPV

- Early age at first intercourse, especially < 16 years old or within 1 year of menarche
- Multiple partners or a partner with multiple partners
- Smoking as well as secondhand smoke (to a lesser extent)
- Immunosuppression, e.g., woman with HIV or an organ transplant recipient
- Oral Contraceptives
- High parity
- Genetic predisposition
- Poverty
- Infectious agents

Progression

- Latency is measured in years or decades
  - 12-month risk of CIN3 developing from cytology negative, HPV-positive result is 0.8-4.1%
  - Cervical cancer occurs a median of 15-25 years after HPV infection
- For carcinoma in situ:
  - 30-70% will develop invasive carcinoma over a period of 10-12 years
  - 10%, however, will progress to invasive in < 1 year
- Women treated in the past for CIN2 or higher are at risk for persistent or recurrent disease for at least 20 years after treatment.
  - 3-fold increased risk of invasive ca for 20 years post-treatment.

Cervical Cancer Incidence

Global - 2nd most common female malignancy in terms of incidence and mortality (2016)

U.S. - 14th among all female cancers (2014)

- >50% decrease of cervical cancer over past 30 years, mainly due to enhanced screening; mortality lowered from 5.55 to 2.3/100,000.
- Most cases occur in women either never or inadequately screened.
- In males, 8.3/100,000 oropharyngeal cancer/year diagnosed; 65% associated with HPV 16 or 18; Risk of anal cancer is 17 times higher in active gay and bisexual men

Women treated for precursor lesions have a 5-year survival rate of nearly 100%.

U.S. Racial and Ethnic Cervical Cancer Incidence

New cases diagnosed by race/ethnicity (CDC 2011-2015):

- Blacks (not Hispanic) 8.4/100,000
- Hispanics 9.1/100,000
- Whites 7.0/100,000
- Asian/Pacific Islanders 5.8/100,000
- American Indian/Alaska Natives 6.2/100,000

Healthy People 2020 Goals and Markers

Cervical Cancer Screening Target: 93.0% of eligible persons

- In 2015: 81.2%
- Groups with lowest screening percentages:
  - Hispanic/Latino, uninsured, older age groups, lower education, lower income, single w/o children, country of birth outside of U.S.

Cervical Cancer Death Target: 2.2/100,000

- In 2016, states not yet achieving this goal with higher poverty and higher underserved populations:
  - AL, MS, TN, SC, GA, FL, TX, OK, AR, TX, NM
- In 2016, by race/ethnicity not yet achieving this goal:
  - Blacks not Hispanic or Latino 3.2
  - Hispanic or Latino Black 2.7

Cervical Cancer: Primary Prevention
Cervical Cancer Primary Prevention

HPV2 (Merck 2009) & Cervarix (GSK 2009) - protected against HPV 16 & 18
Gardasil (Merck 2006) - protected against HPV 6, 11, 16, & 18 and genital warts

- No longer distributed in the US
Gardasil 9 (Merck 2014) protects against HPV types:
  - 6, 11, 16, 18, 31, 33, 45, 52, 58
- Essentially 100% effective for HPV 16, & 18
- 96.7% of HPV 31-58 cervical & penile cancers and > 90% genital warts HPV 6 & 11
- Precancer and cancer of the anus, vulva, and vagina

The CDC recommends HPV vaccination for all adolescents at age 11-12 years old.
- It can be started as young as age 9 or as old as age 26.
- Vaccination is recommended even if patient is tested for HPV DNA and it is positive, with an abnormal Pap test, or history of genital warts.
- While HPV vaccination is not recommended in pregnancy, there have been no reports of negative maternal/fetal outcomes associated with the vaccine.
- It can be given while a woman is breastfeeding.

In October 2018, the FDA approved supplemental application for Gardisil 9 to include women and men ages 27-45 years.
Gardisil was 88% effective in a 3.5-year study of 27-45 year-olds, in the prevention of persistent HPV infection, genital warts, vulvar/vaginal/cervical precancerous lesions, and cervical cancer related to HPV types covered by the vaccine.

2 doses if first dose is before 15 years of age
  - 2nd dose is 6-12 months later
- If interval is < 5 months, a third dose is recommended
3 doses if first dose is > 15 years of age
  - 1-2 months between doses 1 and 2
  - 4 months between doses 2 and 3
- If late or miss a dose, do not restart the series, just complete it.

According to the CDC......
If HPV vaccination rates in eligible recipients could be increased to 80% (Healthy People 2020 goal)......
- An additional 53,000 cases of cervical cancer could be prevented during the lifetime of those < 12 years.
- For every year that the vaccination rate does NOT increase, an additional 4,400 women will develop cervical cancer.

BUT......

ONLY 41.9% of females and 28.1% of males in the recommended age group have received all recommended doses. (Reagan-Steiner, et.al)
In 2017 in Kentucky, only 38.2% of females age 13-15 had received 2 of 3 recommended doses. (HealthyPeople.gov)
NPs & CNMs - we still have much work to do!
Cervical Cancer Screening: Recommendations

2018 USPSTF Recommendations for Average-Risk Women (August 2018)

<table>
<thead>
<tr>
<th>Population</th>
<th>Recommendations</th>
<th>Recommendation Grade</th>
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<tbody>
<tr>
<td>Women aged &lt; 21 years</td>
<td>No screening</td>
<td>D</td>
</tr>
<tr>
<td>Women aged 21-29 years</td>
<td>Cervical cytology alone every 3 years</td>
<td>A</td>
</tr>
<tr>
<td>Women aged 30-65 years</td>
<td>Cervical cytology alone every 3 years OR hrHPV testing alone every 5 years OR Co-testing every 5 years (Pap+hrHPV)</td>
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<td>Women &gt;65 years with adequate screening</td>
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<td>D</td>
</tr>
<tr>
<td>Women w/ hysterectomy and no risk factors</td>
<td>No screening</td>
<td>D</td>
</tr>
</tbody>
</table>

ASCCP Mobile Device


App Store Preview: This app is only available on the App Store for iOS devices.

Cervical Cancer Cytology Screening Methods

- Conventional Slide Method
- Spatula + Cytobrush
- Cytobroom
- Liquid-Based Method: ThinPrep, BD SurePath

So... which is better to use?

**Conventional slide Pap Smear:**
- Same efficacy as liquid-based cytology
- Lower cost

**But...**
- Higher incidence of unsatisfactory specimens
- Unable to test for HPV, gonorrhea, chlamydia
- Although trichomoniasis is noted, it is NOT diagnostic and patient should be receive NAAT or wet prep testing to confirm

In U.S., well over 90% now analyzed by liquid-based cytology
Cytology vs HPV testing
Sensitivity vs Specificity
- HPV test has greater sensitivity for CIN2+ and CIN3+ but has higher risk of false positive for precancer and cancerous changes
  - 5-year interval diminishes the risk of false positive results
- Cytology has greater specificity but lower sensitivity
- A negative HPV test is more reassuring than a negative cytology test due to higher risk of false negative Pap result
- A negative hrHPV test + negative cytology test =
  - Extremely low risk of developing CIN2 or 3 during the next 4-6 years
- One HPV test for primary screening first approved by the FDA in 2014 (cobas HPV Test by Roche)

But...what should I do with an ASC-US result???
With ASC-US (atypical squamous cells of undetermined significance) cytology and a negative HPV test results:
- Very low risk of CIN3 but slightly higher than those with completely normal cytology.
- Recommendation is to have cotesting in 3 years.

You can see why the ASCCP mobile app is so helpful!

ATHENA Study - HPV as first-line screening test
HPV screening with cobas HPV test (Roche Diagnostics), 2014
- Screened for HPV, positive results reflexed to genotyping; if 16 or 18 +, colposcopy performed
- Detected about 50% more CIN3+ compared with cytology
- Lower incidence of CIN3 and cancer at 3-years in women ≥25 years who were hrHPV negative at enrollment
- Cotesting provided minimal increased protection against development of CIN2+ or CIN3+ compared to HPV primary screening
- Doubled the number of colposcopies
  - Mostly attributed to inclusion of women ≥25 years old

hrHPV test for Primary Screening
ACOG Interim Clinical Guidance 2016, Reaffirmed in 2018
- A neg hrHPV test provides greater reassurance of low CIN3+ risk than a neg cytology result.
- Primary screening can be considered as an alternative to current US cytology-based cervical cancer screening methods.
- Positive HPV should be genotyped for HPV 16 & 18; If pos for 16 or 18, perform colposcopy. If neg for 16 or 18, perform cytology.
- Re-screening after a negative primary hrHPV screen should occur no sooner than every 3 years.
- Primary hrHPV screening should not be initiated before 25 years of age.
- Major guidelines still recommend starting at age 30.

HPV Self-Sampling Screening
- Self-sampling - further validation of efficacy is required
  - Method
    - Efficacy depends on device, HPV tests used
    - A number of new devices are being developed
    - Self vs clinician-sampled cobas HPV test (Roche) results were concordant
  - Advantages
    - Self-sampled has better sensitivity than cytology
    - Better patient acceptance
    - Potential to reach underserved persons

Cervical Cancer Screening: Risks, Benefits, and Harms
Risks vs. Benefits of Screening

Risks and harms of overscreening
● 9 of 10 abnormal Pap tests will revert to normal even without treatment
● 90% of HPV infections are resolved by a woman’s immune response
● Increased number of colposcopies and biopsies
● Excessive, unnecessary treatment, (e.g., LEEPs, cold-knife conizations)
● Anxiety and stigma
● Cost to patient and the system
● Risks to reproductive outcomes (i.e., incompetent cervix) from LEEPs, CKCs

Risks, Benefits, and Harms of Screening

Benefits of HPV-only screening
● Detection of hrHPV variants earlier is associated with CIN3+
● Cost of co-testing (cytology + HPV) is higher.
● If HPV self-screening is validated by research and instituted:
  ○ Possible increase population screening for precancer and cancerous changes
  ○ Possible increase in reaching underserved population
  ● Self-screening could be offered in the home as well as sites serving low-income, underserved groups

Balancing Benefits, Risks, and Harms

Take home point is this.....

Co-testing (recommended by most organizations) or hrHPV testing only are currently the preferred screening methods and should be done only every 5 years to diminish risks and harms from overscreening.

Breast Cancer Screening Modalities
● Self Breast Examination
● Clinical Breast Examination
● Mammography
  ○ Film
  ○ Digital (2D)
  ○ Tomosynthesis (3D)
● MRI
● Ultrasound
● Thermography
● BRCA mutation type 1 & 2 genetic testing

Before we start: These decisions are deeply personal.

BR CA risk and more about that “1 in 8” figure....

- 2nd most common cause of cancer death in women = breast
- BR CA accounts for 30% of all new cancer diagnoses in women.
- **Most important risk factors:** being female and getting older.
  - MOST women with a BR CA diagnosis have NO OTHER RISK FACTORS.

1 IN 8 WOMEN **WHO LIVE UNTIL AGE 85** WILL DEVELOP BREAST CANCER (Zahl, et al., 2004)

Average lifespan for women in the U.S. = 81.3 years.
In KY: 78.5 years (Kaiser Foundation)

Who is really “high risk”, clinically?

- Resources often list multiple potential factors that increase risk, but don’t quantify that risk...leading to misunderstandings for women and clinicians (Morère et al., 2018).
- **The sole risk factor in about 85% of women with breast cancer is older age.**
- BR CA mutations significantly increase risk, so referral and screening is important.
- Early life chest radiation increases BR CA risk significantly, and we should ask our patients about childhood and adolescent cancers.
- Personal history of BR CA = most predictive of another BR CA.
- Fibrocystic breasts also increase risk to a small degree.

Higher Risk for BR CA: Modifiable factors

- Obesity post-menopause
- Alcohol consumption
- Sedentary Lifestyle
- Poor Diet

**If ALL of these factors could be changed, we’d eliminate about 45% of breast cancers in the U.S.**

- Smoking: depends on the study; findings are mixed.
- Risk factors may be additive or multiplicative.

(Morère et al., 2018)

Factors that INCREASE relative risk to at > 4.0

- Ionizing radiation exposure before age 30 (RR 22-40)
- Ductal or lobular carcinoma in situ (RR = 8 - 10)
- Inherited mutations (RR = 4 to 8)
- Advanced age (65 years +)
- Biopsy-proven atypical BR hyperplasia
- Family hx of early ovarian CA
- MULTIPLE first degree relatives with BR CA
- Personal history of early BR CA (before age 40)

(Katz, 2019)

Factors that REDUCE relative risk to <1.0

- Asian, Hispanic, American Indian or Pacific Islander ethnicity
- Breastfeeding
- Age < 20 at first pregnancy
- Tamoxifen use
- Prior risk-reduction breast surgery (for known genetic mutations)
- History of cervical CA
- History of oophorectomy
- Exercise/Active Lifestyle
- Low bone mineral density

(Katz, 2019)

Breast CA Screening: the Recommendations
A few statements about the obvious (and not so obvious)

1. Breast cancer screening is one approach, and addressing symptoms a woman finds is another.
2. Screening is believed to work because early detection is believed to be key in surviving diseases like cancer. In cervical cancer, that is undoubtedly true:
   - Precursor lesions with a long lead time between HPV changes and invasive cancer.
   - Precursor lesions can be treated, and cancer can be prevented.
3. In the past, early detection of breast cancer was very important. Since 1990, advances in treatment have made early detection less important to survival.

**Breast CA Screening: USPSTF**

- Self Breast Exam: harm outweighs benefit D recommendation: do not recommend
- Clinical Breast Exam: no evidence it adds benefit beyond mammography.
- Mammography: start at age 50 and do q 2 years until 74.
- May start at 40 if desired by patient after counseling, especially if 1st degree relative with Breast CA.

**Breast CA Screening: ACOG**

- May start mammography at age 40, q 1-2 years, or wait until 50 depending on woman’s values. Recommend at 50.
- 50+ screen every 1–2 years (shared decision)
- Continue until age 75, but afterwards it’s a shared decision.
- Clinical breast exam MAY be offered every 1–3 years starting at 40, as part of shared decision making and with information.
- Breast awareness may include self breast exam.

**Breast CA Screening: American Cancer Society**

- May offer mammograms to women 40-44.
- Start mammography at age 45, do annual tests until age 54.
- Women 55+ should have a mammogram every 2 years, continue as long as in good health with 10 year+ life expectancy. May continue annually if desired.
- Clinical Breast Exams and SBE not recommended.
- *All women should be familiar with the known benefits, limitations, and potential harms linked to breast cancer screening.* - ACS

**BR CA 1 & 2 mutation testing**

- These mutations are known to increase risk of breast and ovarian cancer.
- They aren’t the only ones, but the most common. About 5 - 10% of the population carries genetic risks for breast cancer
- Lifetime risk of breast cancer for BRCA1 mutations is 50 - 85%, and 45% for BRCA2
- Women of ALL ethnicities may carry BRCA1 or 2 mutations, not just Ashkenazi Jewish descent (higher prevalence in this population does not mean no prevalence in others)
- Use risk factors to decide whom to offer counseling and screening for BRCA mutations.
  (Monticciolo et al., 2018)

**Risk Assessment Tools**

- Varied in sensitivity/specificity for BR CA incidence or genetic mutations (Panchal et. al., 2008)
- USPSTF app has several point of care options that can be used to determine whether to refer for BRCA counseling & testing
- IBIS has slightly better evidence for calculating overall risk (Monticciolo et al., 2018)
IBIS Risk Assessment Tool (Tyrer-Cuzick)

Online IBIS (http://ibis.ikonopedia.com/) Gives 10-year and lifetime % risk.
Age, BMI, age at menarche
Childbirth, menopause, HRT
BRCA status
Ovarian CA history
Breast Bx history
Family history

Breast CA Screening for NORMAL risk women: the Evidence

Evidence re: Self Breast Exam
- HUGE studies show no benefit in breast CA mortality for routine monthly self-breast exam vs no screening at all, and in fact show harm (n=388,535, 2x the biopsies in the SBE group) (Cochrane database, 2003 & 2008)
- Women normally have lumpy breasts. How do they know what’s concerning? How can we leave it alone once they tell us there’s an issue?
- Formal monthly SBE leads to increased radiology and biopsy, but not better or faster diagnosis of BR CA.
- Yes, most women find their own lumps...but they will find them in the shower or during sex or while getting dressed, too, and not necessarily any slower.

Evidence re: Clinical Breast Exam
- If you perform these, how did you learn them?
- Comprehensive CBE should take about 10 minutes: 5 per breast
  - Sitting and supine.
  - Tail of Spence
  - Don’t squeeze the nipple, but do palpate over it
  - Axillae
- The bottom line: evidence says ineffective. Since professional guidelines disagree, use shared decision making with your client.

Evidence re: Screening Mammography
- Many mammograms need to be done to detect cancer that is in the sweet spot: going to develop into a life-threatening problem, AND early detection makes a difference in survival.
- Many “cancers” detected by mammography were never destined to become a problem for that woman. Overdiagnosis leads to overtreatment, and treatment has side effects.
- 37 million mammograms done annually in the U.S.
- Treatment has improved drastically, making early detection less important to survival.

Not all breast cancers are the same.
For 1000 women screened every 2 years, starting at age 50 & continuing 20 years.

RCT Efficacy of Screening Mammography by Age

Age 40-49: 3 women in 10,000 will not die of breast CA due to annual mammography. 1 of every 2 women will have a false positive result. 249/2000 will have an unnecessary biopsy. No reduction in advanced breast cancer risk.

Age 50-59: 8 breast cancer deaths averted per 10,000 annually screened women. Reduced risk for advanced breast cancer diagnosis (RR 0.62)

Age 60-69: 21 breast CA deaths averted per 10,000 annually screened women.

Screened women die as often as unscreened women, but from other causes. No reduction in overall mortality. (Nelson et al, 2009 & 2016)

Overdiagnosis ≠ False Positive Screening

Overdiagnosis = a real finding, but one that would not result in the death of the patient.
Examples: a cancer that was not going to progress in time to kill someone who was ill with something else, or a carcinoma in situ that was never destined to progress at all (immune system takes it out before invasiveness.)

A 1987 study found that ⅓ of all women aged 40-59 had breast cancer lesions found on autopsy, but actually died of something else! (Jørgensen & Gøtzsche, 2009)

Overdiagnosis and Overtreatment are Invisible.

● Right now we have no good way to determine which low-grade, node-negative “cancers” will become invasive...so we treat them all.

● Based on a 30 year cohort design, from 1978 to 2008, approximately 1 in 4 mammographically diagnosed breast cancers was overdiagnosed – 1.3 million women were diagnosed with a “cancer” that would never have harmed them (Bleyer et al., 2012)

● Women won’t know whether their mammogram-detected “cancer” was destined to progress, or whether it was destined to regress or remain stable.

The cause of excess death in the screened group isn’t yet known....

● Stress?

● Overtreatment? (chemo, radiation, medications)

● Something else? (individual factors? Social factors?)

MOST women don’t know that screening can lead to harm.

● 90% of US citizens in a sample of 300 were unaware that overdiagnosis and unnecessary treatment were an inherent risk of cancer screening.

● In a representative sample of 5000+ women in 9 European countries: 92% overestimated the reduction of breast cancer mortality by mammography 10x - 200x, or did not know how much mammography reduces breast CA mortality risk.

(Wegwarth & Gigerenzer, 2018)
Many clinicians don’t know this, either.

- 412 US primary care physicians (Wegwarth & Gigerenzer, 2018)
  - 47% mistakenly believed that if more cancers are detected, this proves the test saves lives.
  - 76% wrongly thought that if screen-detected cancers have better 5-year survival rates than cancers detected by symptoms, this proves the screening test saves lives.
- **Why not?** Because these numbers don’t account for other variables that affect cancer survival rates. People with health insurance are more likely to be screened, and also are more likely to be able to complete treatment courses. Overdiagnosis and overtreatment make screening look more effective than it really is.

Bottom Line: Screening mammography is an ETHICAL and PERSONAL choice, not a scientific one.

- Capture ALMOST ALL women with BR CA and incur significant costs to quality of life with NO reduction in overall mortality....
- **VS**
  - Missing a FEW women (2/1000) with BR CA that screening mammography would catch early enough to save from dying of BR CA—but **without a significant reduction in overall mortality**.
  - **AND**
  - Later diagnosis causing more intensive treatment need for unscreened group.

Digital Breast Tomosynthesis and Digital Mammography: What’s the Difference?

Digital mammography: 2D, side and front view, where overlapping breast tissue can create challenges in interpretation. ACA covers 100%.

Digital Breast Tomosynthesis: 3D, where “slices” can be separated out. Lower recall rates for unclear findings. Costs more. Insurance coverage varies (Medicare covers, individual insurance may not). Takes a few seconds longer but reduces radiation exposure.

Film Mammography: analog film, used alongside 2D

Digital Breast Tomosynthesis (DBT), Mammography & Dense Breasts

- Women 40 – 49 have denser breasts; digital breast tomosynthesis is more sensitive than 2D mammography and may be more useful. DBT Detects more node-negative, small (<1 cm) invasive cancers than digital mammography (Conent et al., 2019)
- Current evidence suggests **film mammography screening in women 40 – 49 does not reduce BR CA mortality**.
- However, use of digital mammography will also result in more false positives and higher levels of overdiagnosis.

Breast Density: How important is it?

- Not a major risk factor for BR CA.
- No clear criteria for determining who has dense breasts. Radiologists use a 4-level scale but this is qualitative and impressionistic.
- No clinical guidelines recommend additional or different screening on this basis.
- In theory, denser breasts make mammography less accurate. Clinically, it’s uncertain how important this really is.
- Nevertheless, many state legislatures in their woman-protecting ways have mandated reporting. (ACOG, 2018)
Breast Density & State Laws
- Mammographically-dense breasts first mandated to be reported to patients in Connecticut in 2009.
- “ACOG does NOT recommend routine use of alternative or adjunctive tests in women with dense breasts who are asymptomatic and have no additional risk factors” (ACOG, 2018)
- 35 states have passed laws mandating patient notification.
- FDA mandates reporting of breast parenchymal density on the provider report, but not the patient summary.
- Most laws require the facility to report, not the ordering clinician.
- Language used by each state to report to patients varies.

Kentucky BR density language
"Your x-ray mammogram shows that your breast tissue is dense. Dense breast tissue is common among women and is not abnormal. However, women with dense breast tissue may have a slightly increased risk for developing breast cancer. Dense breast tissue may also make it more difficult to detect an early breast cancer on your x-ray mammogram. At this time, there are no specific recommendations for additional screening or other measures related to having dense breast tissue. However, you may want to talk to your doctor about other ways that you might be able to reduce your risk of breast cancer. A report of your results was sent to your ordering physician. If you are self-referred, a report of your results was sent to you in addition to this summary." (ACOG, 2018)

Thermography
- Painless, no radiation. Maps heat & blood flow near the surface of the body.
- FDA warning against its use due to lack of scientific evidence for efficacy. Recently (Feb 2019) reissued.
- Lower sensitivity and specificity than mammography or ultrasound (25% sensitivity, 24% positive predictive value)
- Lots of consumer interest and direct marketing to consumers; marketing includes scare tactics re: the pain and radiation of mammography.

Ultrasound
- Used first-line for DIAGNOSIS in palpated masses for women under 30.
- Used adjunctively in SCREENING to characterize radiologically-identified masses (e.g., solid vs cystic)
- No benefit to routine adjunctive use with mammograms.
- American College of Radiology recommends adjunctively for high risk women who can’t access MRI, and ACOG supports this as well.
- Adding ultrasound to a negative mammogram SIGNIFICANTLY increases likelihood of biopsy (by 5 - 10x), with no significant benefit in CA detection.
- No clear benefit for women with dense breasts.
(Scheel et al., 2015)

MRI: reserve for high-risk individuals
Per the American Cancer Society (2007), do annual breast MRIs for these groups based on evidence:
- BRCA mutation carrier
- First degree relative of a BRCA mutation carrier, untested
- Women with a 20-25% lifetime risk for developing BR CA:
  - Women who were treated for Hodgkin’s disease
  - Women with a strong family history of ovarian or BR CA

Recommend Annual Breast MRI for:
(Expert consensus opinion, ACS, 2007)
- Radiation to chest between age 10 and 30 years
- Li-Fraumeni syndrome (and first-degree relatives)
- Cowden and Bannayan-Riley-Ruvalcaba syndromes (and first-degree relatives)
Insufficient evidence for MRI (ACS, 2007)

- Personal history of BRCA
- Lobular carcinoma in situ (LCIS) or atypical lobular hyperplasia (ALH)
- Atypical ductal hyperplasia (ADH)
- Heterogeneously or extremely dense breast on mammography
- Ductal carcinoma in situ (DCIS)

Health Disparities and Breast Cancer Screening

Health Disparities and BR CA: How should disparate outcomes inform screening?

- Short answer: we don’t know yet.
- Recommendations are mostly based on women of average risk without regard for social determinants of health (race, class, sexual orientation).
- We know that slightly more White women than Black women develop BRCA...yet many more Black women die of the disease (risk of death is 20-40% higher).
- Black women are more likely to develop aggressive tumor types earlier in life.
- The reasons for this disparity are unlikely to be primarily genetic. But remember that Ashkenazi Jewish women aren’t the only ones to have BRCA mutations! (Monticciolo et al., 2018)

Epidemiology of BR CA

White and Black women are most likely to be diagnosed—numbers are evening out currently.

Black women are 2x as likely to have harder-to-treat, more aggressive triple negative (negative for E,P, and Her-2 receptor) tumors.

BRCA mutations higher (10.7% for BRCA1 and 5.7% for BRCA2) in women of African ancestry than in women of European ancestry (6.9% and 5.2%).

22% of Black women with breast CA had inherited mutations. (Monticciolo et al., 2018)

Sgt. Rashida Mahoney

Black women wait longer for treatment** even with early detection.

<table>
<thead>
<tr>
<th>Treatment Type</th>
<th>White Non-Hispanic, 95th%</th>
<th>Black Non-Hispanic, 95th%</th>
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<td>First Treatment</td>
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<tr>
<td>Surgery</td>
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<td>Endocrine Therapy</td>
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* Private insurance reduced wait time by 1.2 days, but disparities persisted.
** These differences probably do not account for survival differences from an oncology standpoint, but point to access issues.
Preliminary Evidence that Epigenetic Changes predate the development of BRCA

- Epigenetic changes are where the environment meets the body.
- Black women experience environmental threats at much higher levels due to where our society locates highways and plants that produce pollution.
- Black women experience high levels of chronic stress from multiple sources, including interpersonal racial discrimination.
- Epigenetic marker changes consistent with the development of differentially aggressive BRCA show up in healthy White and Black women prior to the onset of disease (Song et al., 2015).
- American College of Radiologists is the ONLY organization to recommend risk assessment for Black women by age 30 to determine screening frequency.

As with other health disparities, inherent biological differences are not responsible.

Rather, these biological outcomes result from the differential exposures to environmental toxicants and stress, and differential access to care… and are thus modifiable.
References


