Should the following women be screened for breast cancer? If so, how?

• Ms. Smith is a 45 year old Caucasian woman with no children

• Mrs. Jones is a 78 Hispanic woman and has type 2 diabetes mellitus

• Mrs. Williams is a 35 year old Black woman with 2 first degree relatives who died of breast cancer. She has had 2 children and had menarche at age 14. She has no history of breast biopsies.
The Controversy

- Routinely after age 40, or routinely after age 50?
- At what age to stop screening?
- For the first question, the issue is differences of opinion regarding the risks and harms of screening
- For the second question, the issue is lack of data
- Self breast exam no longer recommended

USPSTF Breast Cancer Screening 2009

- The US Preventive Services Task Force (USPSTF) recommends against routine screening mammography between the ages of 40 and 49 years (Grade C recommendation).
- They continue to recommend screening every other year between the ages of 50 and 74 years (Grade B)
- They also recommend against teaching breast self-examination (Grade D)
- "Insufficient evidence" rating (Grade I) to clinical breast examining, digital mammography, and magnetic resonance imaging.
- These guidelines are more in step with recommendations in other countries. In the United States, the American College of Physicians is the only other group that does not recommend screening mammography in women younger than 50 years.
Let’s Review the Evidence

Small Benefit For Most Women: Meta-analysis

- This meta-analysis was conducted to support the new guidelines from the USPSTF
- Based on 8 fair to good quality studies of women between the ages of 40 years and 49 years, yearly screening mammography will result in a 15% relative risk reduction in death due to breast cancer (CrI = 4%-25%)
- Absolute benefit is small: absolute risk reduction of 0.025%.
- Number needed to screen annually (NNS): 1904 women (CrI = 929 - 6378) women screened yearly for 10 years to prevent 1 from dying of breast cancer.
- 50 to 69 years: NNS is 1339 for 10 years to prevent one death from breast cancer
- 60 to 69: NNS is 377 for 10 years to prevent one death from breast cancer
- Only one study included patients older than 70 years, and no studies have evaluated mammography screening in women older than 74 years
- No research has shown a decrease in all-cause mortality as the result of mammography screening
- Self breast exam is ineffective (from two large RCTs)

Mammography and Over-Diagnosis

- Approximately 1/3 of women between the ages of 40 years and 54 years who die from other causes will have breast cancer found on autopsy (Br J Cancer 1987;56:814-9).
- Researchers calculated the expected cancer rates in screened and unscreened women after screening began.
- Data were compiled from 6 countries that have national screening programs and the before-after data needed for this analysis.
- Approximately 1 in 3 women were “over-diagnosed.”
- For every 1000 women older than 50 years who are screened for breast cancer annually for 10 years:
  - 1 woman will avoid dying from breast cancer.
  - 2 to 10 women will be over-diagnosed and treated with no benefit.
  - 10 to 15 women will be told they have breast cancer earlier than they would otherwise have been told, but this will not affect their prognosis.
  - 100 to 500 women will have at least one “false alarm” and approximately half these women will undergo a biopsy (Welch HG. Overdiagnosis and mammography screening. BMJ 2009;339:b1425).

Breast Cancer Mortality Reduction: Is it due to Screening or Treatment?

- Norway rolled out its mammography program systematically by county over a 9-year period, creating groups that were and were not screened.
- They have good data on mortality from breast cancer dating back to the 1980s.
- Incidence-based mortality (how many women per 100,000 die of breast cancer in a given year) is a much more valid measure of benefit than 5-year survival, which is heavily biased by overdiagnosis and overtreatment.
- Authors compared counties with and without screening during the years that it was implemented (1996 - 2005) and then compared women in these counties with women in the same counties 10 years earlier, when no one was being screened.
- Compared with the same counties 10 years earlier, they found that the rate of death was reduced by 7.2/100,000 in the screened counties and 4.8/100,000 in the unscreened counties.
- The reduction in mortality that can be attributed to screening was 2.4 deaths per 100,000 person-years, or 2.4 deaths/10,000 women screened for 10 years.

Breast Cancer Screening with Other Imaging Modalities

• The primary role of ultrasound is the evaluation of palpable or mammographically identified masses.

• A review of the literature and expert opinion by the European Group for Breast Cancer Screening concluded that there is little evidence to support the use of ultrasound in population breast cancer screening at any age.

MRI and Breast Cancer Screening (NCI)

- Direct back-to-back comparisons of breast MRI and mammography in young high-risk women report MRI sensitivities ranging from 71% to 100% versus mammography sensitivities of 20% to 50%. The low sensitivities of mammography are consistent with previous experience in young women and those with dense breasts.
- These same studies show that MRI is also associated with threefold to fivefold higher recall rates, higher false-positive rates (with specificities varying from 37%–97%), and substantially worse positive predictive value. Thus, women who are screened with MRI have more negative surgical biopsies.
- It is unknown whether the increase in cancer detection confers a mortality benefit given the large increase in false-positive rates, and overdiagnosis.
- All of the published studies are observational studies, and none of the published studies have assessed whether patient outcomes (including morbidity, survival, or mortality) are improved when women are screened with breast MRI.
- Studies of screening MRI in women of high genetic risk are ongoing


MRI recommendations of the ACS

- Women at high risk (greater than 20% lifetime risk) should get an MRI and a mammogram every year. Women at moderately increased risk (15% to 20% lifetime risk) should talk with their doctors about the benefits and limitations of adding MRI screening to their yearly mammogram. Yearly MRI screening is not recommended for women whose lifetime risk of breast cancer is less than 15%.
- Women at high risk include those who:
  - Have a known BRCA1 or BRCA2 gene mutation
  - Have a first-degree relative (parent, brother, sister, or child) with a BRCA1 or BRCA2 gene mutation, but have not had genetic testing themselves
  - Have a lifetime risk of breast cancer of 20% to 25% or greater, according to risk assessment tools that are based mainly on family history (such as the Claus model - see below)
  - Had radiation therapy to the chest when they were between the ages of 10 and 30 years
  - Have Li-Fraumeni syndrome, Cowden syndrome, or Bannayan-Riley-Ruvalcaba syndrome, or have first-degree relatives with one of these syndromes
- Women at moderately increased risk include those who:
  - Have a lifetime risk of breast cancer of 15% to 20%, according to risk assessment tools that are based mainly on family history
  - Have a personal history of breast cancer, ductal carcinoma in situ (DCIS), lobular carcinoma in situ (LCIS), atypical ductal hyperplasia (ADH), or atypical lobular hyperplasia (ALH)
  - Have extremely dense breasts or unevenly dense breasts when viewed by mammograms
ACS MRI Recommendations

• If MRI is used, it should be in addition to, not instead of, a screening mammogram. This is because while an MRI is a more sensitive test (it's more likely to detect cancer than a mammogram), it may still miss some cancers that a mammogram would detect.

• For most women at high risk, screening with MRI and mammograms should begin at age 30 years and continue for as long as a woman is in good health. But because the evidence is limited regarding the best age at which to start screening, this decision should be based on shared decision making between patients and their health care providers, taking into account personal circumstances and preferences.

• Several risk assessment tools, with names like the Gail model, the Claus model, and the Tyrer-Cuzick model, are available to help health professionals estimate a woman's breast cancer risk.

• It is recommended that women who get screening MRI do so at a facility that can do an MRI-guided breast biopsy at the same time if needed.

• There is no evidence right now that MRI will be an effective screening tool for women at average risk because of low specificity.

Gail Risk Model for Breast Cancer

• Named after Mitchell Gail, a biostatistician at NCI

• Provides 5 year risk estimate of developing breast cancer, and estimates up to age 90

• Risk factors included
  – Patient's age
  – Age at menarche
  – Age of first child
  – History of breast biopsies and results
  – First degree relatives with breast cancer
  – Race, ethnicity


• [www.halls.md/breast/riskcom.htm](http://www.halls.md/breast/riskcom.htm)
Back to our cases. . . Who should be screened?

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• Mrs. Jones, who is a 78 Hispanic woman and has type 2 diabetes mellitus

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