1. Truth or Myth: After heart disease, breast cancer is the leading cause of death in women.
Facts

* Breast cancer kills ~40,000 women / year in USA
* Stroke: 96,000 deaths
* Lung cancer: 71,000 deaths
* Lower respiratory disease 67,000 deaths

Health.com
### World: Leading Causes of Death in Females

<table>
<thead>
<tr>
<th>Rank</th>
<th>Cause</th>
<th>000s</th>
<th>%</th>
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<tbody>
<tr>
<td>1</td>
<td>Ischemic Heart Disease</td>
<td>670</td>
<td>14.9</td>
</tr>
<tr>
<td>2</td>
<td>Stroke</td>
<td>461</td>
<td>10.2</td>
</tr>
<tr>
<td>3</td>
<td>Alzheimer /other dementia</td>
<td>260</td>
<td>5.8</td>
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<tr>
<td>4</td>
<td>Lower Respiratory infections</td>
<td>183</td>
<td>4.1</td>
</tr>
<tr>
<td>5</td>
<td>Lung , Tracheal, Bronchial CA</td>
<td>182</td>
<td>4.0</td>
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<tr>
<td>6</td>
<td>Breast CA</td>
<td>173</td>
<td>3.8</td>
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<tr>
<td>7</td>
<td>Colorectal CA</td>
<td>141</td>
<td>3.1</td>
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<td>8</td>
<td>COPD</td>
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<tr>
<td>9</td>
<td>Hypertensive Heart Disease</td>
<td>128</td>
<td>2.8</td>
</tr>
<tr>
<td>10</td>
<td>Diabetes</td>
<td>126</td>
<td>2.8</td>
</tr>
</tbody>
</table>

WHO, 2008, High Income Countries
2. Truth or Myth: Only women with a family history are at risk of breast cancer?
Biological Risk factors for Breast Cancer

* Current Age 65 or older: RR 5.8
* Age at first child <20: RR 1.7-1.9
* Late menopause >55: RR 1.3

Singletary, Ann Surg 2003
Risk Factors: Biopsy Results

* Ductal hyperplasia of usual type: RR 1.9
* Atypical ductal hyperplasia (ADH): RR 5.3
* ADH with family history: RR 11
* LCIS: RR 16.4
Lifestyle risk factors for breast cancer

* Alcohol intake (2 drinks per day): RR 1.2
* Alcohol intake (3 drinks per day): RR 1.4
* Elevated BMI (older than 55): RR 1.2-1.5
* HRT with estrogen and progesterone: (current user for >=5 years) RR 1.3
* Radiation exposure (Hodgkin/fluoroscopy) RR 1.6
* Antibiotic Usage RR 1.4-2.1
* Indeterminate: exposure ethylene oxide, shift work, mechanics (petroleum solvents)

* Singletary, Ann of Surg, 2003
* World Cancer Research Fund, AJCR 2007
* Weiderpass Saf Health Work, 2011
* Velicer, Jama 2004
<table>
<thead>
<tr>
<th>Antibiotic Usage</th>
<th>HR (CI)</th>
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<tbody>
<tr>
<td>No Antibiotic use</td>
<td>1.0</td>
</tr>
<tr>
<td>1-50 days</td>
<td>1.45 (1.24-1.69)</td>
</tr>
<tr>
<td>51-100 days</td>
<td>1.53 (1.28-1.83)</td>
</tr>
<tr>
<td>101-500 days</td>
<td>1.68 (1.42-2.00)</td>
</tr>
<tr>
<td>501-1000 days</td>
<td>2.14 (1.60-2.88)</td>
</tr>
<tr>
<td>&gt; 1000 days</td>
<td>2.07 (1.48-2.89)</td>
</tr>
</tbody>
</table>
3. Truth or Myth: Exposing tumor to air can cause cancer to spread?
Myth

* VA hospital study of patient with lung cancer or pulmonary disease
  * 45% patients had heard of this myth
  * 37% patients believed it to be true
Why people might think this

- Patients might feel worse after surgery
- Surgeon might find more cancer than what was expected from preoperative imaging
- The cancer was already there
4. Truth or Myth: Antiperspirants increase the risk for breast cancer
Mixed
Antiperspirants block the release of toxins when you sweat and toxins build up within breast

**WRONG BECAUSE**

- **Even the strongest antiperspirant doesn’t block the perspiration under your arm**
- **Most cancer causing substances are excreted by the kidney into the urine**
Truths: Aluminum Salts

- Aluminum Salts (Eur J. Cancer Prevention, 2004)
  - 437 women with breast cancer surveyed
  - Frequent and early onset of deodorant usage with underarm shaving → Associated with earlier age of breast cancer diagnosis
    - Hypothesis: Enhanced absorption of aluminum salts with dermal barrier disruption

- Nipple fluid (Mannello, J App Tox, 2011)
  - 19 women with breast cancer had higher aluminum concentration (268) in nipple fluid versus 16 women without breast cancer (131).
    - Hypothesis: Exposure to antiperspirant salts
Truths: Parabens

- Parabens (Barr, Lester J Applied Toxicology)
  - Parabens prevent growth of microorganism in cosmetics/shampoo
  - Have estrogen-like effects
  - 99% of 160 tissue samples from 40 mastectomies found paraben esters
    - 7/40 women never used deodorant with parabens

- NO CLEAR CAUSE AND EFFECT OF UNDERARM PRODUCTS AND CANCER
5. Truth or Myth: You can’t get breast cancer after a mastectomy
Facts: Recurrence after a mastectomy

* 5-10% of patients undergoing mastectomy for breast cancer will have a chest wall or regional nodal recurrence within 10 years

* Recurrence with mastectomies tend to be earlier (2-3 years) versus 3-4 years with breast conserving therapy

* Up to one third of patients with local recurrence have no evidence of distant disease and can be rendered disease free with local and/or systemic therapy... SO BE AGGRESSIVE IF IT OCCURS

Hirsch et al, Up-to-date, Jan 2013
6. Truth or Myth: If I am at risk for breast cancer there is little to do but wait for it to happen
Breast Cancer Prevention: Lifestyle Modifications

- Exercise > 4 hours /week: May decrease breast cancer by 30-40% (may be greatest benefit for premenopausal, norm to low body wt

- Early pregnancy (<20 years old): 50% decrease in breast cancer vs nulliparous or birth > 35

- Breast feeding: Decrease risk 4.3% for every 12 months of breast feeding, in addition to 7% for each extra birth

- Vitamin D: Levels above 40 ng/ml were associated with decreased cancer risk
  - OR .56 (CI 0.41-0.78)

NCI PDQ, 2/2013
Crew K, Cancer Prevention Research 2009
Exercise Study at Penn State
Breast Cancer Prevention: Medications

* SERM
  * Tamoxifen: Decreases risk of invasive and non-invasive breast cancer by 50% for pre and post menopausal women
  * Evista: Decreases invasive risk by 50%. Not as helpful for non-invasive breast cancer
    * Side effects may be less

* Aromatase inhibitor
  * Exemestene: HR .35
    * Absolute risk reduction 21 cancers avoided for every 2380 participants.

NCI-PDQ, 2/2013
Zhang, Am J Health- Sys Pharm, 2012
Breast Cancer Prevention: Prophylactic Surgery

* Oophorectomies or ablation: 50% risk reduction
* Prophylactic Mastectomies: Over 90% risk reduction
It is not your mother’s mastectomy
Today: Skin Sparing Incisions May Be Possible

- Lateral extension can increase axillary exposure
- Wise pattern
- Incision when biopsy site near areola
- Incision when biopsy site remote from areola with axillary incision for lymphadenectomy
Skin Sparing: Tissue Removed
Skin Sparing Mastectomy: Technique
Raising thin flaps

Skin Sparing Mastectomy: Technique
Nipple Sparing Mastectomy
Nipple sparing (Right) versus Skin Sparing (Left) Mastectomies
"Breast implants?! There must be some mistake, I have you down for knee surgery not breast implants!"
7. Truth or Myth: Mastectomy provides better survival than a lumpectomy with radiation?
Truth: Survival after Mastectomy

* NSABP trial showed equivalent survival rates for mastectomy versus lumpectomy with radiation

* European trial showed equivalent survival rates for mastectomy versus lumpectomy with radiation (van Dongen, J Natl Canc Inst, 2000)
Survival may be improved with lumpectomy and RT

- Hwang et al, Cancer 2012
- 112,154 women with T1 or T2 Stage 1 or 2 breast cancer between 1990 and 2004. Median follow-up 10 years.
- Lumpectomy with RT compared with Mastectomy patients for OS and DSS
BCT patients (Lumpectomy+RT)

- 28% less likely to die from any cause
- Up to 16% less likely to die from breast cancer
- OS HR .81 95% CI .80-.83
- Death from
  - Chronic respiratory disease HR .46
  - Heart disease HR. 51
  - Cerebrovascular disease HR .64

**CONCLUSION:**
- Breast Conserving therapy (BCT) demonstrated survival benefit over mastectomy for T1, T2, Stage I or 2 disease
8. Truth or Myth: Living near powerlines increases the risk for breast cancer
**Truths: Powerlines**

- 576 breast cancer patients from the Long Island Breast Cancer Study Project.
  - Lived >15 years in their home (Nassau/Suffolk)
  - Measured EMF at Front door, bedroom, most lived in room and ground current

FOUND: NO ASSOCIATION BETWEEN EMF and BREAST CANCER RISK

Schoenfeld, AM J of Epid, 2003
Truly: Powerlines

* England and Wales
  * 58,404 breast cancer cases within 1000 meters of a power line versus control
  * Looked at distances 0-49 versus 600-1000 meters

* FOUND: NO MEANINGFUL EXCESS RISK FOR BREAST CANCER (OR 1.08, CI .77-1.51)

* Elliot, Epidemiology, 2013
9. Truth or Myth: Are all breast cancers treated the same?
Treatments for Breast Cancer

**Breast**
- Lumpectomy with Radiation → Depends on extent of disease, location, ability to have RT
- Mastectomy

**Nodes**
- Sentinel Node
- Axillary dissection

**Rest of Body**
- ?Chemotherapy → depends on ER, HER2, nodes, size, genomic profiling
- ?Anti-hormonal therapy → depends on ER status
**Oncotype DX™ 21-Gene Recurrence Score (RS) Assay**

16 Cancer and 5 Reference Genes From 3 Studies

<table>
<thead>
<tr>
<th>Category</th>
<th>RS (0-100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk</td>
<td>RS &lt;18</td>
</tr>
<tr>
<td>Int risk</td>
<td>RS ≥18 and &lt;31</td>
</tr>
<tr>
<td>High risk</td>
<td>RS ≥31</td>
</tr>
</tbody>
</table>

### PROLIFERATION
- Ki-67
- STK15
- Survivin
- Cyclin B1
- MYBL2

### ESTROGEN
- ER
- PR
- Bcl2
- SCUBE2

### INVASION
- Stromelysin 3
- Cathepsin L2

### HER2
- GRB7
- HER2

### CD68
- GSTM1
- BAG1

### REFERENCE
- Beta-actin
- GAPDH
- RPLP0
- GUS
- TFRC

RS = 0.47 x Her2 GRP Score -0.34 x ER GRP Score +1.04 x Prolif GRP Score +0.1 x Invasion GRP Score +0.05 x CD-68 -0.08 x GSTM1 -0.07 x BAG1
**Oncotype DX™ Clinical Validation: RS as Continuous Predictor**

My RS is 30. What is the chance of recurrence within 10 years?

95% CI
Penn State Cancer Institute

* 247 patients evaluated with Oncotype Dx score
* 133 patients (54%) changed systemic treatment based on Oncotype score
* 126 (51%) patients changed to endocrine therapy
* 7 (3%) patients changed to chemotherapy and endocrine

* Smith, Kass et al, ASBS abstract, 2012
10. Truth or Myth: I’m too old to get breast cancer!
* The incidence of breast cancer increases with age.
Can you be too young?

- Can occur in teens and 20’s – these are unusual tumors, related to genetic mutations.
- 5% of breast cancers occur < 40 y
  - 70,000 men and women per year

11. Do fibrocystic changes increase the chance of developing cancer?

Doshi D J et al. Radiographics 2007;27:S53-S64
* Fibrocystic changes are benign
* common
  * after 30, peak in perimenopausal years
  * influenced by hormone levels
* palpable mass, cannot differentiate from a breast cancer lump
  * mammogram
  * ultrasound
* Pain, tenderness, heaviness, nipple itching
process involves inflammation and cell death within the milk ducts of the breast
* chronic inflammation has been implicated in oxidative stress and as a possible etiology of breast cancer

* Can this be mediated by suppressing the effects of hormones and supplementing anti-oxidants?
baseline (left) and 2 years (right) after beginning treatment with tamoxifen for contralateral breast cancer.
Genetics

Australia and North America - mammograms in 951 twin pairs aged 40 – 70 y

60 – 67% Breast Density related to genetics
One third related to parity, age, menopause, BMI.


Core biopsies
Stromal cells in dense regions have higher levels of aromatase IR than the epithelial cells.
Enhanced estrogen synthesis
Greater lifetime exposure to estrogen
Stromal cells – CAF’s (carcinoma assoc. FBs)

* can promote tumorigenic conversion of initiated epithelial cells
* fibroblasts from normal tissue suppress this transition
* suppression is also proven for myoepithelial cells
  * key in transition to invasive disease

Frontiers in Bioscience 15, 226-236, January 1, 2010. Role of myoepithelial cells in breast tumor progression. Puspa Raj Pandey¹, Jamila Saidou¹, Kounosuke Watabe
Postmenopausal women with increased breast density
breast density as a surrogate biomarker for risk
  Volumetric measurement

Interventions (5 treatment groups) – chemoprevention data
  Raloxifene
  Omega 3 Fa’s – Fish oil
Serum biomarkers, BMI, annual screening mammograms x3.
12. If the mammogram is normal, I have nothing to worry about, right?
* Mammograms are the best way to detect cancer at its earliest stages
* Mortality reduction
  * 15 – 30% in women 40 – 49
  * 29 – 40% in women 50 – 74

did you feel something different?
problem solving is necessary if a woman has symptoms
Pitfall: Mammograms are less sensitive in younger women, and women with dense breasts.
* Digital breast tomosynthesis
13. Do Needle biopsies spread cancer cells in the breast and to the rest of the body?
Needle biopsies

* standard of care for breast masses
* 2004 study showed no spread of cancer vs. surgical biopsies
* some “seeding” can occur along the tract
  * negative consequences are rare
* exceptions: ovary and testes, sarcomas

Figure 3a. Effect of needle placement during core needle biopsy.


©2007 by Radiological Society of North America
14. If you find a lump, is it cancer?
Breast lumps are common and **80%** of breast lumps are NOT related to cancer

- fibrocystic changes – Cysts can be large
- hormone fluctuations
- fibroadenomas
- papillomas
- traumatic fat necrosis
15. Can men get breast cancer?
* 1% of all breast cancers occur in men (2,200 per year)

* tender breast enlargement can occur in men (gynecomastia)
  * this is NOT related to cancer
16. Will having a mammogram every single year, after age 40 expose me to TOO much radiation?
* low dose,
* decreased since digital
* greater impact on developing breasts

* How much? average of 70 mrem
  * = environmental exposure over 2.5 months (340 mrem/y)
  * soil (uranium/thorium), cosmic (protons), gases (radon)
Mehmet Oz, MD, - incidence of thyroid cancers has been increasing among women over the past 30 years. (truth)

attributed radiation exposures during dental x-rays and mammograms as possibly contributing to this increase. (myth)
Title: "Scatter Radiation Dose During Routine Screening Mammography to the Thyroid Gland, Salivary Glands, Lens of Eye, Red Bone Marrow of Sternum, and Uterus."
Results

- thyroid gland received less than 2% of normal background radiation
- thyroid shields can interfere with imaging of the breast
  - cannot see breast tissue
  - may need to repeat images

- Radiation to the Thyroid gland, lens of eye, salivary glands and uterus are less than 4% of annual background radiation
17. Is my mother’s family history more important than my father’s?
* much emphasis placed on mothers, aunts and grandmothers

* particularly important in the genetic mutations related to breast and ovarian cancer
BRCA1 and BRCA2 genes function to repair double-strand DNA breaks

BRCA1 and BRCA2 genes act as tumor suppressor genes

Mutations in these genes may lead to transcriptional activation of the Estrogen Receptor leading to altered hormonal regulation of the breast and ovarian epithelium
BRCA1 Gene Mutation

* **BRCA1 mutation**
  * Risk of breast cancer is 60% (compared to 12.5%)
  * Risk of contralateral breast cancer is 65% (compared to 1% per year)
  * Risk of ovarian cancer is 45% (compared to 1.5%)
  * Male breast cancer is 3% (compared to 0.1%)
BRCA2 Gene Mutation

- BRCA2 mutation
  - Risk of breast cancer is 55% (compared to 12.5%)
  - Risk of contralateral breast cancer is 50% (compared to 1% per year)
  - Risk of ovarian cancer is 25% (compared to 1.5%)
  - Risk of prostate cancer is 40% (compared to 15%)
  - Risk of male breast cancer is 12% (compared to 0.1%)
- Mutations in the BRCA2 gene have a significant affect on male breast cancer and prostate cancer
Who should be tested for BRCA1 or BRCA2 gene mutations?

* Women with breast cancer:
  * Age < 30 years of age
  * Age < 50 years of age with at least one relative with breast or ovarian cancer < 50 years of age
  * At any age with breast cancer < 50 years of age or one relative with ovarian cancer
  * With both breast and ovarian cancer or multiple primary breast cancers