Identification and Management of Women at Increased Risk of Breast Cancer

June C. Carroll MD CCFP FCFP
Sydney G. Frankfort Chair in Family Medicine
Associate Professor, Dept. of Family Medicine
Mount Sinai Hospital, University of Toronto

Andrea Eisen MD FRCPC
Assistant Professor, Dept. of Medicine, University of Toronto
Medical Oncologist, Odette Cancer Centre

Ontario College of Family Physicians
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Identification and Management of Women at Increased Risk of Breast Cancer

- No conflict of interest to declare
Identification and Management of Women at Increased Risk of Breast Cancer

Objectives:

- Identify women at increased risk of breast cancer
  - family history, risk assessment tools
- Understand the benefits, risks and limitations of genetic testing
- Identify and counsel women who might benefit from chemoprevention
- Understand lifestyle factors and their role in breast cancer risk
- Provide appropriate screening and management advice based on risk
Identification and Management of Women at Increased Risk of Breast Cancer

Seminar Plan

- Breast cancer risk assessment tools
- Case illustrating hereditary breast cancer
  - Criteria for referral to genetics
  - Benefits and limitations of genetic testing
  - Screening and management
    - MRI screening program
- Cases illustrating chemoprevention
- Lifestyle factors
## Risk Factors for Breast Cancer

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>BRCA1</em> or <em>BRCA2</em> mutation</td>
<td>10.0-32.0</td>
</tr>
<tr>
<td>FH of Cancer:</td>
<td></td>
</tr>
<tr>
<td>- 1 first-degree relative</td>
<td>1.5-2.0</td>
</tr>
<tr>
<td>- 2 first-degree relatives</td>
<td>3.0</td>
</tr>
<tr>
<td>- 3 or more first-degree relatives</td>
<td>4.0</td>
</tr>
<tr>
<td>Therapeutic radiation to chest &lt;age 30</td>
<td>7.0-17.0</td>
</tr>
<tr>
<td>Hormonal Factors</td>
<td></td>
</tr>
<tr>
<td>- Late (age&gt;30) parity or nulliparity</td>
<td>1.2-1.7</td>
</tr>
<tr>
<td>- Early (age&lt;12) menarche or late menopause (&gt;55)</td>
<td>1.2-1.3</td>
</tr>
<tr>
<td>- Combined HRT (≥10 yrs)</td>
<td>1.5</td>
</tr>
</tbody>
</table>

- *Warner NEJM 2011*
## Risk Factors for Breast Cancer

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postmenopausal obesity</td>
<td>1.2-1.9</td>
</tr>
<tr>
<td>Alcohol consumption (2 drinks/day vs. none)</td>
<td>1.2</td>
</tr>
<tr>
<td>Smoking before first live birth</td>
<td>1.2</td>
</tr>
<tr>
<td>Sedentary lifestyle</td>
<td>1.1-1.8</td>
</tr>
<tr>
<td>White race</td>
<td>1.1-1.5</td>
</tr>
<tr>
<td>Breast density (very dense vs. mainly fatty)</td>
<td>5.0</td>
</tr>
<tr>
<td>Atypical ductal or lobular hyperplasia or lobular carcinoma in situ on previous breast biopsy</td>
<td>4.0</td>
</tr>
</tbody>
</table>

- Warner NEJM 2011
Select Modifiable Risk Factors
Percentage of adults with select modifiable risk factors, Ontario, by sex, 2007-2008

Data source: Canadian Community Health Survey 2007-2008 (Statistics Canada)
Prepared by: Cancer Care Ontario, Prevention and Cancer Control
Notes: 1. Data is adjusted to the age distribution of the 2006 Canadian population.
Fertility rate among women 35 to 44 years old, Canada, 1926 to 2006
Risk Assessment

- What is the likelihood that this woman will develop breast cancer?
  - Informal assessment
  - Formal assessment using models

- What is the probability that this woman has a mutation in BRCA1 or BRCA2?
  - Family history criteria
  - Statistical models
EDITORIALS


Joann G. Elmore, Suzanne W. Fletcher

Journal of the National Cancer Institute, Vol. 98, No. 23, December 6, 2006
Models

Absolute risk prediction

Ottman et al. (13)
Anderson et al. (14)
Gail et al. (15)
Taplin et al. (16)
Claus et al. (17); Claus et al. (18)
Rosner et al. (19); Colditz et al. (20)
Ueda et al. (21)
Tyrer et al. (22) IBIS
Models

Risk prediction of gene carrier status

Couch et al. (23)
Shattuck-Eidens et al. (24)
Parmigiani et al. (25); Berry et al. (26) BRCAPRO
Frank et al. (27); Frank et al. (28)
Antoniou et al. (29) BOADICEA
de la Hoya et al. (30)
Vahteristo et al. (31)
Hartge et al. (32)
Apicella et al. (33)
Jonker et al. (34)
Gail Model

http://www.cancer.gov/bcrisktool/
IBIS Model (Tyrer-Cuzick Model)

- IBIS ibis@cancer.org.uk
BOADICEA uses the following information to determine risks:

- The family history of breast, ovarian, prostate and pancreatic cancer
- Information on any BRCA1 or BRCA2 testing that has been performed
- The ages at which these cancers were diagnosed in the family
- Age information on unaffected family members
- Ashkenazi Jewish origin
- Information on cohorts

**Assessing Women at High Risk of Breast Cancer: A Review of Risk Assessment Models**

Eitan Amir, Orit C. Freedman, Bostjan Seruga, D. Gareth Evans

<table>
<thead>
<tr>
<th></th>
<th>Gail</th>
<th>Claus</th>
<th>BRCAPRO</th>
<th>IBIS</th>
<th>BOADICEA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1&lt;sup&gt;st&lt;/sup&gt; DR with breast cancer</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>2&lt;sup&gt;nd&lt;/sup&gt; DR with breast cancer</strong></td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>3&lt;sup&gt;rd&lt;/sup&gt; DR with breast cancer</strong></td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Age of br ca in relative</strong></td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Bilateral br ca in a relative</strong></td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Ov ca in a relative</strong></td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Male breast cancer</strong></td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

# Comparing Breast Cancer Risk Assessment Models

Mitchell H. Gail, Phuong L. Mai

## Table 1. Features of models for projecting breast cancer risk*

<table>
<thead>
<tr>
<th>Model (reference)</th>
<th>Calibrated to</th>
<th>Breast cancer outcome predicted</th>
<th>Conditions that preclude use of model (exclusions)</th>
<th>Accounts for competing risks of mortality other than breast cancer</th>
<th>References for studies done to assess model calibration</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCRAT (10)</td>
<td>US SEER</td>
<td>Invasive</td>
<td>LCIS</td>
<td>Yes</td>
<td>(10,11,12)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Invasive and DCIS†</td>
<td>No affected first-degree relatives</td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>Claus (15)</td>
<td>US SEER</td>
<td></td>
<td></td>
<td></td>
<td>(13)</td>
</tr>
<tr>
<td>BRCAPRO (4,5)</td>
<td>Meta-analysis for carriers (5); US SEER for noncarriers</td>
<td>Invasive for noncarriers</td>
<td>None</td>
<td>No</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(13)</td>
</tr>
<tr>
<td>BOADICEA (6)</td>
<td>England and Wales</td>
<td>Invasive</td>
<td>None</td>
<td>No</td>
<td>NA</td>
</tr>
<tr>
<td>IBIS (7)</td>
<td>England and Wales</td>
<td>Invasive and DCIS</td>
<td>None</td>
<td>No</td>
<td>NA</td>
</tr>
</tbody>
</table>

* BCRAT incorporates Gail model 2 (10). BCRAT = Breast Cancer Risk Assessment Tool; BOADICEA = Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm; DCIS = ductal carcinoma in situ; IBIS = International Breast Cancer Intervention Study; LCIS = lobular carcinoma in situ; NA = none available; SEER = Surveillance, Epidemiology, and End Results.

† DCIS was rare in this study, which accrued women with breast cancer from 1980 to 1982.
Hereditary Breast Cancer

- Judy - healthy 40 year old
  - Concerned about her risk for cancer
  - Family history of both breast & ovarian cancer
Case: Judy

LEGEN D
- Breast cancer
- Ovarian cancer

Judy, age 40

Br Ca  Dx 30

Ov Ca  Died 48

Br Ca  Dx 38

Ov Ca  Dx 40
Red flags for hereditary disorders

- Multiple affected relatives on same side of family
- More than 1 generation affected
- Closely related
- Early age of onset
- Clustering of diseases
- Multiple primary cancers in an individual
80% of breast cancer is sporadic

~20% of women with breast cancer have a family history

15% is familial
  - Due to some factor in the family
    - Environmental
    - Undiscovered gene mutation
    - Chance

5% is hereditary
  - Inherited single gene mutation which causes increased risk for cancer
    - About 2/3 of these - BRCA1 or BRCA2 mutations
Genes involved in hereditary breast/ovarian cancer

- *BRCA1* (chrom 17) and *BRCA2* (chrom 13)
- >2600 mutations
- Autosomal dominant transmission
- Carrier frequency of *BRCA1* & 2 mutations
  - \(\approx 1/800\) in general population
  - 1/40 - 1/50 in Ashkenazi Jewish population
    - 3 common mutations in Ashkenazi Jews
    - Unique French Canadian mutations
- Genes are tumor suppressors
- Mutation leads to:
  - Inability to regulate cell death
  - Uncontrolled growth
Genes involved in hereditary breast/ovarian cancer

- **TP53**
  - Li Fraumeni syndrome (P53 mutation)

- **PTEN**
  - Cowden syndrome

- **CDH1**
  - Hereditary diffuse gastric cancer (HDGC)
Hereditary Breast Cancer

Autosomal Dominant Inheritance

Legend

B: BRCA gene with mutation

b: normal BRCA gene

Susceptible BRCA gene

Population Risk

Population Risk
What family history criteria suggest offering referral for genetic counselling and/or genetic testing?....

- Multiple cases of breast cancer or at least 2 cases $\leq$ age 50
  - same side of family (paternal or maternal)
- Any case of:
  - Ovarian cancer
  - Male breast cancer
  - Breast cancer in an Ashkenazi Jewish woman (especially if at age $<60$)
  - Primary cancer occurring in both breasts ($\leq$ age 50)
- An identified $BRCA1$ or $BRCA2$ mutation in any blood relative
Red Flags & Judy’s History

- Multiple affected relatives
- More than 1 generation affected
- Closely related
- Early age of onset
- Clustering of diseases

Judy’s family history indicates increased risk of breast cancer.
*BRCA1* and *BRCA2* mutations greatly increase breast and ovarian cancer risk.

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Estimated Risk in <em>BRCA</em> Mutation Carriers (by Age 70)</th>
<th>In General Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast Cancer ♂</td>
<td><em>BRCA1</em> 1%</td>
<td>&lt;0.1%</td>
</tr>
<tr>
<td></td>
<td><em>BRCA2</em> 7%</td>
<td></td>
</tr>
<tr>
<td>Breast Cancer ♂</td>
<td>49% - 57%</td>
<td>11%</td>
</tr>
<tr>
<td>Ovarian Cancer</td>
<td>40%</td>
<td>1.5%</td>
</tr>
<tr>
<td><em>(BRCA1)</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ovarian Cancer</td>
<td>18%</td>
<td>1.5%</td>
</tr>
<tr>
<td><em>(BRCA2)</em></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Why refer to genetics clinics?

- A genetics consultation involves:
  - Detailed family history information
  - Pedigree documentation
    - Confirmation of cancer history: pathology reports/death certificates
  - Medical & exposure history
  - Hereditary cancer / genetic risk assessment
  - Psychosocial assessment
Why refer to genetics clinics?

A genetics consultation involves:

- Assessment of eligibility for genetic testing
  - Estimated risk of a mutation must be $\geq 10\%$
  - Most appropriate family member to test first
- Discussion of risks, benefits & limitations
- Testing and disclosure of genetic test results
- Discussion of results and what they mean
- Screening/management recommendations
Genetic Testing

- Available at regional genetic centres and familial cancer clinics
- Covered by OHIP if criteria are met

<table>
<thead>
<tr>
<th>Genetic Testing Type</th>
<th>Price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full gene testing</td>
<td>$1400</td>
</tr>
<tr>
<td>Ashkenazi panel</td>
<td>$350</td>
</tr>
<tr>
<td>Familial mutation</td>
<td>$250</td>
</tr>
</tbody>
</table>

- Testing is only offered if the risk of mutation is \( \geq 10\% \)
- Test highest risk *affected* individual first
- Only in exceptional circumstances will testing be offered to unaffected individuals
Results from Genetic Testing

- **Positive**
  - Deleterious mutation identified

- **Negative**
  - Interpretation differs if a mutation has previously been identified in the family
    - Mutation known – true negative
    - Mutation unknown – uninformative

- **Variant of unknown significance**
  - Significance will depend on how variant tracks through family - i.e. is variant present in people with disease?
  - Can use software to predict functional significance
  - Check with lab to see if reported previously
Risks/Benefits/Limitations of genetic testing:

Positive test result

**Potential Benefits:**
- Clinical intervention may improve outcome
- Family members at risk can be identified

**Potential Risks:**
- Adverse psychological reaction
- Family issues/distress
- Uncertainty - incomplete penetrance
- Insurance/job discrimination
- Confidentiality issues
Risks/Benefits/Limitations of genetic testing: Negative test result

Potential Benefits:
- Emotional relief
- Children can be reassured
- Avoidance of unnecessary clinical interventions

Potential Risks:
- Adverse psychological reaction (i.e. survivor guilt)
- Dysfunctional family dynamics
- Complacent attitude to health
Risks/Benefits/Limitations of genetic testing

Uninformative test result
Judy’s Story

- Affected family member must be tested first
  - Deceased
  - Unwilling to contact
    - Guilt
    - Relationship difficulties
    - Illness
- Family member may be unwilling to be tested
Judy’s test results...

LEGEND

- Breast cancer
- Ovarian cancer

Judy

*BRCA1* 185delAG

--- Normal

--- Mutation
Hereditary Breast Cancer

Benefits of knowing GT results

- Clarification of risk of cancer for her & offspring
- Clinical interventions in \textit{BRCA} mutation carriers can save lives
  - Risk reduction surgery
  - Increased screening
  - Chemoprevention
  - Lifestyle modification
Risk Reducing Surgery

- Bilateral risk reducing mastectomy
  - ~ 90% risk reduction in Br Ca incidence
- Bilateral salpingo-oophorectomy
  - 80% reduction in risk of \textit{BRCA 1/2}-associated ovarian/fallopian tube cancer
  - 50% reduction in risk of breast cancer in \textit{BRCA 1/2} mutation carriers
  - Optimal age of SO – possibly before 40 (after childbearing completed)

Ontario Breast Cancer Screening Program for women at high risk of breast cancer

Recommendation:

- Annual screening with combined mammography and breast MRI from age 30-69
Ontario Breast Cancer Screening Program for women at high risk of breast cancer

- Systematic review of MRI screening of women at high risk for breast cancer (*Warner 2007*):

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRI and Mammography combined</td>
<td>87.4%</td>
<td>94.2%</td>
</tr>
<tr>
<td>MRI alone</td>
<td>80.1%</td>
<td>97.0%</td>
</tr>
<tr>
<td>Mammography alone</td>
<td>36.8%</td>
<td>97.1%</td>
</tr>
</tbody>
</table>

Example: 1000 women at high risk of breast cancer (2% risk) screened with MRI and MM - Expect 17 cancers detected with 57 falsely screened positive
Category A:
Eligible for screening with annual MRI + mammography through OBSP due to high risk criteria

Please check at least one box:
- Known to be a carrier of a deleterious gene mutation (e.g., BRCA1, BRCA2).
- First-degree relative of a mutation carrier (e.g., BRCA1, BRCA2), has previously had a genetic assessment and has currently declined genetic testing.
- Determined to be at ≥25% lifetime risk of breast cancer (must have been assessed using IBIS or BOADICEA tools – See reverse side for definitions).

IBIS: 10 year risk: _______ Lifetime Risk: _______
BOADICEA: 5 year risk: _______ Lifetime Risk: _______

If results are available, fax a copy with referral form.

- Received chest radiation (not x-ray) before age 30 and at least 8 years previously (e.g., as treatment for Hodgkin’s lymphoma).

Please complete section on the woman’s history, sign and fax to OBSP. OBSP will arrange further assessment through genetics or high risk cancer clinics to determine the woman’s eligibility for breast screening through the OBSP high risk program.

Category B:
May be eligible for screening with annual MRI + mammography through OBSP because of history suggestive of hereditary breast cancer

Please check at least one box:
- First-degree relative of a mutation carrier (e.g., BRCA1, BRCA2), has not had a genetic assessment or genetic testing.
- A personal or family history (paternal or maternal) of at least one of the following:

Please check all that apply:
- Multiple cases of breast cancer (particularly where diagnosis occurred at ≤50 years) and/or ovarian* cancer (any age) in the family – especially in closely related relatives†, on the same side of the family.
- Primary cancer occurring in both breasts, especially if one or both cancers were diagnosed ≤50 years.
- Both breast and ovarian* cancer in the same woman.
- Breast cancer at ≤35 years.
- Invasive serous ovarian* cancer.
- Breast and/or ovarian* cancer in Ashkenazi Jewish families.
- An identified BRCA1 or BRCA2 mutation in any blood relative.
- Male breast cancer.

*Includes cancer of the Fallopian tubes and primary peritoneal cancer.
† Closely related relative: 1st degree = parent, sibling, child or 2nd degree = grandparent, aunt, uncle, niece, nephew
Eligibility Criteria for High Risk Program

- Asymptomatic women 30-69 years of age

- **Category A:** Eligible for screening with annual MRI + Mammography through OBSP
  - Known to be a carrier of a deleterious gene mutation (e.g. *BRCA1*, *BRCA2*)
  - First-degree relative of a mutation carrier, has previously had a genetics consultation and has currently declined genetic testing.
  - Received chest radiation before age 30 and at least 8 years previously (e.g. as treatment for Hodgkin’s lymphoma).
  - Determined to be at ≥25% lifetime risk of breast cancer (must have been assessed using IBIS or BOADICEA tools)
Eligibility Criteria for High Risk Program - Requisition

☐ **Category B**: May be eligible for screening with annual MRI + MM through OBSP because of history suggestive of hereditary breast cancer

- First-degree relative of a mutation carrier (e.g. *BRCA1*, *BRCA2*), who has not had a genetic consultation or genetic testing.
- A personal or family history...
Eligibility Criteria for High Risk Program - Requisition

- A personal or family history (paternal or maternal) of at least one of the following:
  - Breast cancer at \( \leq 35 \) years.
  - Invasive serous ovarian cancer.
  - Male breast cancer.
  - Breast and/or ovarian cancer in Ashkenazi Jewish families.
  - Primary cancer occurring in both breasts, especially if one or both cancers were diagnosed \( \leq 50 \) years.
  - Both breast and ovarian cancer in the same woman.
  - Multiple cases of breast cancer (particularly where diagnosis occurred at \( \leq 50 \) years) and/or ovarian* cancer (any age) in the family – especially in closely related relatives\(^\dagger\), on the same side of the family.
  - An identified BRCA1 or BRCA2 mutation in any blood relative.
Ontario Breast Screening Program (OBSP): Program Details

Media Trigger · Doctor Visit

Health Care Provider (HCP)*

Assess Risk:
Symptoms, Family history, Clinical history

High Risk (30-69)

Complete and fax ‘Risk assessment & referral form for women at high risk for breast cancer’ to OBSP

OBSP navigator books (a) mammogram (MM) and MRI, if appropriate and eligible OR (b) genetic assessment

Not high risk (b) High risk

Refer back to PCP for average risk screening

Genetic counseling (and testing, if eligible and consent)

Not eligible for genetic testing or declines

Genetics clinic assesses whether woman has ≥25% risk of breast cancer**

Genetics clinic sends PCP and OBSP letter with screening recommendation

If woman is at high risk and eligible for OBSP high risk program, receives MM and MRI

OBSP sends results of MM and MRI screening to PCP and woman

Abnormal

OBSP arranges follow-up

Normal

OBSP recalls in 1 year

Notes:

* Any health care provider (FP, GP oncologist, oncologist) can assess risk and make referrals

** using a risk assessment tool (IBIS or BOADICEA)
Provider Roles

Primary Care Provider

- Collect family and clinical history; completes risk assessment and referral form and sends to OBSP
- Conduct formal assessment of familial breast cancer risk, offer genetic testing if appropriate and/or complete risk assessment tool, refer back to OBSP

Genetic Counseling/Testing Clinics

- Provide navigation for genetic counseling/testing
- Schedule breast MRI and mammography
- Provide results to patient and referring provider
- Coordinate follow-up of abnormal results

Ontario Breast Screening Program Sites

Radiologist

- Interpret breast MRI and mammography results
Chemoprevention of Breast Cancer
Case 1

A healthy 52 yo woman comes to see you following the press coverage of ASCO 2011. She is concerned about her risk of breast cancer, and wants to discuss taking a medication to reduce her risk. Her LMP was 8 mos ago.

Your approach is:

A  Take hx, calculate 5 y risk of br ca, prescribe tamoxifene if eligible
B  Take hx, calculate 5 y risk of br ca, prescribe raloxifene if eligible
C  Take hx, calculate 5 y risk of br ca, prescribe exemestane if eligible
D  recommend regular exercise and low fat diet
Case 2

You have referred a 38 yo woman in your practice for genetic counselling because of a family history of breast cancer. She is G2 P2 and healthy. Her mother died of breast cancer when she was 12 yrs old. She comes back to see you 6 mos later to discuss the results. A BRCA2 mutation has been identified in her maternal aunt. The patient is uncertain about genetic testing but wants to “do everything” to reduce her risk of cancer.

You advise her to:
A Have the genetic test to clarify her risk.
B Have a BSO and prophylactic mastectomy
C Take tamoxifen.
D Take exemestane
<table>
<thead>
<tr>
<th>Treatment</th>
<th>Number of patients</th>
<th>Median duration of follow-up (months)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tamoxifen 20 mg daily</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Royal Marsden trial(^{14})</td>
<td>2471</td>
<td>158</td>
<td>0.61 (0.43–0.86)</td>
</tr>
<tr>
<td>NSABP P-1(^{15})</td>
<td>13 388</td>
<td>84</td>
<td>0.38 (0.28–0.50)</td>
</tr>
<tr>
<td>Italian study(^{16})</td>
<td>5408</td>
<td>132</td>
<td>0.77 (0.51–1.16)</td>
</tr>
<tr>
<td>IBIS-1(^{17})</td>
<td>7139</td>
<td>96</td>
<td>0.66 (0.50–0.87)</td>
</tr>
<tr>
<td><strong>Raloxifene 60 mg daily</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CORE(^{18+})</td>
<td>4011</td>
<td>96</td>
<td>0.24 (0.22–0.40)</td>
</tr>
<tr>
<td>RUTH(^{19})</td>
<td>10 101</td>
<td>67</td>
<td>0.45 (0.28–0.72)</td>
</tr>
<tr>
<td>STAR(^{20})</td>
<td>19 747</td>
<td>81</td>
<td>1.24 (1.05–1.47) vs tamoxifen</td>
</tr>
<tr>
<td><strong>Lasofoxifene 0.25 mg or 0.5 mg daily</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEARL(^{21})</td>
<td>8556</td>
<td>60</td>
<td>0.19 (0.07–0.56)</td>
</tr>
<tr>
<td><strong>Arzoxifene 20 mg daily</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GENERATIONS(^{22})</td>
<td>9354</td>
<td>48</td>
<td>0.30 (0.14–0.63)</td>
</tr>
<tr>
<td><strong>Anastrozole 1 mg daily</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IBIS-2(^{23})</td>
<td>4000 planned</td>
<td>Continuing</td>
<td></td>
</tr>
</tbody>
</table>
ALL INVASIVE BREAST CANCERS, 0-10y
SERM vs. placebo

Tamoxifen vs. placebo
  Italian
  NSABP B-1
  IBIS1
  Marsden
Raloxifene vs. placebo
  MORE/CORE
  RUTH
  STAR
Lasofoxifene vs. placebo
  PEARL 25 mg
  PEARL 50 mg
  Combined

Fixed-effect model: -38.3% [-44.2%; -29.6%], p<0.001
Random-effect model: -39.3% [-51.1%; -24.7%], p<0.001
Test for heterogeneity: Q(8df) = 23.79, p=0.002, Cuzick et al ASCO 2010
NCIC CTG MAP.3 Prevention Trial

Postmenopausal women at increased risk for breast cancer

Stratification
Aspirin use
Gail score (<2.0 vs. > 2.0)

Double-Blind

Randomize

Exemestane
25 mg/day x 5 years
n = 4560
February 2004 – March 2010

Placebo
1 pill/day x 5 years
<table>
<thead>
<tr>
<th>Treatment</th>
<th>Annual Incidence rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exemestane</td>
<td>0.19% (0.08-0.30%)</td>
</tr>
<tr>
<td>Placebo</td>
<td>0.55% (0.36-0.73%)</td>
</tr>
</tbody>
</table>

Hazard Ratio 0.35 (95% CI =0.18–0.70)  
Stratified log rank p-value=0.002
## Side effects by severity and treatment arm

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Exemestane (n=2240)</th>
<th>Placebo (n=2248)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤ gr 2</td>
<td>≥ gr 3</td>
<td>Total (%)</td>
</tr>
<tr>
<td>Any</td>
<td>1395</td>
<td>568</td>
<td>1963 (88)</td>
</tr>
<tr>
<td>Hot flashes</td>
<td>833</td>
<td>67</td>
<td>900 (40)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>492</td>
<td>33</td>
<td>525 (23)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>215</td>
<td>15</td>
<td>230 (10)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>109</td>
<td>9</td>
<td>118 (5)</td>
</tr>
<tr>
<td>Nausea</td>
<td>149</td>
<td>3</td>
<td>155 (7)</td>
</tr>
<tr>
<td>Arthritis</td>
<td>215</td>
<td>32</td>
<td>247 (11)</td>
</tr>
<tr>
<td>Joint pain</td>
<td>587</td>
<td>78</td>
<td>665 (30)</td>
</tr>
<tr>
<td>Muscle pain</td>
<td>131</td>
<td>16</td>
<td>147 (7)</td>
</tr>
<tr>
<td>Depression</td>
<td>213</td>
<td>23</td>
<td>236 (11)</td>
</tr>
<tr>
<td>Vaginal dryness</td>
<td>351</td>
<td>1</td>
<td>352 (16)</td>
</tr>
</tbody>
</table>

NCI CTCAE version 3
MAP.3 Conclusions

- Exemestane reduced the incidence of invasive breast cancer by 65% (from 0.55% to 0.19%)
- Exemestane also reduced pre-invasive DCIS and pre-cancerous ADH, ALH and LCIS
- Serious toxicities over 3 years were not seen, particularly fractures, self reported osteoporosis, cardiovascular toxicities or second cancers
- Minimal meaningful changes in health related QOL occurred
The challenge

- Poor uptake of tamoxifen,
- Which care providers should do this work?
- Cardiology paradigm
# Prevalence of Tamoxifen Use for Breast Cancer Chemoprevention Among U.S. Women

Erika A. Waters, Kathleen A. Cronin, Barry I. Graubard, et al.

*Cancer Epidemiol Biomarkers Prev* 2010;19:443-446. Published online February 7, 2010.

## Table 1. Prevalence estimates for use of tamoxifen in two nationally representative U.S. data sources (NHIS 2000, NHIS 2005)

<table>
<thead>
<tr>
<th>NHIS 2000*</th>
<th>Percentage</th>
<th>NHIS 2005†</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of women using tamoxifen (95% CI)</td>
<td>120,737 (95% CI, 75,416-183,219)</td>
<td>0.20 (95% CI, 0.13-0.31)</td>
<td>51,575 (95% CI, 19,596-109,936)</td>
</tr>
</tbody>
</table>

*Weighted estimate from a sample of 27 women who report using tamoxifen of a total sample size of 10,601.

†Weighted estimate from a sample of 8 women who report using tamoxifen of a total sample size of 10,690.
Case 1

A healthy 52 yo woman comes to see you following the press coverage of ASCO 2011. She is concerned about her risk of breast cancer, and wants to discuss taking a medication to reduce her risk. Her LMP was 8 mos ago.

Your approach is:
A  Take hx, calculate 5 y risk of br ca, prescribe tamoxifen if eligible
B  Take hx, calculate 5 y risk of br ca, prescribe raloxifene if eligible
C  Take hx, calculate 5 y risk of br ca, prescribe exemestane if eligible
D  recommend regular exercise and low fat diet
You have referred a 38 yo woman in your practice for genetic counselling because of a family history of breast cancer. She is G2 P2 and healthy. Her mother died of breast cancer when she was 12 yrs old. She comes back to see you 6 mos later to discuss the results. A BRCA2 mutation has been identified in her maternal aunt. The patient is uncertain about genetic testing but wants to “do everything” to reduce her risk of cancer.

You advise her to:
A Have the genetic test to clarify her risk.
B Have a BSO and prophylactic mastectomy
C Take tamoxifan.
D Take exemestane
Lifestyle modification
STEP 10
Discover Curcumin: Nature’s Anticancer Secret Agent 106

STEP 11
Make the Most of Melatonin: Nature’s Cancer-Preventing Hormone 111

STEP 12
Reduce Your Risk with Other Nutrients 119

STEP 13
Avoid Chemicals That Cause Breast Cancer 126

STEP 14
Raise Your B₁₂ and Folate Levels 136

STEP 15
Strengthen Your Cancer-Fighting Immune Cells 141

STEP 16
Detoxify to Reduce Your Breast Cancer Risk 149

STEP 17
Eat Right to Reduce Risk 155

STEP 18
Determine If SERMs Are Right for You 164

STEP 19
Start Exercising to Lower Your Risk 168

STEP 20
Putting It All Together 173
Lifestyle modification

- Diet and Exercise
- AICR report: systematic review
SUMMARY

Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective

http://www.dietandcancerreport.org
<table>
<thead>
<tr>
<th>RECOMMENDATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BODY FATNESS</strong></td>
</tr>
<tr>
<td>Be as lean as possible within the normal range of body weight</td>
</tr>
<tr>
<td><strong>PHYSICAL ACTIVITY</strong></td>
</tr>
<tr>
<td>Be physically active as part of everyday life</td>
</tr>
<tr>
<td><strong>FOODS AND DRINKS THAT PROMOTE WEIGHT GAIN</strong></td>
</tr>
<tr>
<td>Limit consumption of energy-dense foods</td>
</tr>
<tr>
<td>Avoid sugary drinks</td>
</tr>
<tr>
<td><strong>PLANT FOODS</strong></td>
</tr>
<tr>
<td>Eat mostly foods of plant origin</td>
</tr>
<tr>
<td><strong>ANIMAL FOODS</strong></td>
</tr>
<tr>
<td>Limit intake of red meat and avoid processed meat</td>
</tr>
<tr>
<td><strong>ALCOHOLIC DRINKS</strong></td>
</tr>
<tr>
<td>Limit alcoholic drinks</td>
</tr>
<tr>
<td><strong>PRESERVATION, PROCESSING, PREPARATION</strong></td>
</tr>
<tr>
<td>Limit consumption of salt</td>
</tr>
<tr>
<td>Avoid mouldy cereals (grains) or pulses (legumes)</td>
</tr>
<tr>
<td><strong>DIETARY SUPPLEMENTS</strong></td>
</tr>
<tr>
<td>Aim to meet nutritional needs through diet alone</td>
</tr>
<tr>
<td><strong>BREASTFEEDING</strong></td>
</tr>
<tr>
<td>Mothers to breastfeed; children to be breastfed</td>
</tr>
<tr>
<td><strong>CANCER SURVIVORS</strong></td>
</tr>
<tr>
<td>Follow the recommendations for cancer prevention</td>
</tr>
</tbody>
</table>
RECOMMENDATION 1

BODY FATNESS

Be as lean as possible within the normal range\(^1\) of body weight

PUBLIC HEALTH GOALS

Median adult body mass index (BMI) to be between 21 and 23, depending on the normal range for different populations\(^2\)

The proportion of the population that is overweight or obese to be no more than the current level, or preferably lower, in 10 years

PERSONAL RECOMMENDATIONS

Ensure that body weight through childhood and adolescent growth projects\(^3\) towards the lower end of the normal BMI range at age 21

Maintain body weight within the normal range from age 21

Avoid weight gain and increases in waist circumference throughout adulthood
Lifestyle modification

- Vitamin D
  - IARC report
  - IOM report
  - recommendations
Vitamin D and Cancer

Figure 13.4 - Dose-response relative risks for breast cancer due to an increase of 1 unit of ng/mL serum level of 25-hydroxyvitamin D. All studies are on breast cancer incidence, but Freedman et al., 2007, that used breast cancer mortality as endpoint. The relative risk "pooled Co or NCC" is calculated after exclusion of case-control studies (Co is cohort studies, NCC is nested case-control studies)

Berton-Johnson, 2005
Colsto, 2006
Abba, 2007
Freedman, 2007
Freedman, 2008
Pooled Co or NCC
Pooled Overall

RR=0.994 (0.964, 1.024)
RR=0.984 (0.964, 1.004)
## RCTs of vitamin D and Cancer

### Table 14.1 - Summary of randomised trials on vitamin D and invasive cancer

<table>
<thead>
<tr>
<th>Study reference and endpoint</th>
<th>Type of randomised trial</th>
<th>Vitamin D daily dose</th>
<th>Elementary calcium daily dose</th>
<th>Mean trial duration (years)</th>
<th>No. in intervention group</th>
<th>No. in control group</th>
<th>Age at inclusion</th>
<th>No. cases in intervention group</th>
<th>No. cases in control group</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wactawski-Wende et al., 2006</td>
<td>Double-blind, placebo controlled</td>
<td>10 µg</td>
<td>1.0 g</td>
<td>7</td>
<td>18,176 women</td>
<td>18,106 women</td>
<td>50-79</td>
<td>168</td>
<td>154</td>
<td>1.08</td>
<td>0.86-1.34</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>128</td>
<td>126</td>
<td>1.00</td>
<td>0.78-1.28</td>
</tr>
<tr>
<td>Colon cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>44</td>
<td>30</td>
<td>1.46</td>
<td>0.92-2.32</td>
</tr>
<tr>
<td>Rectal cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SEER stage of invasive CRC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Localised</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Regional</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distant</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All cancers</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1634</td>
<td>1655</td>
<td>0.98</td>
<td>0.91-1.05</td>
</tr>
<tr>
<td>Chlebowski et al., 2008</td>
<td>id.</td>
<td>id.</td>
<td>id.</td>
<td>id.</td>
<td>id.</td>
<td>id.</td>
<td>id.</td>
<td>528</td>
<td>545</td>
<td>0.96</td>
<td>0.85-1.09</td>
</tr>
<tr>
<td>Breast cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SEER stage of breast cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trivedi et al., 2003</td>
<td>Double-blind, placebo controlled</td>
<td>21 µg</td>
<td>No calcium supplement</td>
<td>5</td>
<td>1345 men and women</td>
<td>1341 men and women</td>
<td>65-84</td>
<td>28</td>
<td>27</td>
<td>1.02</td>
<td>0.60-1.74</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>144</td>
<td>130</td>
<td>1.11</td>
<td>0.86-1.42</td>
</tr>
<tr>
<td>All cancers</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lappe et al., 2007</td>
<td>Double-blind, placebo controlled</td>
<td>27.5 µg</td>
<td>1.5 g</td>
<td>4</td>
<td>&gt;55</td>
<td></td>
<td></td>
<td>446 women</td>
<td>733 women</td>
<td>0.99</td>
<td>0.32-1.10</td>
</tr>
<tr>
<td>All cancers (intervention is vitamin D supplements)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>13</td>
<td>37</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All cancer (intervention is calcium supplements)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>30</td>
<td>20</td>
<td>0.50</td>
<td>0.29-0.87</td>
</tr>
</tbody>
</table>

No difference between the two groups (data not reported)
BOX S-2

Potential Indicators of Health Outcomes for Nutrient Adequacy for Calcium and Vitamin D

Cancer/neoplasms
- All cancers
- Breast cancer
- Colorectal cancer/colon polyps
- Prostate cancer
Closing Remarks

At this time, the scientific data available indicate a key role for calcium and vitamin D in skeletal health and provide a sound basis for DRIs. The data do not, however, provide compelling evidence that either nutrient is causally related to extra-skeletal health outcomes or that intakes greater than those established in the DRI process have benefits for health. The last chapter of this report specifies the research needs and reflects an urgent and worthwhile agenda. If carried out, this research will assist greatly in clarifying DRIs for vitamin D and calcium in the future.
<table>
<thead>
<tr>
<th>Life Stage Group</th>
<th>Calcium</th>
<th>Vitamin D</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimated Average</td>
<td>Recommended Dietary</td>
</tr>
<tr>
<td></td>
<td>Requirement (mg/day)</td>
<td>Allowance (mg/day)</td>
</tr>
<tr>
<td>Infants 0 to 6 months</td>
<td>*</td>
<td>1,000</td>
</tr>
<tr>
<td>Infants 6 to 12 months</td>
<td>*</td>
<td>1,500</td>
</tr>
<tr>
<td>1-3 years old</td>
<td>500</td>
<td>2,500</td>
</tr>
<tr>
<td>4-8 years old</td>
<td>800</td>
<td>2,500</td>
</tr>
<tr>
<td>9-13 years old</td>
<td>1,100</td>
<td>3,000</td>
</tr>
<tr>
<td>14-18 years old</td>
<td>1,100</td>
<td>3,000</td>
</tr>
<tr>
<td>19-30 years old</td>
<td>800</td>
<td>2,500</td>
</tr>
<tr>
<td>31-50 years old</td>
<td>800</td>
<td>2,500</td>
</tr>
<tr>
<td>51-70 year old males</td>
<td>800</td>
<td>2,000</td>
</tr>
<tr>
<td>51-70 year old females</td>
<td>1,000</td>
<td>2,000</td>
</tr>
<tr>
<td>&gt;70 years old</td>
<td>1,000</td>
<td>2,000</td>
</tr>
<tr>
<td>14-18 years old, pregnant/lactating</td>
<td>1,100</td>
<td>3,000</td>
</tr>
<tr>
<td>19-50 years old, pregnant/lactating</td>
<td>800</td>
<td>2,500</td>
</tr>
</tbody>
</table>

*For infants, Adequate Intake is 200 mg/day for 0 to 6 months of age and 260 mg/day for 6 to 12 months of age.
**For infants, Adequate intake is 400 IU/day for 0 to 6 months of age and 400 IU/day for 6 to 12 months of age.
Lifestyle modification

- Alcohol
  - Are guidelines for safe drinking safe for cancer?
  - Nurses Health Study, JAMA
Alcohol consumption and cancer risk: revisiting guidelines for sensible drinking

Paule Latino-Martel PhD, Pierre Arwidson MD, Raphaëlle Ancellin MSc, Nathalie Druesne-Pecollo PhD, Serge Hercberg MD PhD, Martine Le Quellec-Nathan MD, Thanh Le-Luong MD, Dominique Maraninchi MD PhD

CMAJ, November 8, 2011, 183(16)
<table>
<thead>
<tr>
<th>Country</th>
<th>Alcohol content of a standard drink, g</th>
<th>Recommended limit for adult men</th>
<th>Recommended limit for adult women</th>
<th>Institutional source</th>
<th>Average annual consumption of alcohol per capita (2003–2005), L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>10</td>
<td>2 drinks/d (20 g/d)</td>
<td>2 drinks/d, (20 g/d)</td>
<td>National Health and Medical Research Council</td>
<td>10.0</td>
</tr>
<tr>
<td>Austria</td>
<td>8</td>
<td>24 g/d</td>
<td>16 g/d</td>
<td>Ministry of Health</td>
<td>13.2</td>
</tr>
<tr>
<td>Bulgaria</td>
<td>15</td>
<td>&lt; 20 mL or 16 g/d</td>
<td>&lt; 10 mL or 8 g/d</td>
<td>National Center of Public Health Protection</td>
<td>12.4</td>
</tr>
<tr>
<td>Canada</td>
<td>13.6</td>
<td>2 drinks/d (27.2 g/d), up to 14 drinks/w (190.4 g/w)</td>
<td>2 drinks/d (27.2 g/d) up to 9 drinks/w (122.4 g/w)</td>
<td>Center for Addiction and Mental Health</td>
<td>9.8</td>
</tr>
<tr>
<td>Denmark</td>
<td>12</td>
<td>21 drinks/w (252 g/w)</td>
<td>14 drinks/w (168 g/w)</td>
<td>Ministry of Health and Prevention, National Board of Health</td>
<td>13.4</td>
</tr>
<tr>
<td>France</td>
<td>10</td>
<td>3 units/d (30 g/d)</td>
<td>2 units/d (20 g/d)</td>
<td>French Institute for Prevention and Health Education</td>
<td>13.7</td>
</tr>
<tr>
<td>Great Britain</td>
<td>8</td>
<td>3–4 units/d (24–32 g/d)</td>
<td>2–3 units/d (16–24 g/d)</td>
<td>National Health Service</td>
<td>13.4</td>
</tr>
<tr>
<td>Ireland</td>
<td>10</td>
<td>21 drinks/w (210 g/w)</td>
<td>14 drinks/w (140 g/w)</td>
<td>Health Service Executive</td>
<td>14.4</td>
</tr>
<tr>
<td>Italy</td>
<td>12</td>
<td>20–40 g/d (2–3 units/d), ≥ 65 yr, 12 g/d</td>
<td>10–20 g/d (1–2 units/d), ≥ 65 yr, 12 g/d</td>
<td>Ministry of Health</td>
<td>10.7</td>
</tr>
<tr>
<td>Spain</td>
<td>10</td>
<td>17 units/w (170 g/w)</td>
<td>11 units/w (110 g/w)</td>
<td>Ministry of Health</td>
<td>11.6</td>
</tr>
<tr>
<td>United States</td>
<td>13.7</td>
<td>2 drinks/d (27.4 g/d)</td>
<td>1 drink/d (13.7 g/d)</td>
<td>Centers for Disease Control and Prevention; US Department of Health and Human Services</td>
<td>9.4</td>
</tr>
</tbody>
</table>
Appendix 2 (as supplied by the authors): Summary of cohort results published between 2007 and 2010 on alcohol drinking and the risk of upper aerodigestive tract, breast, colon–rectum and liver cancers

<table>
<thead>
<tr>
<th>Country/Study Cancer site</th>
<th>Participants, no.</th>
<th>Cases, no.</th>
<th>Significantly increased risk associated with alcohol drinking*</th>
<th>Dose–response p trend</th>
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</thead>
<tbody>
<tr>
<td>UK/Million Women Study¹</td>
<td></td>
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<tr>
<td>Oral cavity and pharynx</td>
<td>1280 296</td>
<td>758</td>
<td>Yes (women)†</td>
<td>&lt;0.001§</td>
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<tr>
<td>Larynx</td>
<td>138</td>
<td></td>
<td>Yes (women)†</td>
<td>0.008§</td>
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<tr>
<td>Oesophagus</td>
<td>773</td>
<td></td>
<td>Yes (women)†</td>
<td>0.002§</td>
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<tr>
<td>Breast</td>
<td>28 380</td>
<td></td>
<td>Yes (women)†</td>
<td>&lt;0.001§</td>
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<tr>
<td>Colon</td>
<td>4169</td>
<td></td>
<td>No (women)†</td>
<td>0.8§</td>
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<tr>
<td>Rectum</td>
<td>2129</td>
<td></td>
<td>Yes (women)†</td>
<td>0.02§</td>
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<tr>
<td>Liver</td>
<td>337</td>
<td></td>
<td>Yes (women)†</td>
<td>0.03§</td>
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</tbody>
</table>
ORIGINAL CONTRIBUTION

Moderate Alcohol Consumption During Adult Life, Drinking Patterns, and Breast Cancer Risk

Wendy Y. Chen, MD, MPH
Bernard Rosner, PhD
Susan E. Hankinson, ScD
Graham A. Colditz, MD, DrPH
Walter C. Willett, MD, DrPH

JAMA, November 2, 2011—Vol 306, No. 17
<table>
<thead>
<tr>
<th>Alcohol Intake, g/d&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Cases, No.</th>
<th>Incidence Rate&lt;sup&gt;d&lt;/sup&gt;</th>
<th>RR (95% CI)&lt;sup&gt;e&lt;/sup&gt;</th>
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<td>0</td>
<td>1669</td>
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<td>0.1-4.9</td>
<td>3143</td>
<td>309</td>
<td>1.06 (0.99-1.12)</td>
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<tr>
<td>5-9.9</td>
<td>1063</td>
<td>333</td>
<td>1.15 (1.06-1.24)</td>
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<tr>
<td>10-19.9</td>
<td>1091</td>
<td>351</td>
<td>1.22 (1.13-1.32)</td>
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<tr>
<td>20-29.9</td>
<td>362</td>
<td>356</td>
<td>1.20 (1.07-1.35)</td>
</tr>
<tr>
<td>≥30</td>
<td>362</td>
<td>413</td>
<td>1.51 (1.35-1.70)</td>
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<td>RR per 10-g increase</td>
<td></td>
<td></td>
<td>1.10 (1.07-1.12)</td>
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<td>P for trend</td>
<td>7690</td>
<td>316</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

<sup>a</sup> Adjusted for age, sex, race, smoking status, and energy intake.

<sup>d</sup> Per 1000 person-years.

<sup>e</sup> Relative risk compared to the group with alcohol intake of 0 g/d.
Lifestyle modification

- Inconsistent and controversial findings
- Recommend:
  - Healthy diet
  - Physically active lifestyle
  - Healthy weight
  - Limit alcohol
  - Avoid smoking
  - Minimize duration of postmenopausal HRT

  *Tirona Cancer Investigation 2010*
Resources

Identification and Management of Women at Increased Risk of Breast Cancer

- OBSP Provider tools/references
  - www.cancercare.on.ca/obspresources
- Genetics resources for primary care providers
  - http://www.mtsinai.on.ca/FamMedGen
- “My Family Health Portrait” – FH tool
- Genetic Clinics http://www.cagc-accg.ca