WELCOME!!

McMaster University
Evidence-Based Clinical Practice Workshop

June 3-7, 2019
McMaster EBPC

• 1985: First EBPC Workshop run by David Sackett
• 1993: Leadership transition to Gordon Guyatt and Team
• Conservative Estimate: 2,500 learners!!
Logistical Information

• In your binder
  • Maps, schedules, locations…

• Administrative Team
  • Gail Clark, Laurel Grainger, Jennifer Ayers
  • Help with… ANYTHING (copies, small group needs)
  • Location: Student Center Room 206 & 207
Materials

- Web-based content EBCP website
- Flash Drive with modules; will get a link to the answers via drop box at the end of the workshop
- Slides from large groups posted by the end of the week
Locations: Where to Go

• Student Centre – All small group sessions
• Chester New Hall (#104): Large groups
• Exceptions:
  • Tuesday 6-4: Special Interest Group: Student Center Room 315
  • Thursday 6-6: Medical Grand Rounds 8 am in Health Sciences Center Ewart Angus Rm 1A1
Locations: Where to Go

• Computer Labs Structured Teaching Sessions
  • Kenneth Taylor Hall Computer labs Basement Level Rooms B121 and B123
  • McMaster Health Sciences Centre – Room 2B3 (Health Sciences Library)

• Computer drop-in 1:00 – 4:00 pm
  • Rooms B121 and B123 ONLY in the computer labs in Kenneth Taylor Hall.
Course Objectives

• Modeling interactive teaching
• Create opportunities for networking and interaction with educator colleagues
• Practice teaching
• Learn to access information resources
• Practice critical appraisal skills
Small Groups: The Workshop Core

• As adult learners, small group members take responsibility for the majority of the group learning and teach each other

• Tutorial Team facilitate

• Encourage planning of the week to cover ‘core curriculum’
  • Therapy, Harm, Diagnosis, Prognosis, Systematic Review / Meta-analysis
Afternoon Individual Study Time

• Preparation for small group
• Consultations with faculty tutors, tutor trainees and librarians
• Interest Groups
• Computer Lab is open
• PLEASE...

• ....And Thank you!
And Now…

A day in Sheri’s GIM Clinic
Disclosures

• Paid Editorial Role JAMA’s The Rational Clinical Examination

• No other disclosures or conflicts of interest, but…
Sorry about our president.
Perdón por nuestro presidente.
为总统感到抱歉
Désolé pour notre président.
Tut mir leid wegen unseres Präsidenten.
Elnézést az elnökünk miatt.
Oprostite nam za nasega predsednika.
متأسفون على رئيسنا
Undskyldninger for vores præsident.
ما را بخش كه ترامپ را انتخاب كردیم
Mijn excuses voor onze president.
Przepraszam za naszego prezydenta.
우리 대통령 때문에 미안해
What’s in a Number?

A Journey from Evidence to Action
Objectives

• By attending the session, participants will be able to:
  • Apply the 5 elements of the evidence cycle
  • Use evidence to support patients in shared clinical decision making
  • Practice using the key principles involved in translating Evidence-to-Action
  • Role model interactive teaching strategies and mechanisms to promote engagement in large group
Evidence-based medicine cycle

- Ask
- Acquire
- Appraise

Patient dilemma

Hierarchy of Evidence

Values & Preferences

Apply
Written informed consent was obtained to share this story...
Phone call

Will you care for me?
Go to Audio…

• Listen to the audiotape.
• While you listen, please “get to know” our patient. What are her values, preferences, and priorities?
Ask

Acquire

Appraise

Evidence-based medicine cycle

Hierarchy of Evidence

Apply

Values & Preferences

Patient dilemma
How to Frame Clinical Questions

- **P**: Patient, population, problem
- **I**: Intervention, exposure, prognostic factor
- **C**: Comparison (if applicable)
- **O**: Outcome
- **T**: Type of question (e.g. therapy, harm, diagnosis)
- **T**: Type of study design (e.g. RCT, cohort, case-control)
LP Clinical Questions

- **P**: 50 yo woman, breast cancer
- **I**: 
- **C**: 
- **O**: “Cancer Recurrence to Zero”
- **T**: 
- **T**: 
LP Gets Treatment: Go to Audio…

• Listen to the audiotape.

• While you listen, please listen for questions that come up about her treatment. What is she concerned about?

• Consider elements of PICOTT
LP Clinical Questions

- **P**: 50 yo, woman, breast cancer
- **I**:
- **C**:
- **O**: Cancer recurrence
- **T**:
- **T**: 
LP Clinical Questions

- **P**: 50 yo, woman, breast cancer, ER-PR +, HER2 -, recurrence score 17
- **I**: Hormone Treatment ONLY
- **C**: Hormones + Chemotherapy
- **O**: Cancer recurrence, mortality
- **T**: Therapy
- **T**: RCT
LP Clinical Questions

- **P**: 50 yo, woman, breast cancer, ER-PR +, HER2 -, recurrence score 17
- **I**: Ovaries out
- **C**: Ovaries in
- **O**: Cancer recurrence, mortality
- **T**: Therapy
- **T**: RCT
And We Run Into A Paper
Hi Sheri! Hope all is well! I just read this article that Dr [redacted] shared and in the discussion section it talks about ovary suppression and AI for women 50 and under and octotype scores greater than 16 (I was 17 and 50 at time of diagnosis). My heart is saying to remove ovaries. Should I discuss with Dr E?
to remove ovaries. Should I discuss with Dr E?

Adjuvant Chemotherapy Guided by a 21-Gene Expression Assay in Breast Cancer | NEJM
nejm.org

3rd paragraph of discussion. No worries if you’re busy tonight. Please don’t drop your family time. We can discuss at another time but wanted to get my thoughts to you sooner.

Discussion: Paragraph 3
Adjuvant Chemotherapy Guided by a 21-Gene Expression Assay in Breast Cancer


ABSTRACT

BACKGROUND
The recurrence score based on the 21-gene breast cancer assay predicts chemotherapy benefit if it is high and a low risk of recurrence in the absence of chemotherapy if it is low; however, there is uncertainty about the benefit of chemotherapy for most patients, who have a midrange score.

METHODS
We performed a prospective trial involving 10,273 women with hormone-receptor–positive, human epidermal growth factor receptor 2 (HER2)–negative, axillary node–negative breast cancer. Of the 9719 eligible patients with follow-up information, 6711 (69%) had a midrange recurrence score of 11 to 25 and were randomly assigned to receive either chemoendocrine therapy or endocrine therapy alone. The trial was designed to show noninferiority of endocrine therapy alone for invasive disease–free survival (defined as freedom from invasive disease recurrence, second primary invasive breast cancer, or death from any cause).

The authors’ full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Sparano at Montefiore Medical Center, 1695 Eastchester Rd., Bronx, NY 10461, or at jsparano@montefiore.org.

A full list of the investigators in this trial is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on June 3, 2018, at NEJM.org.

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Treatment for Breast Cancer
What Specifically Is Being Tested?

- **Low Recurrence Score ≤ 10**: Hormone

- **Recurrence Score 11 to 25**: Randomized
  - Hormone
  - Hormone + Chemo

- **High Recurrence Score ≥ 26**: Hormone + Chemo
Page 4 of Paper

11,232 Patients were preregistered

959 Did not register
182 Were ineligible
551 Withdrew
33 Had medical reason
159 Had other reasons
34 Did not report a reason

10,273 Registered and were assigned to a treatment group

1629 Had recurrence score \( \leq 10 \) and were assigned to receive endocrine therapy alone
10 Were excluded
3 Were ineligible
7 Did not have trial-period information, follow-up information, or either

3458 Had recurrence score 11–25 and were randomly assigned to receive endocrine therapy alone
59 Were excluded
4 Were ineligible
55 Did not have trial-period information, follow-up information, or either

3449 Had recurrence score 11–25 and were randomly assigned to receive chemoendocrine therapy
137 Were excluded
6 Were ineligible
131 Did not have trial-period information, follow-up information, or either

1737 Had recurrence score \( \geq 26 \) and were assigned to receive chemoendocrine therapy
348 Were excluded
7 Were ineligible
341 Did not have trial-period information, follow-up information, or either

1619 Were included in the main analysis
56 Withdraw consent for continued follow-up
93 Were lost to follow-up

3399 Were included in the main analysis
3214 Received assigned treatment with endocrine therapy only
185 Received adjuvant chemotherapy
116 Withdraw consent for continued follow-up
224 Were lost to follow-up

3312 Were included in the main analysis
2704 Received assigned treatment with adjuvant chemotherapy
608 Did not receive chemotherapy
148 Withdraw consent for continued follow-up
208 Were lost to follow-up

1389 Were included in the main analysis
25 Withdraw consent for continued follow-up
25 Were lost to follow-up
Some clues from the abstract...
Endocrine therapy was noninferior to chemoendocrine therapy in the analysis of invasive disease–free survival (hazard ratio for invasive disease recurrence, second primary cancer, or death [endocrine vs. chemoendocrine therapy], 1.08; 95% confidence interval, 0.94 to 1.24; \( P = 0.26 \)). At 9 years, the two treatment groups had similar rates of invasive disease–free survival (83.3% in the endocrine-therapy group and 84.3% in the chemoendocrine-therapy group), freedom from disease recurrence at a distant site (94.5% and 95.0%) or at a distant or local–regional site (92.2% and 92.9%), and overall survival (93.9% and 93.8%). The chemotherapy benefit for invasive disease–free survival varied with the combination of recurrence score and age (\( P = 0.004 \)), with some benefit of chemotherapy found in women 50 years of age or younger with a recurrence score of 16 to 25.
RESULTS
Endocrine therapy was noninferior to chemoendocrine therapy in the analysis of invasive disease-free survival (hazard ratio for invasive disease recurrence, second primary cancer, or death [endocrine vs. chemoendocrine therapy], 1.08; 95% confidence interval, 0.94 to 1.24; P = 0.26). At 9 years, the two treatment groups had similar rates of invasive disease-free survival (83.3% in the endocrine-therapy group and 84.3% in the chemoendocrine-therapy group), freedom from disease recurrence at a distant site (94.5% and 95.0%) or at a distant or local-regional site (92.2% and 92.9%), and overall survival (93.9% and 93.8%). The chemotherapy benefit for invasive disease-free survival varied with the combination of recurrence score and age (P = 0.004), with some benefit of chemotherapy found in women 50 years of age or younger with a recurrence score of 16 to 25.

CONCLUSIONS
Adjuvant endocrine therapy and chemoendocrine therapy had similar efficacy in women with hormone-receptor-positive, HER2-negative, axillary node-negative breast cancer who had a midrange 21-gene recurrence score, although some benefit of chemotherapy was found in some women 50 years of age or younger. (Funded by the National Cancer Institute and others; TAILORx ClinicalTrials.gov number, NCT00310180.)
Does This Match Our PICOTT?

- **P**: Breast cancer ER-PR +, HER2 –
- **I**: Hormones only (experimental)
- **C**: Hormones + Chemotherapy (standard)
- **O**: Cancer recurrence, mortality
- **T**: Therapy
- **T**: RCT
Ask
Acquire
Appraise

Evidence-based medicine cycle

Patient dilemma

Hierarchy of Evidence

Values & Preferences

Apply
Critical Appraisal Framework

I. How serious is the risk of bias?

II. What are the results?
   • Magnitude of effect
   • Confidence / precision of estimate

III. How can I apply to patient care
Risk of Bias

- Groups begin with similar prognosis?
  - Randomized (permuted blocks, stratified for prognostic factors such as tumor size, or menopausal status)
  - Allocation concealed (central randomization)
  - Groups similar at baseline (table 1)

- Was prognostic balance maintained?
  - 5 groups unaware of group allocation (blinded)
### Table 1. Characteristics of the Patients in the Intention-to-Treat Population at Baseline.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Recurrence Score of ≤10</th>
<th>Recurrence Score of 11–25</th>
<th>Recurrence Score of ≥26</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Endocrine Therapy (N=1619)</td>
<td>Chemoendocrine Therapy (N=3312)</td>
<td>Chemoendocrine Therapy (N=1389)</td>
</tr>
<tr>
<td>Median age (range) — yr</td>
<td>58 (25–75)</td>
<td>55 (23–75)</td>
<td>55 (25–75)</td>
</tr>
<tr>
<td>Age ≤30 yr — no. (%)</td>
<td>429 (26)</td>
<td>1139 (34)</td>
<td>1077 (33)</td>
</tr>
<tr>
<td>Menopausal status — no. (%)‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Premenopausal</td>
<td>478 (30)</td>
<td>1212 (36)</td>
<td>1203 (36)</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>1141 (70)</td>
<td>2187 (64)</td>
<td>2109 (64)</td>
</tr>
<tr>
<td>Tumor size in the largest dimension — cm‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>1.5 (1.2–2.0)</td>
<td>1.5 (1.2–2.0)</td>
<td>1.5 (1.2–2.0)</td>
</tr>
<tr>
<td>Mean</td>
<td>1.74±0.76</td>
<td>1.71±0.81</td>
<td>1.71±0.77</td>
</tr>
<tr>
<td>Histologic grade of tumor — no./total no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>530/1572 (34)</td>
<td>959/3282 (29)</td>
<td>934/3216 (29)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>931/1572 (59)</td>
<td>1884/3282 (57)</td>
<td>1837/3216 (57)</td>
</tr>
<tr>
<td>High</td>
<td>111/1572 (7)</td>
<td>439/3282 (13)</td>
<td>445/3216 (14)</td>
</tr>
<tr>
<td>Estrogen-receptor expression — no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>5 (&lt;1)</td>
<td>6 (&lt;1)</td>
<td>3 (&lt;1)</td>
</tr>
<tr>
<td>Positive</td>
<td>1614 (&gt;99)</td>
<td>3393 (&gt;99)</td>
<td>3309 (&gt;99)</td>
</tr>
<tr>
<td>Progesterone-receptor expression — no./total no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>28/1583 (2)</td>
<td>267/3339 (8)</td>
<td>251/3240 (8)</td>
</tr>
<tr>
<td>Positive</td>
<td>1555/1583 (98)</td>
<td>3072/3339 (92)</td>
<td>2989/3240 (92)</td>
</tr>
<tr>
<td>Clinical risk — no./total no. (%)§</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>1227/1572 (78)</td>
<td>2440/3282 (74)</td>
<td>2339/3214 (73)</td>
</tr>
<tr>
<td>High</td>
<td>345/1572 (22)</td>
<td>842/3282 (26)</td>
<td>855/3214 (27)</td>
</tr>
<tr>
<td>Primary surgery — no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mastectomy</td>
<td>516 (32)</td>
<td>935 (28)</td>
<td>917 (28)</td>
</tr>
<tr>
<td>Breast conservation</td>
<td>1103 (68)</td>
<td>2464 (72)</td>
<td>2395 (72)</td>
</tr>
<tr>
<td>Adjuvant chemotherapy — no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>8 (0.5)</td>
<td>185 (5.4)</td>
<td>2704 (81.6)</td>
</tr>
<tr>
<td>No</td>
<td>1611 (99.5)</td>
<td>3214 (94.6)</td>
<td>608 (18.4)</td>
</tr>
</tbody>
</table>
Risk of Bias

- Groups prognostically balanced at end?
  - Was follow up complete?
  - Trial was NOT stopped early for benefit
  - Were patients analyzed in group to which they were randomized? (ITT: intention to treat)
Risk of Bias (Non-inferiority)

• Did the investigators guard against the unwarranted conclusion of Non-inferiority?
  • Was the effect of standard treatment preserved?
  • Were patients analyzed according to treatment received (per protocol) and group to which they were randomized (ITT)?
  • **Note: recruited until they had a prespecified number of events (835)**
**Summary:** This is a well done multicenter RCT of 10,000 women with hormone receptor positive, HER2 negative breast cancer that represents low risk of bias for the main study outcome of invasive disease free survival.
What Are The Results?
Our Question

- **P:** 50 yo woman, breast cancer, ER-PR +, HER2 - recurrence score 17
- **I:** Hormone Tx ONLY
- **C:** Hormones + Chemo
- **O:** Recurrence, mortality
- **T:** Therapy
- **T:** RCT

Patient’s question

- Should I get chemo?
- Treatment questions: Y/N
Our Question

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GOAL: Ask focused questions that can be answered by studies

Patient’s question

- Should I get chemo?
- Treatment questions: Y/N
Our Questions

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GOAL: Ask questions that can be answered by studies

Patient’s questions

- Should I get chemo?
- Treatment questions: Y/N

GOAL: Action (we treat or don’t treat; there is no fence)
A. Based on this paper, should I get (or have gotten) chemotherapy? (Therapy)
• We are at the point of considering principles to use to link evidence to action

• GRADE framework can help us…
# LINKING EVIDENCE TO ACTION: GRADE principles for clinical decision making

## Quality of the Evidence (or confidence in evidence or certainty of estimates of effect)

<table>
<thead>
<tr>
<th>Quality of a Body of Evidence</th>
<th>Synonyms and related concepts</th>
<th>Categories for Quality of a Body of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk of Bias</td>
<td>Validity</td>
<td>High</td>
</tr>
<tr>
<td>Imprecision</td>
<td>Confidence Intervals, Random error</td>
<td>Moderate</td>
</tr>
<tr>
<td>Indirectness</td>
<td>Generalizability, (PICO), indirect comparisons of effectiveness</td>
<td>Low</td>
</tr>
<tr>
<td>Inconsistency</td>
<td>Heterogeneity of results between studies, forest plots</td>
<td>Very Low</td>
</tr>
<tr>
<td>Publication Bias</td>
<td>Unreported (hidden) studies; funnel plots</td>
<td></td>
</tr>
</tbody>
</table>

*Randomized trials start high and observational studies start low; then quality rating can be decreased or increased.*

## Factors that contribute to determining the Strength of Recommendations

| Balance between desirable and undesirable effects | A larger difference (benefits >> harms or harms >> benefits) favors a strong recommendation |
| Quality of the evidence                           | Higher quality evidence favors a strong recommendation |
| Values and Preferences                             | High variability or greater uncertainty in values and preferences favors a conditional recommendation |
| Resource use (costs)                              | Higher costs favor a conditional recommendation |

## Recommendation

<table>
<thead>
<tr>
<th>Evidence To Action</th>
<th>For</th>
<th>Against</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Strong</td>
<td>“Just do it”</td>
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<tr>
<td></td>
<td>Conditional</td>
<td>“It depends”</td>
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<td></td>
<td>Preference sensitive</td>
<td>Should apply to most people and circumstances</td>
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LINKING EVIDENCE TO ACTION: GRADE principles for clinical decision making (individual trial)

<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>Elements of Quality for an Individual Trial</strong></td>
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| A larger difference (benefits >> harms or harms >> benefits) favors a strong recommendation |
| Higher quality evidence favors a strong recommendation |
| High variability or greater uncertainty in values and preferences favors a conditional recommendation |
| Higher costs favor a conditional recommendation |

Recommendation | Strength of Recommendation
--- | ---
Evidence To Action For | Conditional | “It depends” | Preference sensitive
Against | Strong | “Just do it” | Should apply to most people and circumstances
<table>
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### Factors that contribute to determining the Strength of Recommendations

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</tr>
<tr>
<td>Resource use (costs)</td>
<td>Higher costs favor a conditional recommendation</td>
</tr>
</tbody>
</table>
(GRADE PAPER based on a body of evidence)

**WARNING**: be very careful when making a single recommendation.

(If a single paper is for a body of evidence where **Recommendation** is for a single paper)
Linking Evidence to Action Worksheet

Patient: 50-year-old with breast cancer, 2 lesions in the right breast: 1) 2.3 cm; and 2) 0.9 cm
- Hormone receptor (ER/PR) positive / Human epidermal growth factor receptor-2 (HER-2) negative
- Recurrence Score based on 21-gene breast cancer assay: Recurrence Score 17
- Treatment: Lumpectomy, Axillary Node dissection (neg), Radiation Tx, Tamoxifen (did not receive chemo)
- Menstrual history: periods irregular, + intermittent hot flashes, labs: FSH 27.7 (There is a 90% likelihood that she is perimenopausal)

LP’s Questions when we reviewed the paper

A. Based on this paper, should I get (or have gotten) chemotherapy? (Therapy question)

<table>
<thead>
<tr>
<th>Considerations:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Results including balance of desirable / undesirable effects</td>
</tr>
<tr>
<td>Quality of Evidence: High, Moderate, Low, Very Low</td>
</tr>
<tr>
<td>Values, preferences</td>
</tr>
<tr>
<td>Costs</td>
</tr>
</tbody>
</table>

**Recommendation:**
Yes (recommendation for chemotherapy) or No (recommendation against chemotherapy):
Conditional ("it depends") or Strong ("just do it"):

B. Should I remove my ovaries to decrease cancer recurrence? (Therapy question)

<table>
<thead>
<tr>
<th>Considerations:</th>
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</thead>
<tbody>
<tr>
<td>Results including balance of desirable / undesirable effects</td>
</tr>
<tr>
<td>Quality of Evidence: High, Moderate, Low, Very Low</td>
</tr>
<tr>
<td>Values, preferences</td>
</tr>
<tr>
<td>Costs</td>
</tr>
</tbody>
</table>

**Recommendation:**
Yes (recommendation for chemotherapy) or No (recommendation against chemotherapy):
Conditional ("it depends") or Strong ("just do it"):
**LP’s Questions when we reviewed the paper**

A. *Based on this paper, should I get (or have gotten) chemotherapy?* (Therapy question)

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</tbody>
</table>

**Recommendation:**

- Yes (recommendation for chemotherapy) or **No** (recommendation against chemotherapy):
- **Conditional** (“it depends”) or **Strong** (“just do it”):
**Main Result:** No Difference

**IDFS:** Hazard Ratio 1.08 (0.94-1.24)

**RDS:** Hazard Ratio 1.10 (0.85-1.41)
Exploratory Subgroup Analysis

Interactions according to subgroup in the cohorts with a recurrence score of 11 to 25

We performed exploratory analyses to determine whether any subgroups might have derived some benefit from chemotherapy in the intention-to-treat population, with a focus on covariates that were prognostic or associated with greater benefit from chemotherapy, such as younger age (Section 6F and Fig. S11 in the Supplementary Appendix). There were no significant interactions between chemotherapy treatment and most of the prognostic covariates examined, including recurrence-score category (either 11 to 15 vs. 16 to 20 vs. 21 to 25, or 11 to 17 vs. 18 to 25), tumor size (≤2 cm vs. >2 cm), histologic grade (low vs. intermediate vs. high), clinical risk category (high vs. low), and menopausal status (pre- vs. postmenopausal). There were significant interactions between chemotherapy treatment and age (≤50 vs. 51 to 65 vs. >65 years) for invasive disease-free survival (P=0.03) and for freedom from recurrence of breast cancer at a distant or local-regional site (P=0.02) but not at a distant site (P=0.12). The effect of treatment also varied significantly over the six combinations of menopausal status and recurrence-score category (11 to 15 vs. 15 to 20 vs. 21 to 25) (P=0.02) and over the nine combinations of age and recurrence-score category (P=0.004) for invasive disease-free survival (Figs.
Supplement 1

Subgroup Analysis:
This subgroup did better

IDFS: Hazard Ratio
1.9 (1.27-2.84)
A. *Based on this paper, should I get (or have gotten) chemotherapy?* (Therapy question)

**Considerations:**
- Results including balance of desirable / undesirable effects
- Quality of Evidence: High, Moderate, Low, Very Low
- Values, preferences
- Costs

**Recommendation:**
- Yes (recommendation for chemotherapy) or **No** (recommendation against chemotherapy):
- **Conditional** (“it depends”) or **Strong** (“just do it”):
VOTE: Chemo Yes or No?
Make Recommendation

- YES
- OR
- NO

Conditional
- OR
- STRONG
SK and LP and LP’s oncologist: No Chemotherapy

NO

STRENGTH
B. Should I remove my ovaries to decrease cancer recurrence? (Therapy)
B. **Should I remove my ovaries to decrease cancer recurrence?** (Therapy question)

**Considerations:**
- Results including balance of desirable/undesirable effects
- Quality of Evidence: High, Moderate, Low, Very Low
- Values, preferences
- Costs

**Recommendation:**
- Yes (recommendation for chemotherapy) or **No** (recommendation against chemotherapy):
- **Conditional** (“it depends”) or **Strong** (“just do it”):
A total of 40% of women who were 50 years of age or younger had a recurrence score of 15 (a range of scores that was found in 46% of women in this age group). A greater treatment effect from adjuvant chemotherapy has been noted in younger women, which may be at least partly explained by an antiestrogenic effect associated with premature menopause induced by chemotherapy. We did not collect data on chemotherapy-induced menopause. It remains unclear whether similar benefits could be achieved with ovarian suppression plus an aromatase inhibitor instead of chemotherapy.
Tailoring Adjuvant Endocrine Therapy for Premenopausal Breast Cancer


BACKGROUND
In the Suppression of Ovarian Function and Exemestane Trial (TEXT), and the Suppression of Ovarian Function and Tamoxifen compared with Tamoxifen and Exemestane (SOFT) trial, ovarian suppression was significantly lower among premenopausal women compared with postmenopausal women. Women who received tamoxifen plus ovarian suppression had significantly lower recurrence rates than among those who received tamoxifen plus ovarian suppression. The addition of ovarian suppression to tamoxifen did not result in significantly lower recurrence rates than those with tamoxifen alone. Here, we report the updated results from the two trials.

METHODS
Premenopausal women were randomly assigned to receive 5 years of tamoxifen, tamoxifen plus ovarian suppression, or exemestane plus ovarian suppression in SOFT and to receive tamoxifen plus ovarian suppression or exemestane plus ovarian suppression in TEXT. Randomization was stratified according to the receipt of chemotherapy.
This figure contains data from McKinlay SM, Brambilla DJ, Posner JG (The normal menopause transition. *Maturitas*. 1992;14[2]:103-115), collected during the Massachusetts Women’s Health Study. This was a population-based study of 5547 women aged 45-55 years. The median age of onset of perimenopause was 47.5 years. By age 45 years, 40% of all women have started or completed menopause transition, and by age 50 years, 75% of women have started or completed the transition. By age 55 years, 98% of women are either perimenopausal or have completed the transition.
We are 90% certain: Perimenopausal

PRE
75% perimenopausal

POST
90% perimenopausal
B. *Should I remove my ovaries to decrease cancer recurrence?* (Therapy question)

**Considerations:**
- Results including balance of desirable / undesirable effects
- Quality of Evidence: High, Moderate, Low, Very Low
- Values, preferences
- Costs

**Recommendation:**
- Yes (recommendation for chemotherapy) or No (recommendation against chemotherapy):
- Conditional (“it depends”) or Strong (“just do it”):
VOTE: Remove ovaries Yes or No?
Make Recommendation

YES

OR

NO

Conditional

OR

STRONG
SK and LP / disagreement among other providers: no ovary removal

Conditional

NO
Phone call

Will you care for me?
To Kick OFF A GREAT Week

• Approach this week
  • Unafraid
  • Step out of your comfort zone
  • Never lose sight of the humanity
Thank you

• Please fill in your evaluations