

**PATIENT OUTCOMES ASSOCIATED WITH
BREAST CANCER TREATMENT AND RECURRENCE:
FOCUS ON PATIENT-REPORTED OUTCOMES &
QUALITY OF LIFE**

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FDA Advisory Committee Meeting

November 7, 2024

Disclosures

- Grants- NIH/NCI, the Breast Cancer Research Foundation
- Royalties-Up-to-Date section editor on Survivorship
- Consultant- Genentech/Roche
- Advisory Board-InformedDNA
- DSMB-Astellas

Presentation Outline

- Historic data on quality of life (QOL) after breast cancer treatments
- How have things changed?
- What is early stage, low risk breast cancer?
- QOL data in this population
- Impact of cancer recurrence on QOL

Quality of Life: Conceptual Model

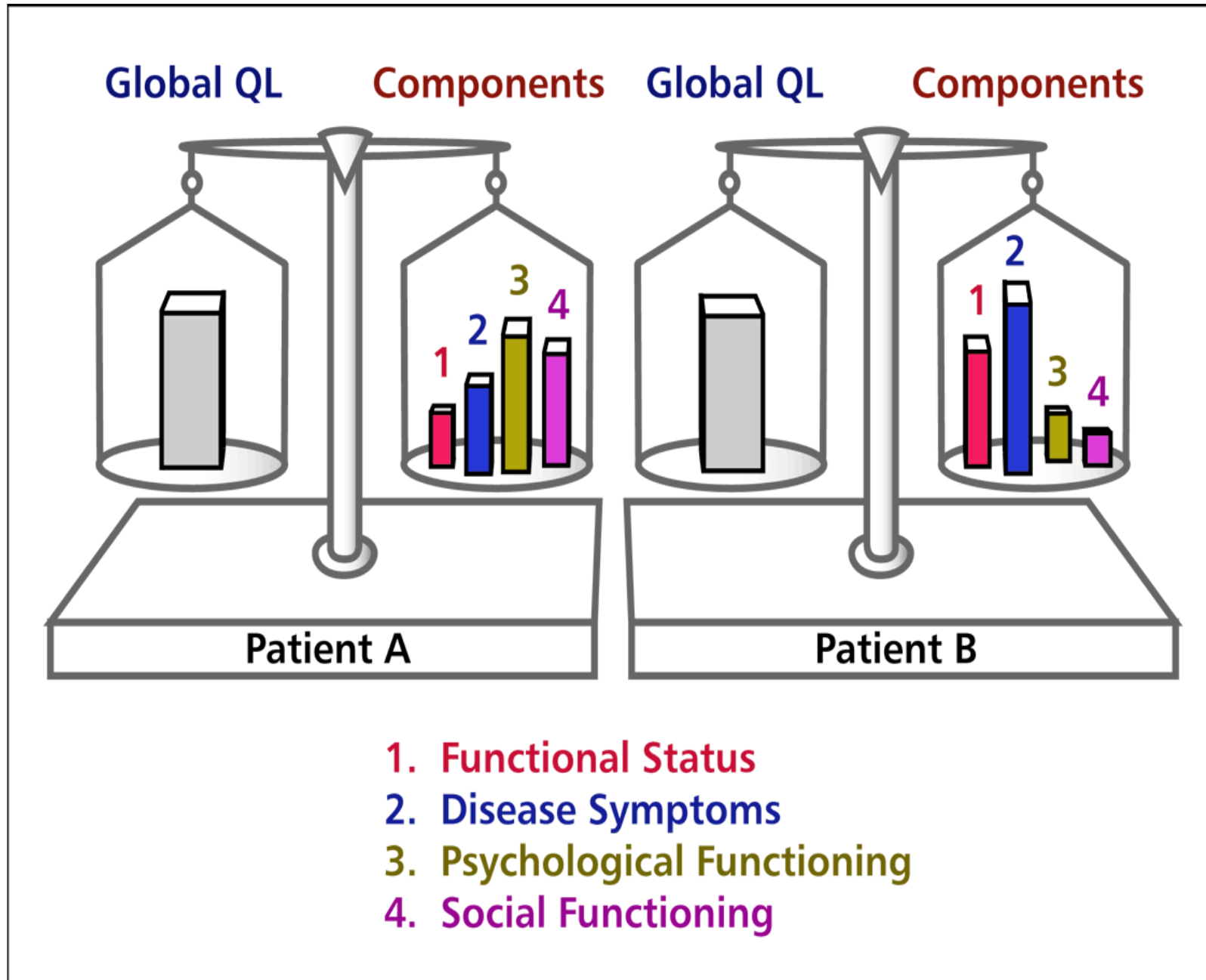


Circa 1990

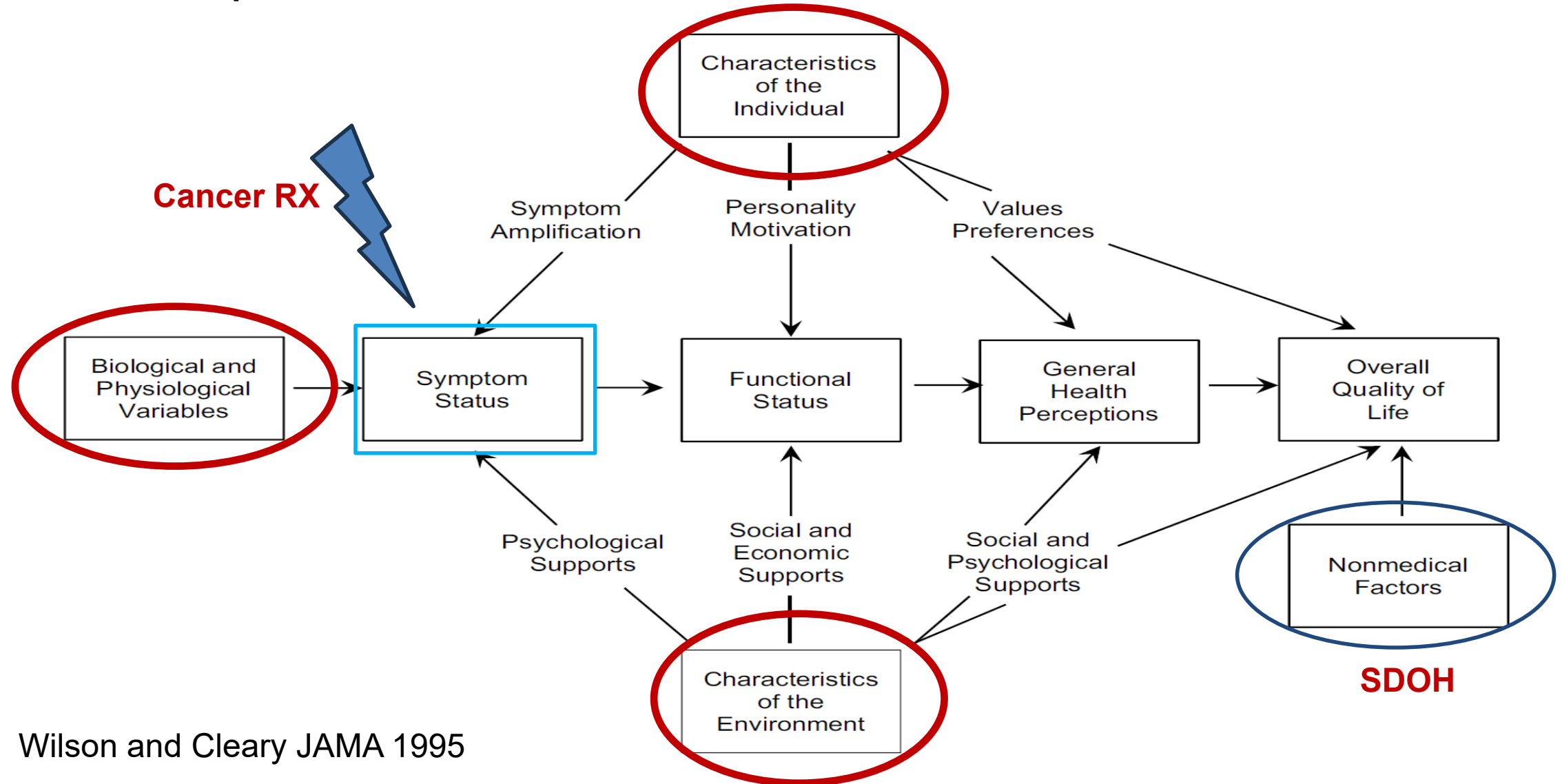
Health-related Quality of Life Dimensions

- Physical Functioning
- Occupational/Role Functioning
- Social Functioning
- Emotional Well-being
- Symptom Status
- Financial Concerns
- Spirituality
- Future Orientation
- Sexuality/Intimacy
- Health Concerns/Worries
- Family Well-Being
- Satisfaction w/Care

Global/Overall Perception of Quality of Life



Linking Clinical Variables With Health-Related Quality of Life: A Conceptual Model of Patient Outcomes.





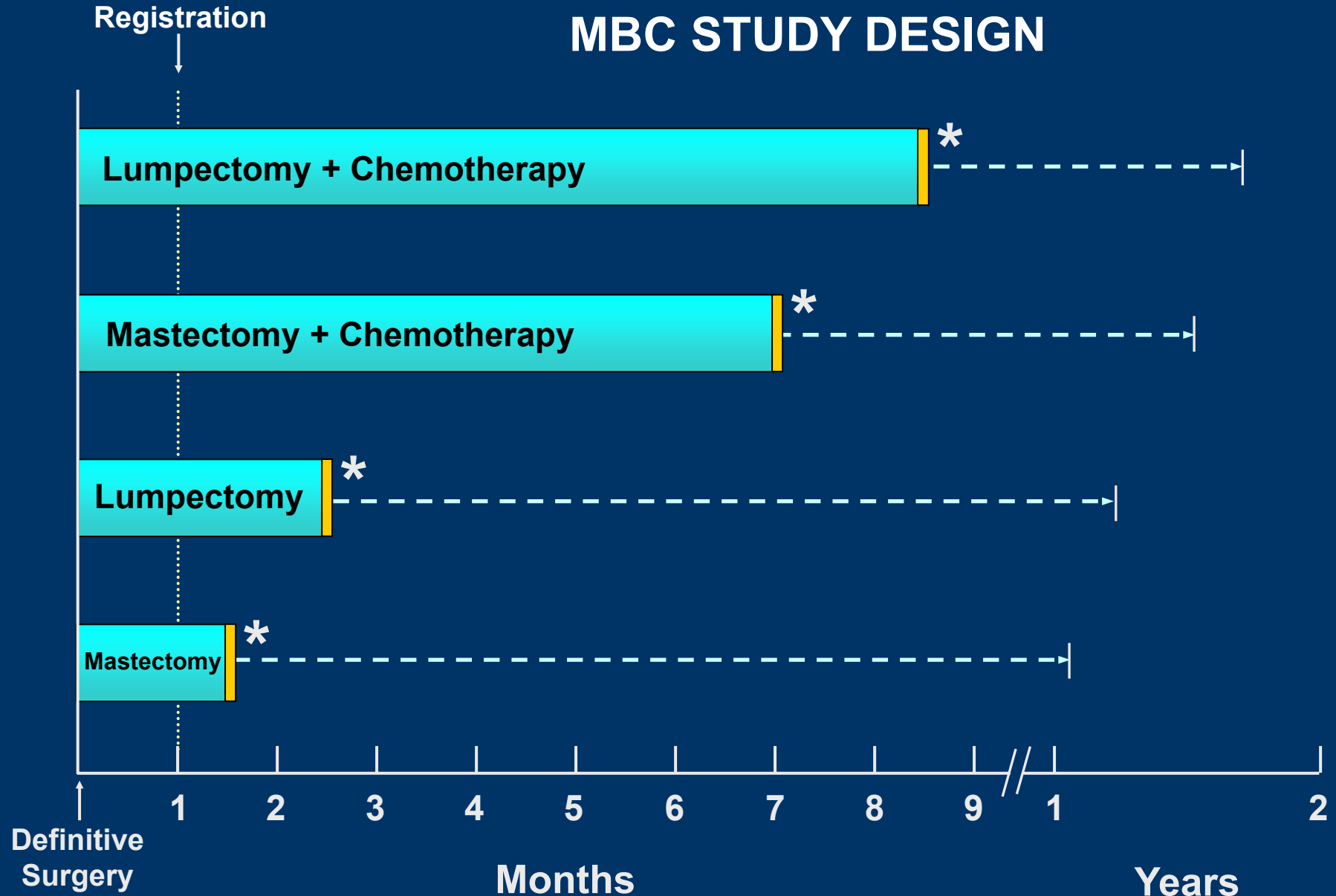
Moving Beyond Cancer (MBC):
**QOL at the end of primary breast
cancer treatment—and thereafter**

NCI R01 CA63028

The MBC Psychosocial Intervention Trial

Ganz et al., JNCI 2004; Stanton et al., JCO, 2005

MBC STUDY DESIGN



Concerns voiced by women at the end of treatment....

- How will I know if my treatments worked?
- When will I get my energy back?
- What is the follow-up plan now that my treatments are over?
- Does this new ache mean that the cancer is coming back?
- Why does my family think that everything is okay now when I know it isn't?
- **MBC was a randomized trial testing three different interventions to help prepare patients for survivorship at the end of primary treatment.**

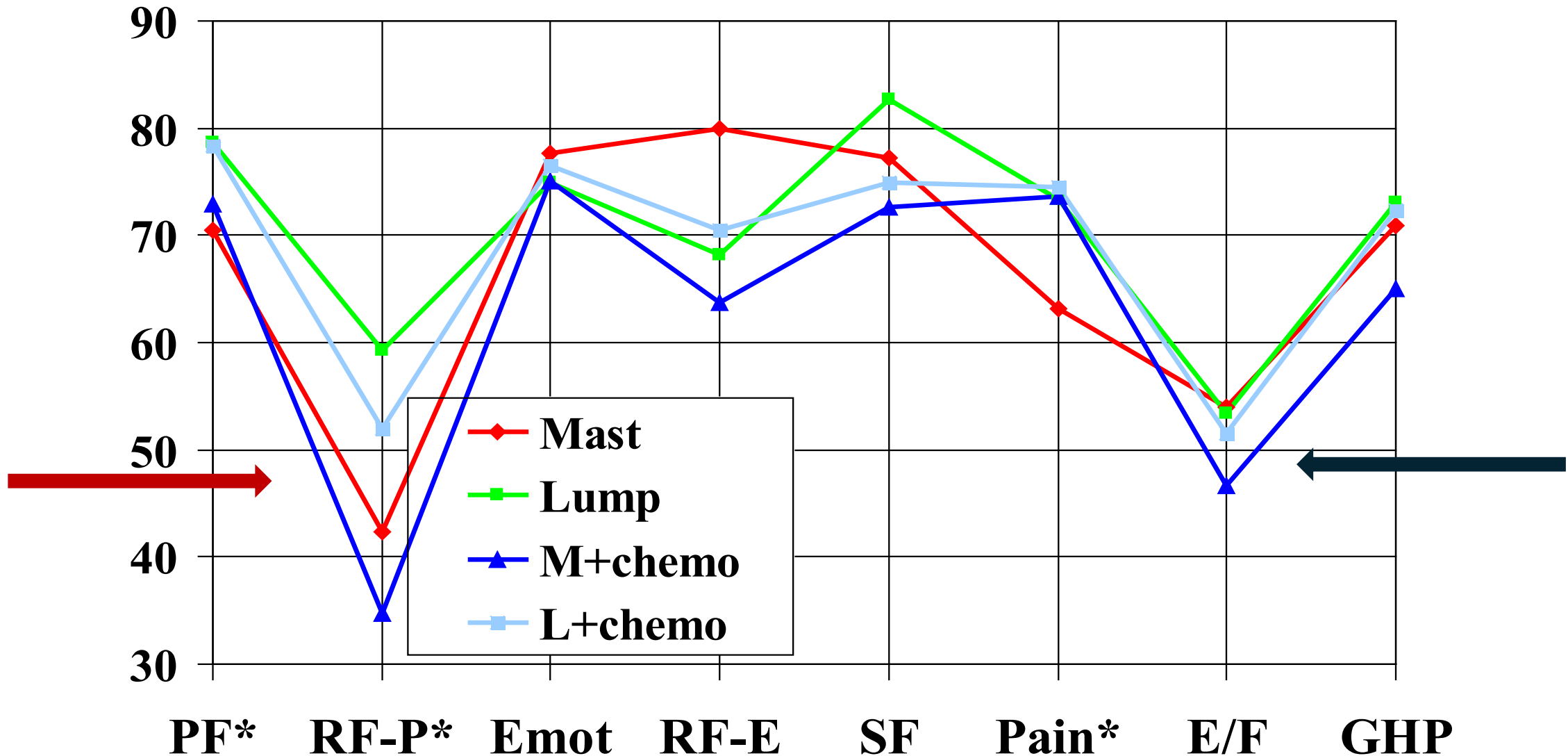
Subject Recruitment

- From offices of surgeons and medical oncologists
- Identified shortly after diagnosis, registered, and then tracked until treatment completed
- Geographic diversity: Los Angeles, Kansas, and Washington DC
- Total of 558 patients enrolled at the end of primary treatment; recruited between July 1, 1999, and June 30, 2002

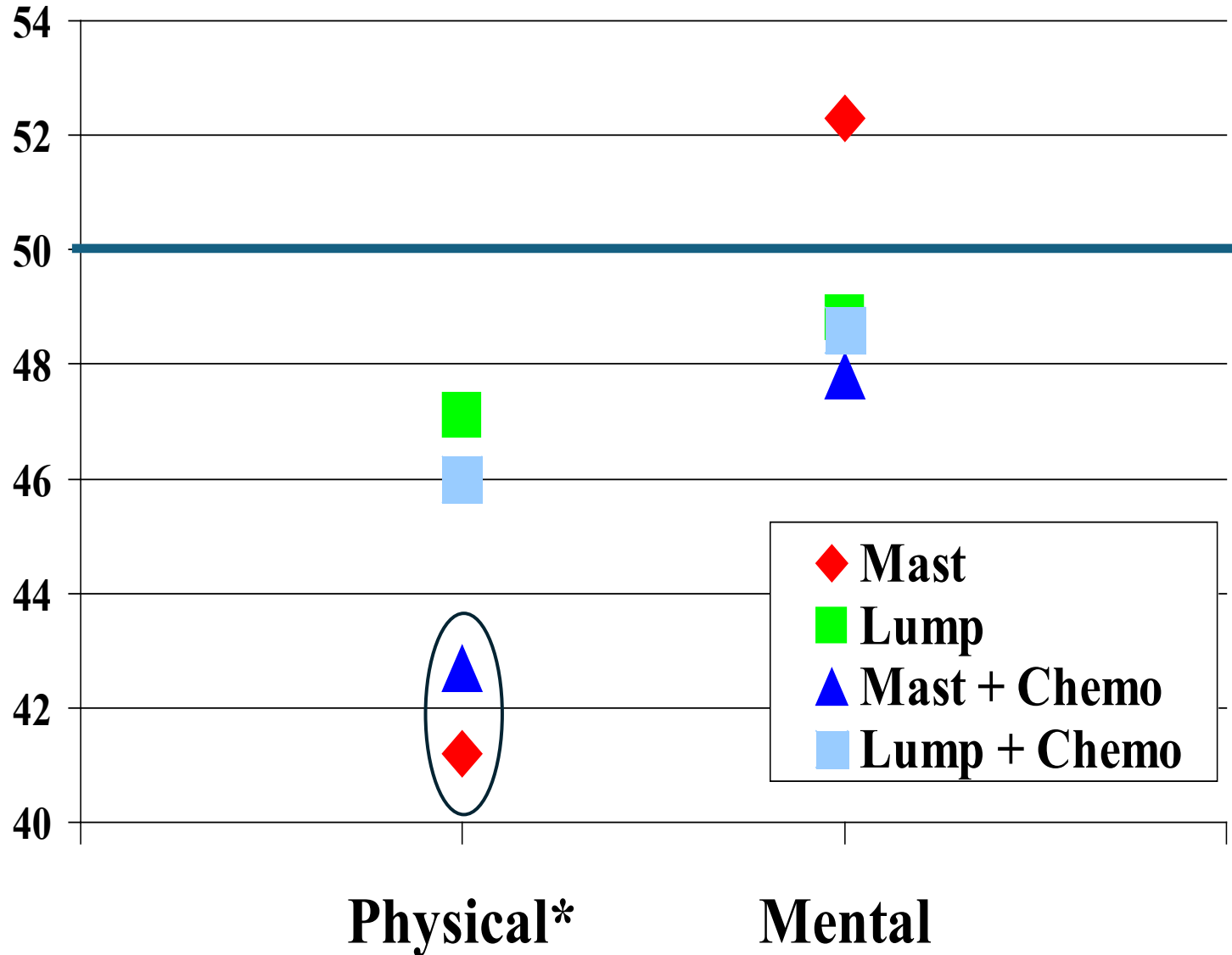
Characteristics of Sample at End of Treatment (N=558)

- Mean age 56.9 years
 - Mean days p/surgery 173.8
 - 86% white
 - 70% married
 - 57% working
 - 63% college graduate or higher
- LA =50%
 - DC =29%
 - Kansas =21%

SF-36 Subscale Scores at End of Treatment



SF-36 Component Summary Scales



* P < .001

Other Findings at the End of Primary Treatment

- Greater sexual problems and impact on sex life for women who received chemotherapy
- >50% of women report being **unhappy with appearance, hot flashes, aches & pains, forgetfulness, breast sensitivity, joint pains, muscle stiffness**
- These symptoms contribute significantly to decreased physical and mental health

How have things changed in the past 20 years?

- More than half of breast cancers are stage 0-1, are screen detected, and require minimal treatment
- Large tumors with more aggressive biological features require extended complex treatments for up to 18 months
- Adjuvant endocrine therapy is given for 5-10 years, including ovarian function suppression for 5 years in younger women
- Quality of life domains (physical, emotional, social well-being) largely return to pre-treatment function, but symptoms persist in about 25%--**fatigue, neuropathy, pain, cognitive complaints, depression, anxiety, vasomotor symptoms.**

What is Early Stage, Low Risk Breast Cancer?

- No textbook definition
- Clinical considerations: small size, low grade, hormone receptor positive, HER2 negative
- How has this been conceptualized in recent clinical trials?

Long-term primary results of accelerated partial breast irradiation after breast-conserving surgery for early-stage breast cancer: a randomised, phase 3, equivalence trial



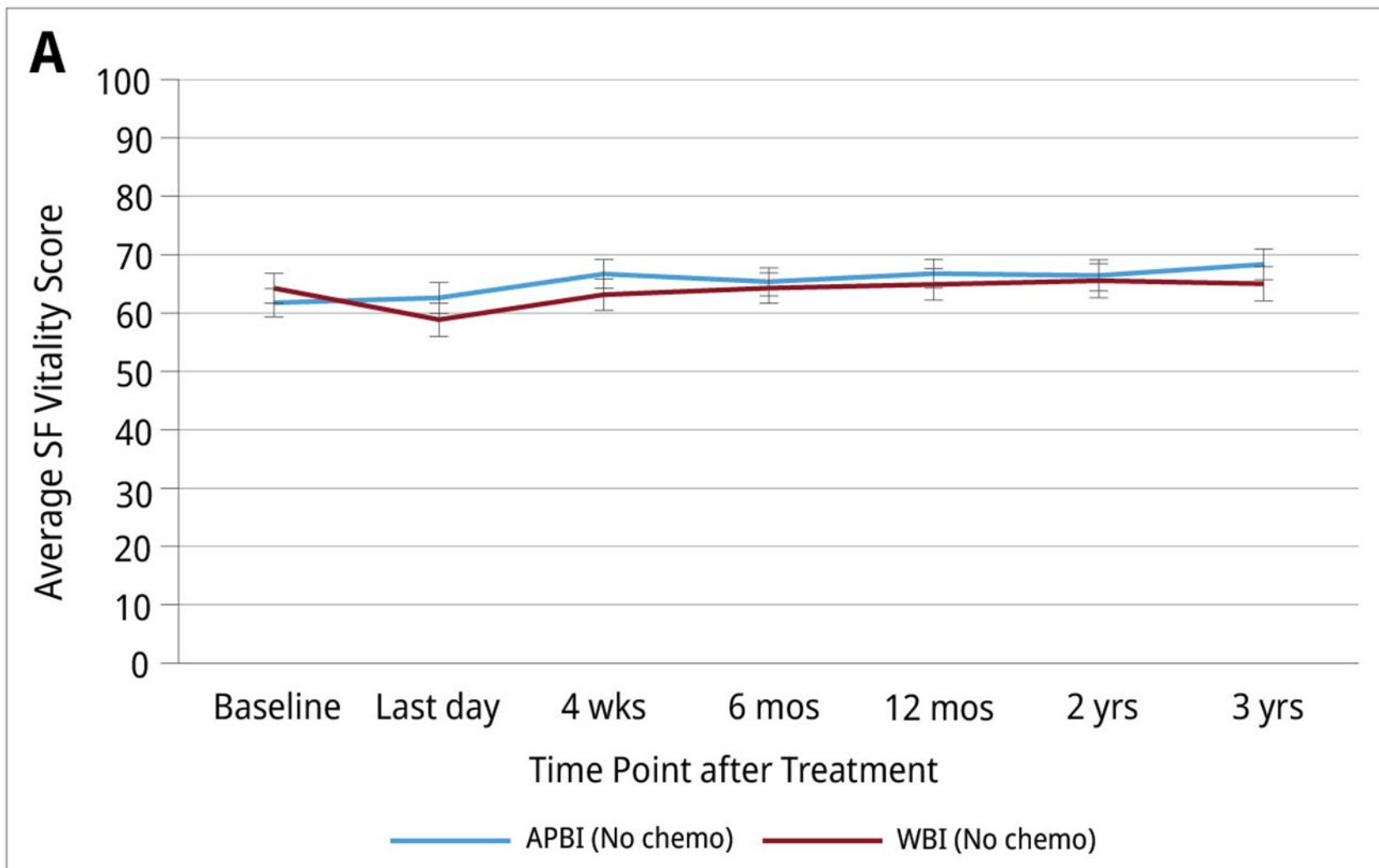
Frank A Vicini, Reena S Cecchini, Julia R White, Douglas W Arthur, Thomas B Julian, Rachel A Rabinovitch, Robert R Kuske, Patricia A Ganz, David S Parda, Michael F Scheier, Kathryn A Winter, Soonmyung Paik, Henry M Kuerer, Laura A Vallow, Lori J Pierce, Eleftherios P Mamounas, Beryl McCormick, Joseph P Costantino, Harry D Bear, Isabelle Germain, Gregory Gustafson, Linda Grossheim, Ivy A Petersen, Richard S Hudes, Walter J Curran Jr, John L Bryant, Norman Wolmark*

Lancet 2019; 394: 2155–64

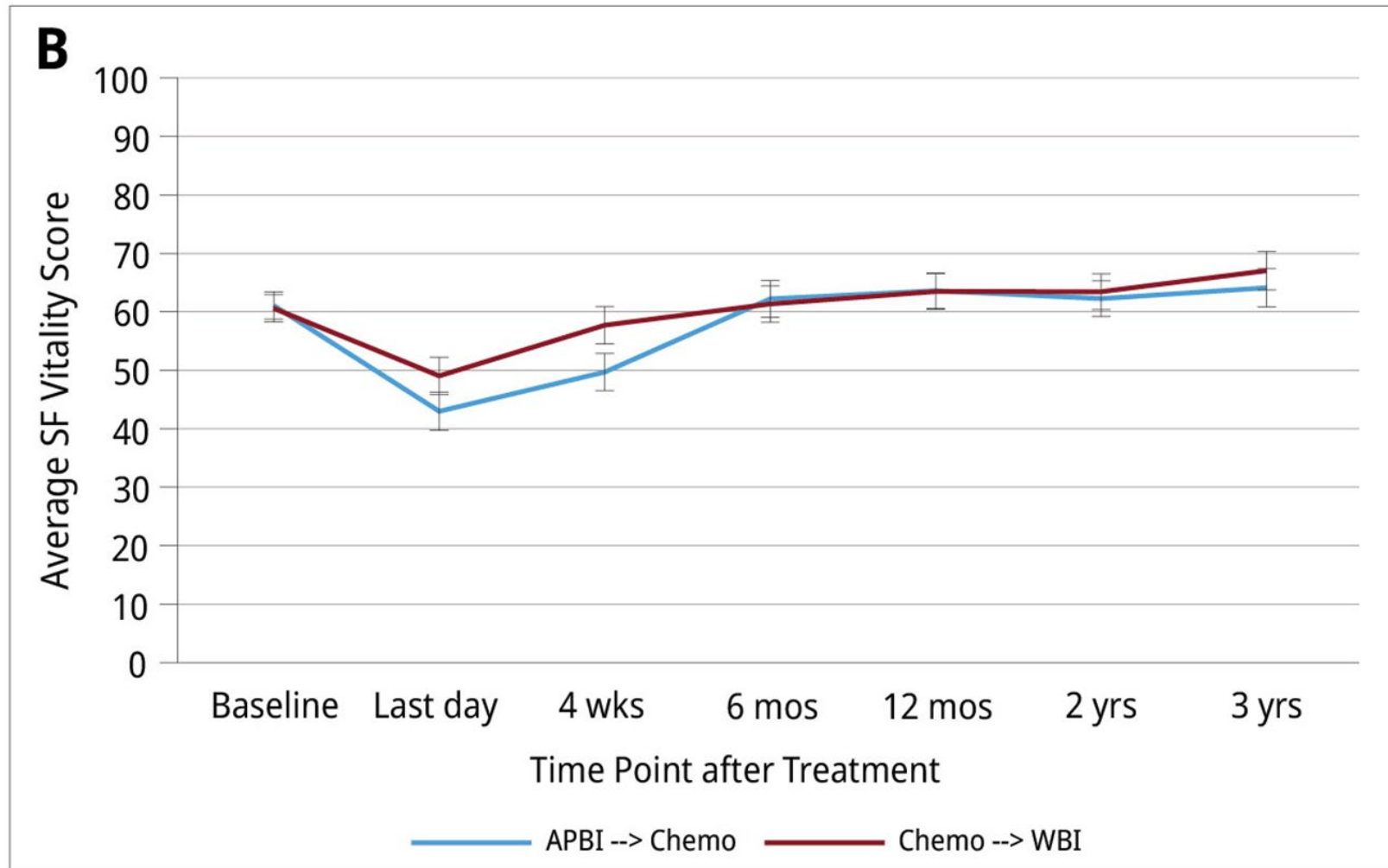
Adult women (>18 years) with early-stage (0, I, or II; no evidence of distant metastases, but up to three axillary nodes could be positive) breast cancer (tumour size ≤ 3 cm; including all histologies and multifocal breast cancers), who had had lumpectomy with negative (ie, no detectable cancer cells) surgical margins, were randomly assigned (1:1) using a biased-coin-based minimisation algorithm to receive either whole-breast irradiation (whole-breast irradiation group) or APBI (APBI group).

Every patient received radiation therapy, and some received chemotherapy and/or endocrine therapy as indicated.

Pattern of Fatigue after Lumpectomy with RT in Follow-up



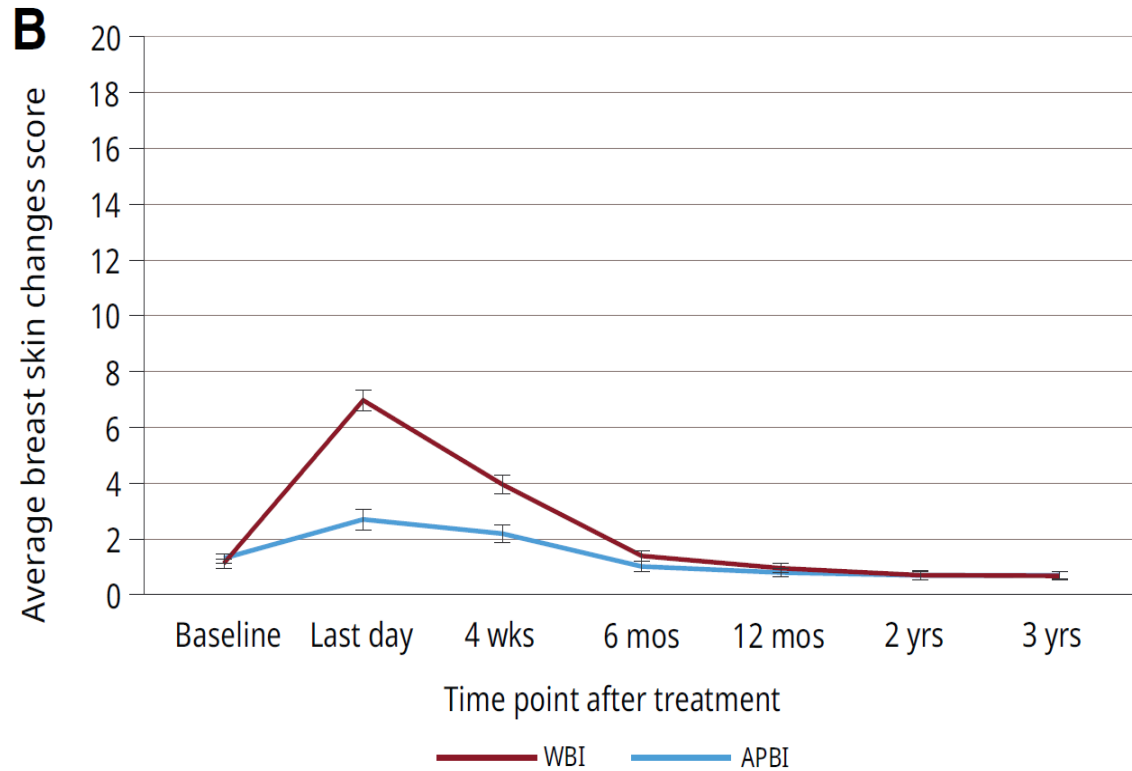
Pattern of Fatigue after Lumpectomy, RT, and Chemotherapy



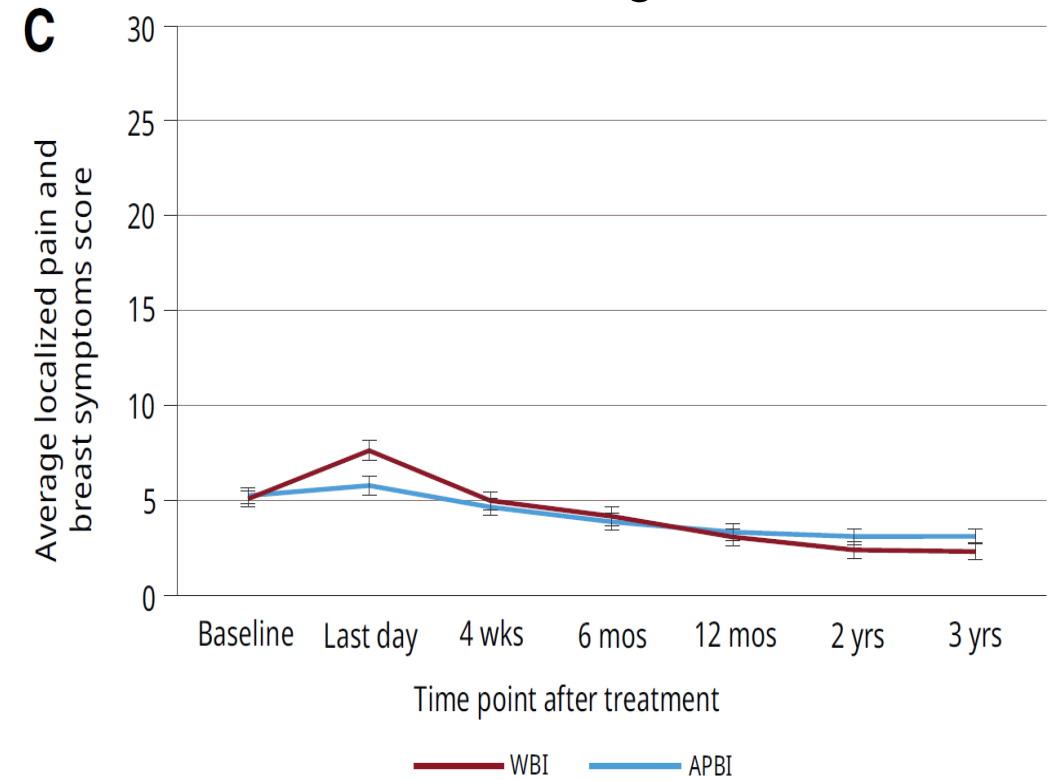
Skin Changes and Localized Pain & Breast Symptoms in NSABP B-39

Higher Score is Worse

Skin Changes-Score Range 0-20



Local Pain and Breast Symptoms Score Range 0-32



NRG-BR007: A PHASE III CLINICAL TRIAL EVALUATING DE-ESCALATION OF BREAST RADIATION FOR CONSERVATIVE TREATMENT OF STAGE I, HORMONE SENSITIVE, HER2-NEGATIVE, ONCOTYPE RECURRENCE SCORE ≤ 18 BREAST CANCER

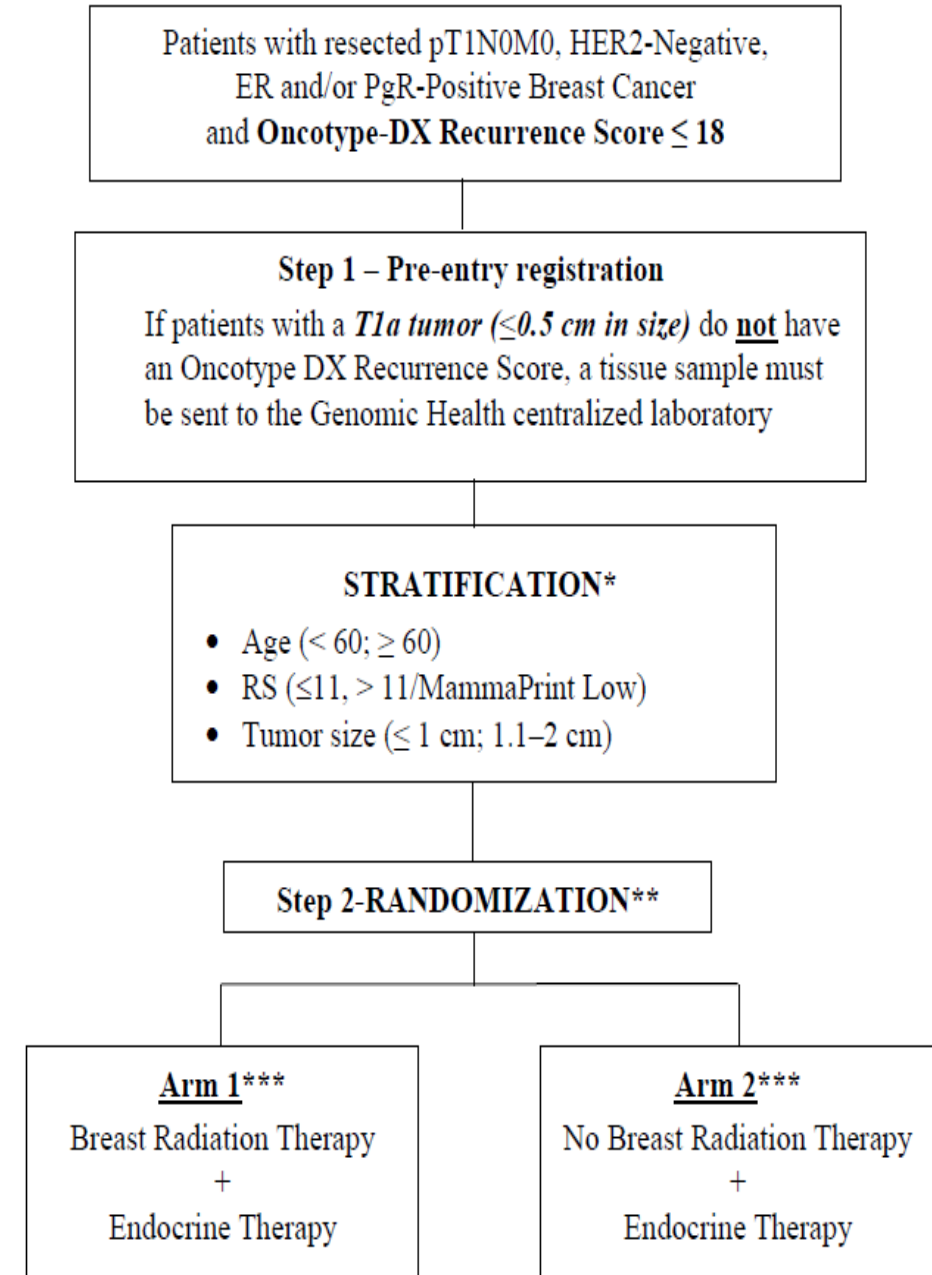
(DEBRA*)

* *DE-escalation of Breast Radiation (DEBRA)*

ClinicalTrials.gov Identifier NCT#04852887

NCI Version Date: (October 20, 2023)

- **Contemporary view of low risk—features:**
 - T1N0, up to 2 cm in size; DCIS excluded
 - Required to be hormone receptor positive/HER2-negative
 - Use of a genomic classifier to determine risk for recurrence
 - Experimental arm omits radiation therapy



BR-007 Objectives

- Primary Objective: Is omission of radiation therapy with endocrine therapy non-inferior to treatment with radiation therapy and endocrine therapy?
- Selected Secondary Objectives:
 - To evaluate whether there is a difference in patient-reported breast pain in women who do and do not receive breast radiation.
 - To evaluate whether there is a difference in patient-reported worry about recurrence in women who do and do not receive breast radiation.
- Other assessments: QOL and Breast Related Symptoms

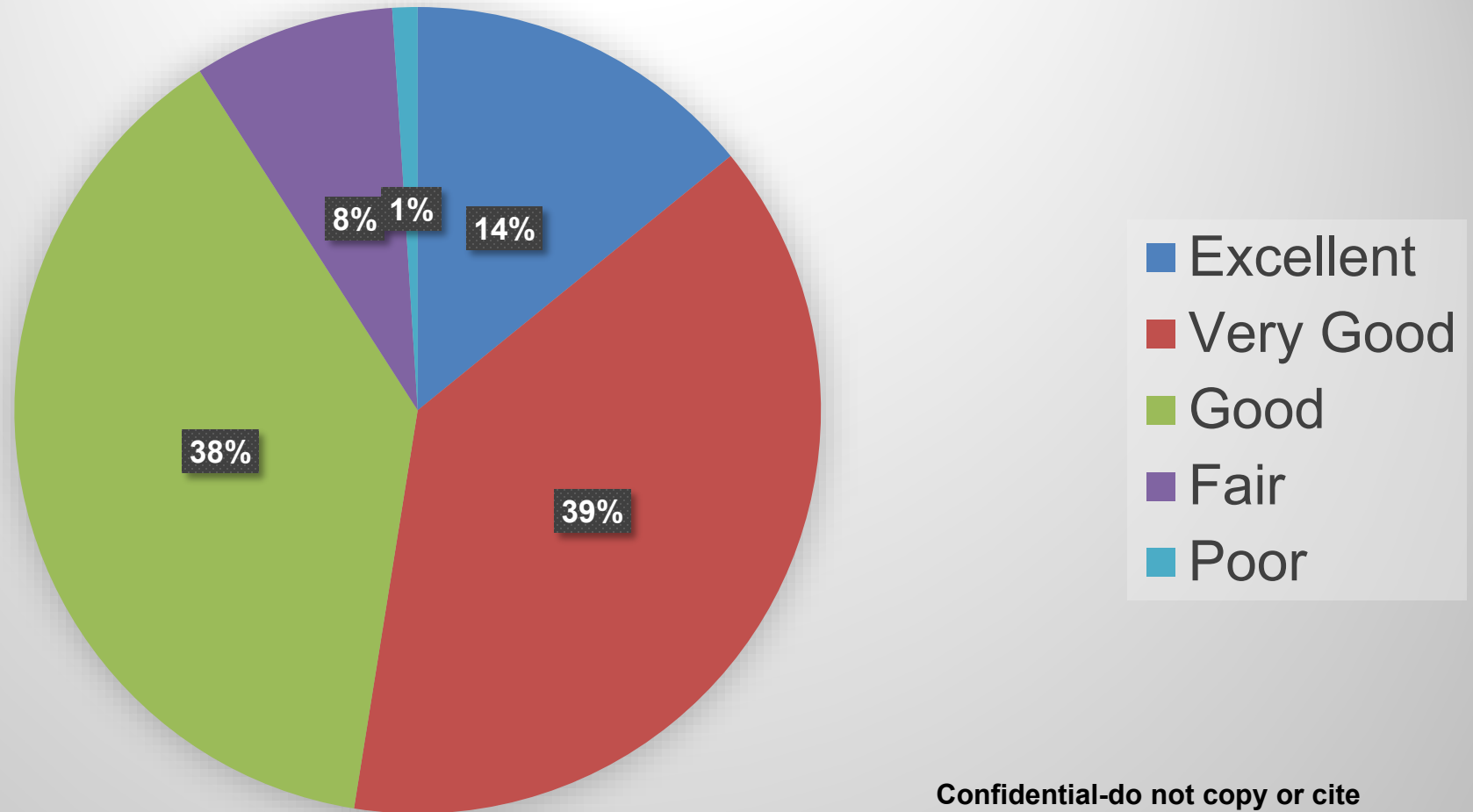
Patient Characteristics in BR-007 QOL Study N=310

Variable	
Age: median and range (yrs)	62 (50-69)
Race/Ethnicity	...
Asian	9 (2.9%)
Black of African Am	16 (5.2%)
White	275 (88.7%)
Other, unknown, not reported	10 (3.3%)
Hispanic or Latino	12 (3.9%)
Tumor Size	...
0.11-0.50 cm (T1a)	45 (14.5%)
0.51-1.00 cm (T1b)	126 (40.6%)
1.05-2.00 cm (T1c)	139 (44.8%)

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In general, would you say your health is.....

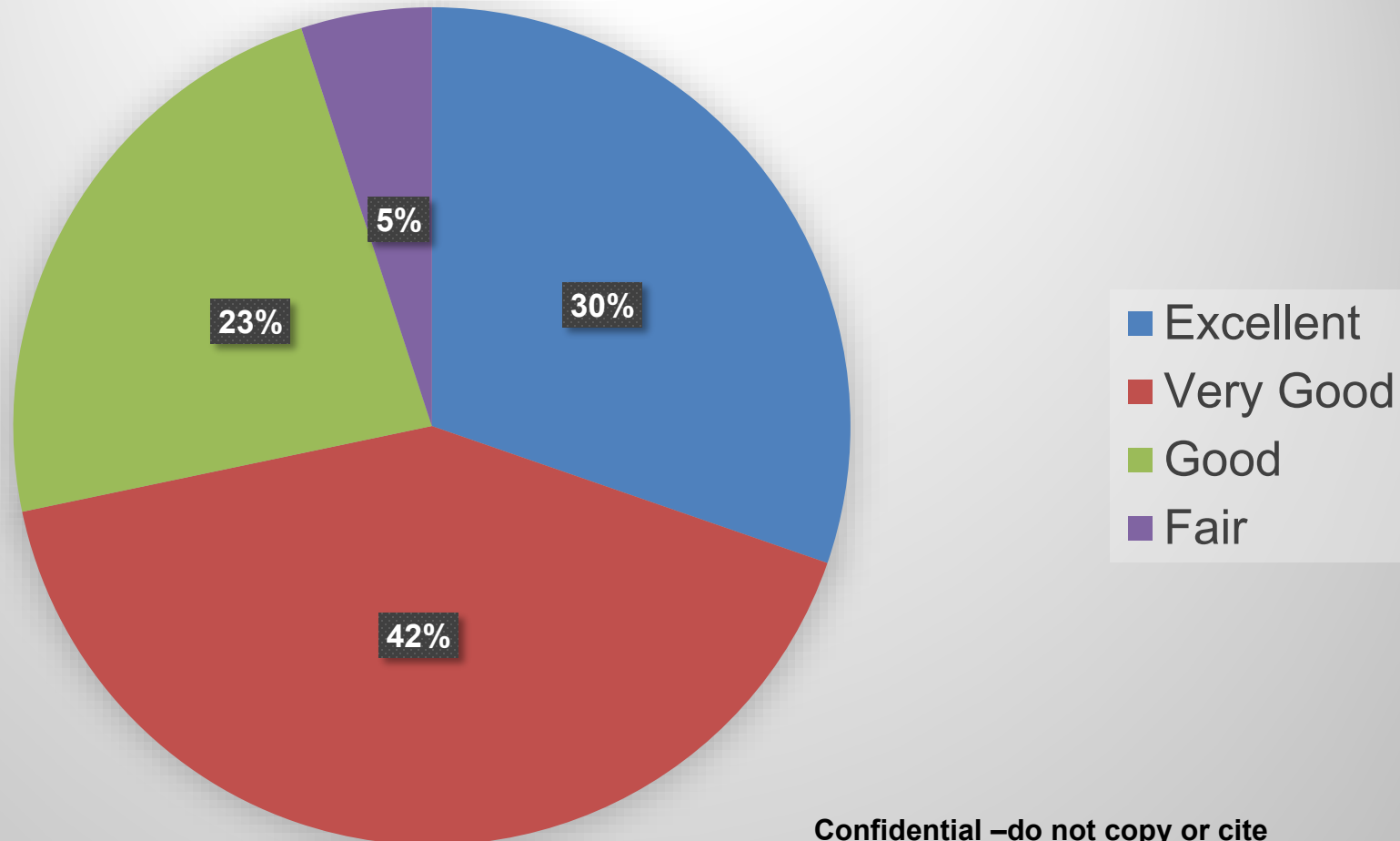
BR-007 Patients after Lumpectomy



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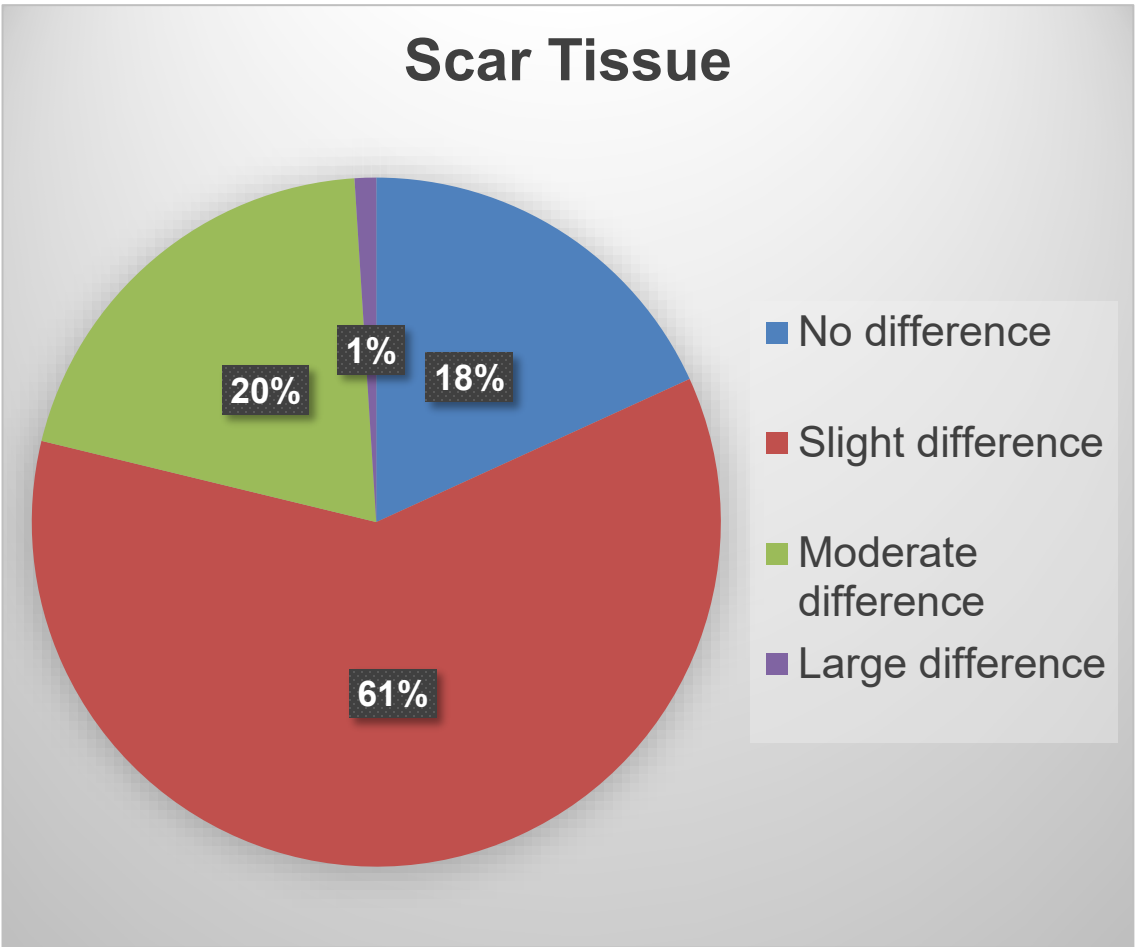
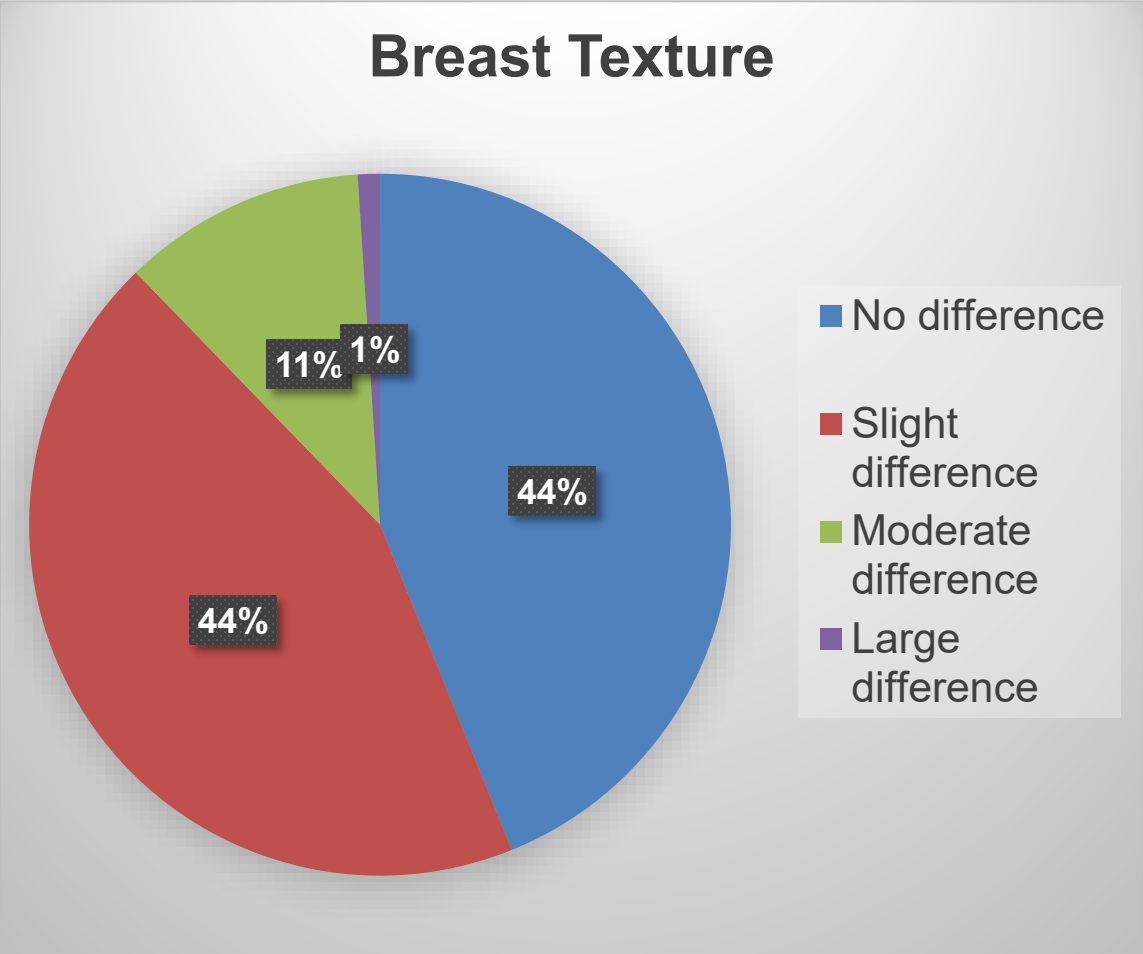
In general, would you say your quality of life is....

BR-007 Patients after Lumpectomy



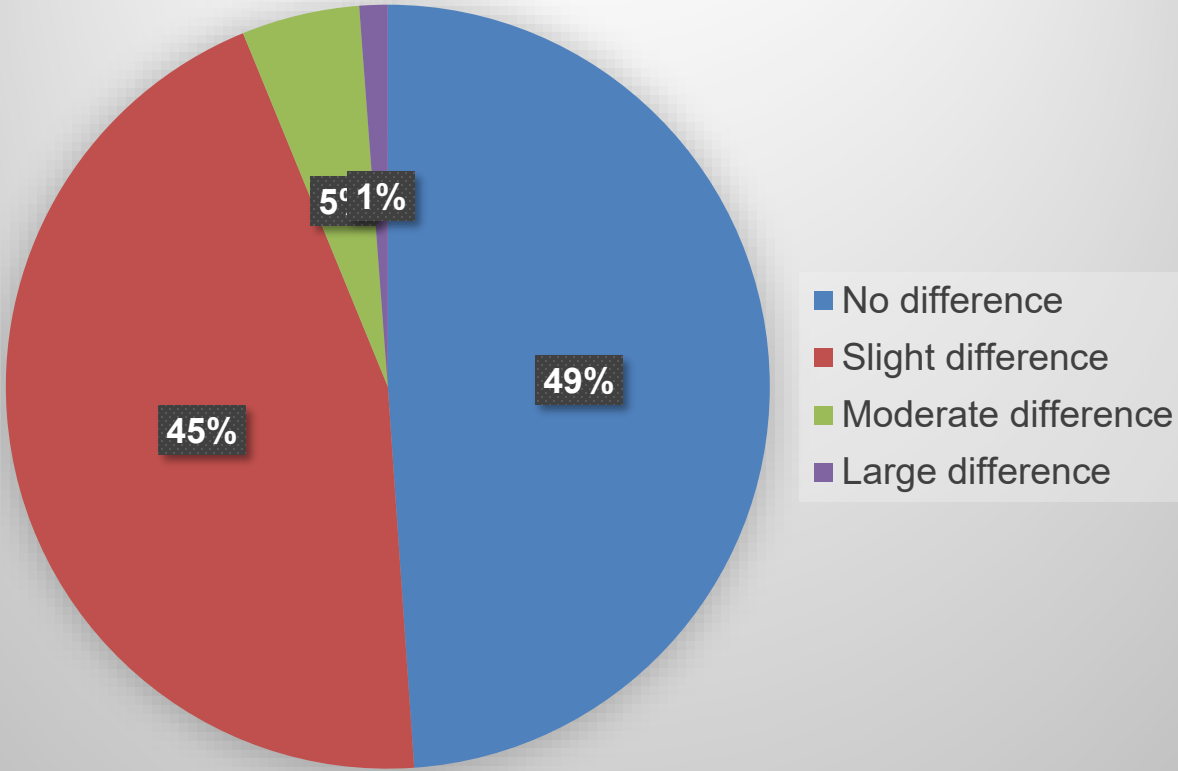
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Breast Cosmesis: affected breast compared to untreated breast

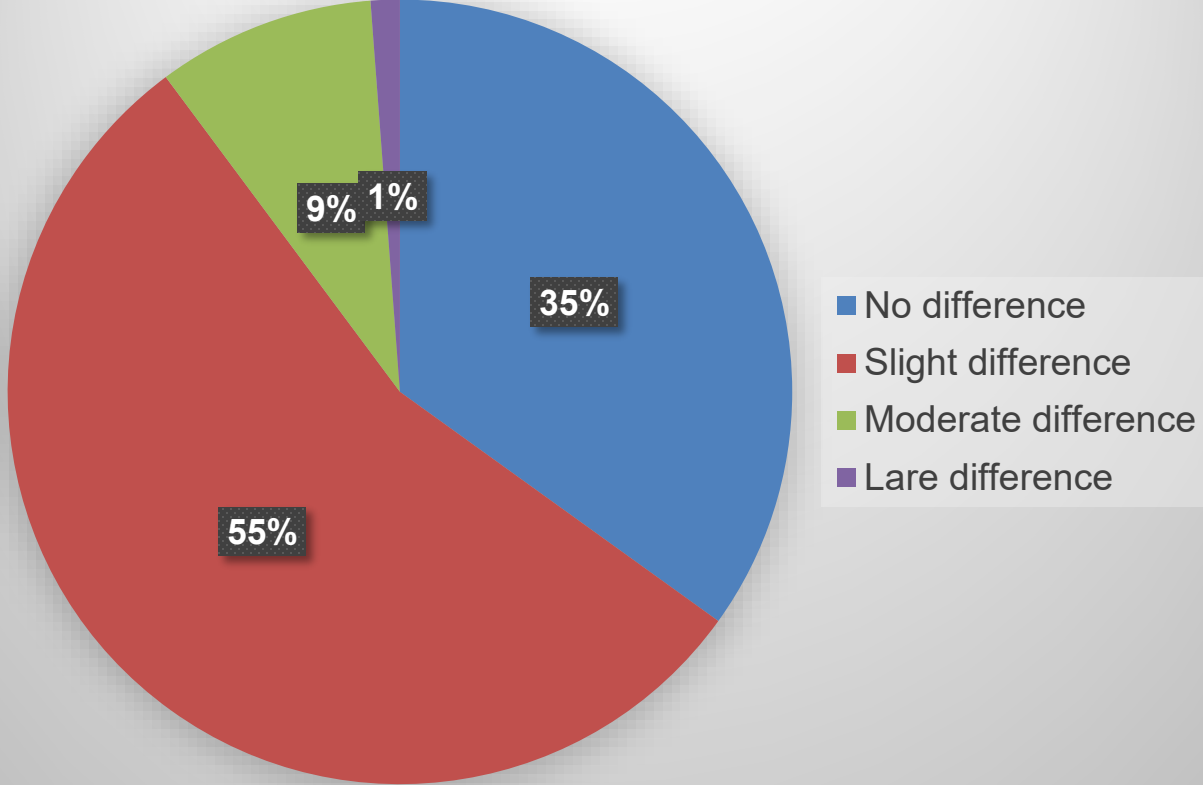


Breast Pain: affected breast compared to untreated breast

Breast Pain



Breast Tenderness



What happens when cancer recurs?

Recurrence can be isolated to the breast/chest wall
Occur in distant metastatic sites
Or, both local and distant metastatic sites

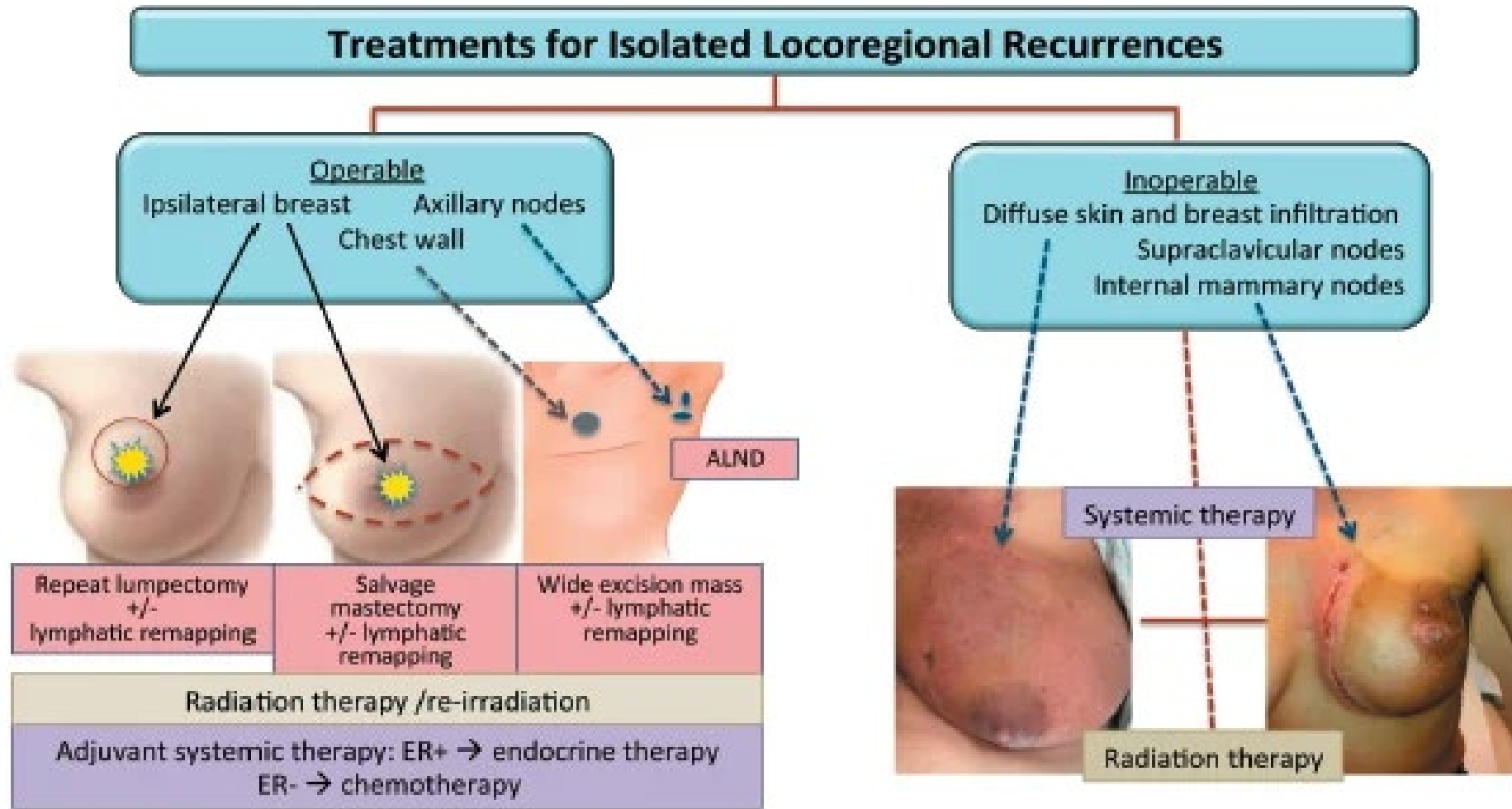


FIGURE 2 Surgical and Adjuvant Treatments for Isolated Locoregional Recurrences of Breast Cancer.

ALND = axillary lymph node dissection; ER = estrogen receptor.

What do we know about QOL after breast cancer recurrence?

Experience and predictors of symptoms, distress and health-related quality of life over time in postmenopausal women with recurrent breast cancer

Elisabeth Kenne Sarenmalm^{1,2*}, Joakim Öhlén², Anders Odén³ and Fannie Gaston-Johansson^{3,4}

- 56 women with breast cancer recurrence in Sweden, followed longitudinally for 6 months after diagnosis
- Compared with baseline, all outcomes were improved by 6 months after recurrence

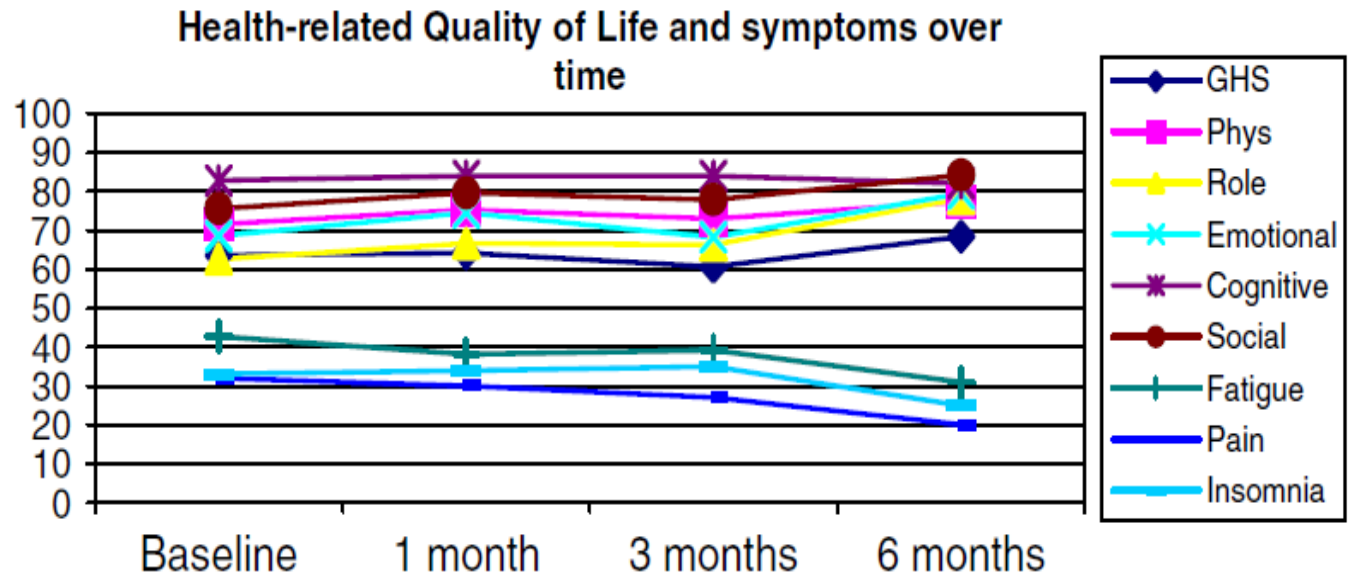


Figure 2. Mean scores of quality of life for 6 months of recurrent breast cancer disease

Quality of Life in Long-Term, Disease-Free Survivors of Breast Cancer: a Follow-up Study

JNCI 2002

Patricia A. Ganz, Katherine A. Desmond, Beth Leedham, Julia H. Rowland, Beth E. Meyerowitz, Thomas R. Belin

- Longitudinal follow of large cohort of breast cancer patients recruited between 1-5 years after diagnosis in Los Angeles and Washington DC in mid-1990s
- Follow-up survey offered to all patients more than 5 years after diagnosis to understand long-term survivorship issues
- 817 women completed the survey (61% response rate)
- 763 were disease-free survivors; average time since diagnosis was 6.3 years
- 54 (6.6 %) reported experiencing a recurrence of breast cancer either in the breast (n=32) or in a distant metastatic site (n=22)



Report

Quality of life of breast cancer survivors after a recurrence: a follow-up study

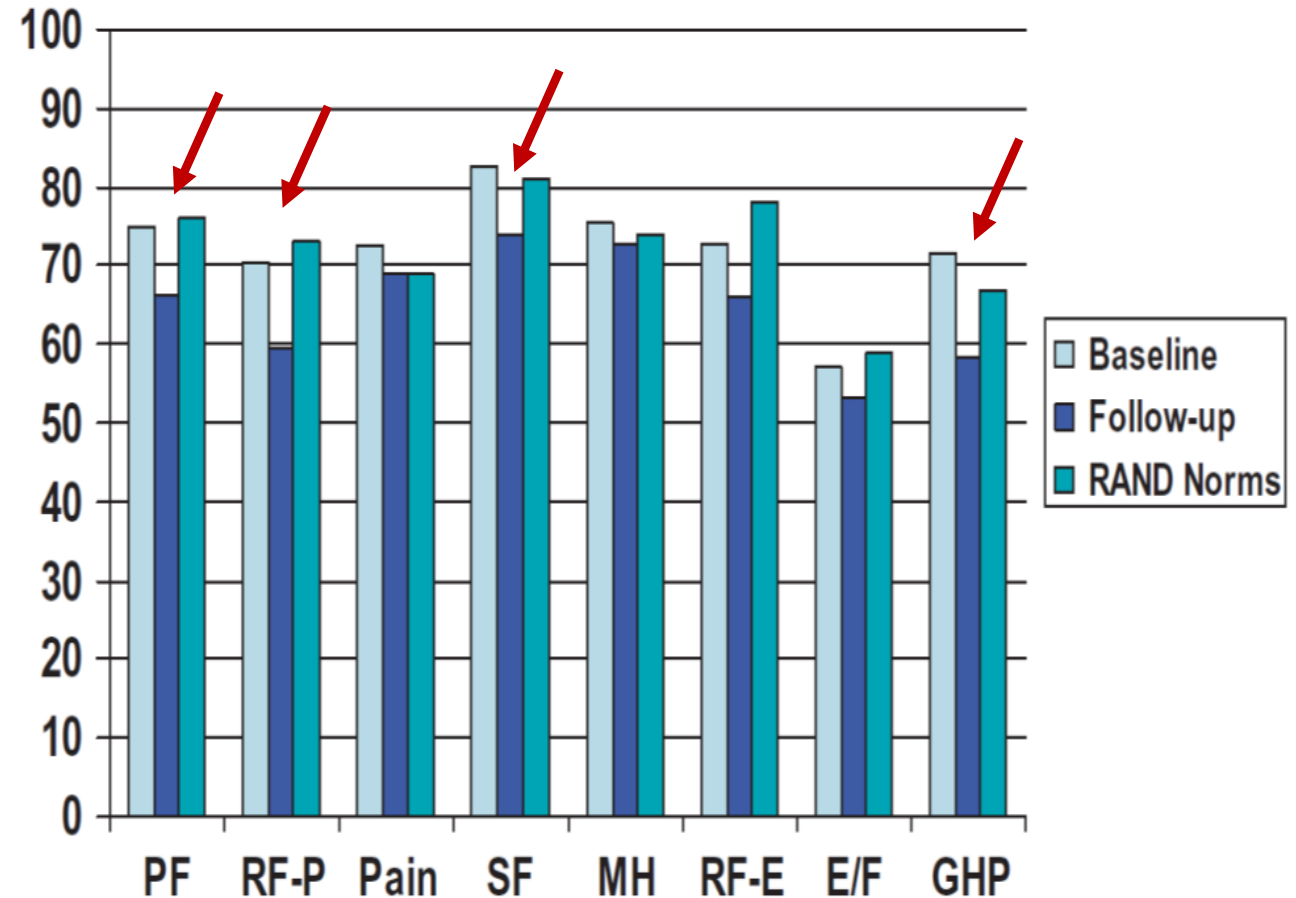
Sindy Oh¹, Lara Heflin¹, Beth E. Meyerowitz¹, Katherine A. Desmond²,
Julia H. Rowland³, and Patricia A. Ganz⁴

¹Department of Psychology, University of Southern California, Los Angeles, CA; ²Consultant; ³Office of Cancer Survivorship, Division of Cancer Control and Population Sciences, National Cancer Institute, Bethesda, MD; ⁴Schools of Medicine and Public Health, and the Jonsson Comprehensive Cancer Center, University of California, Los Angeles, CA, USA

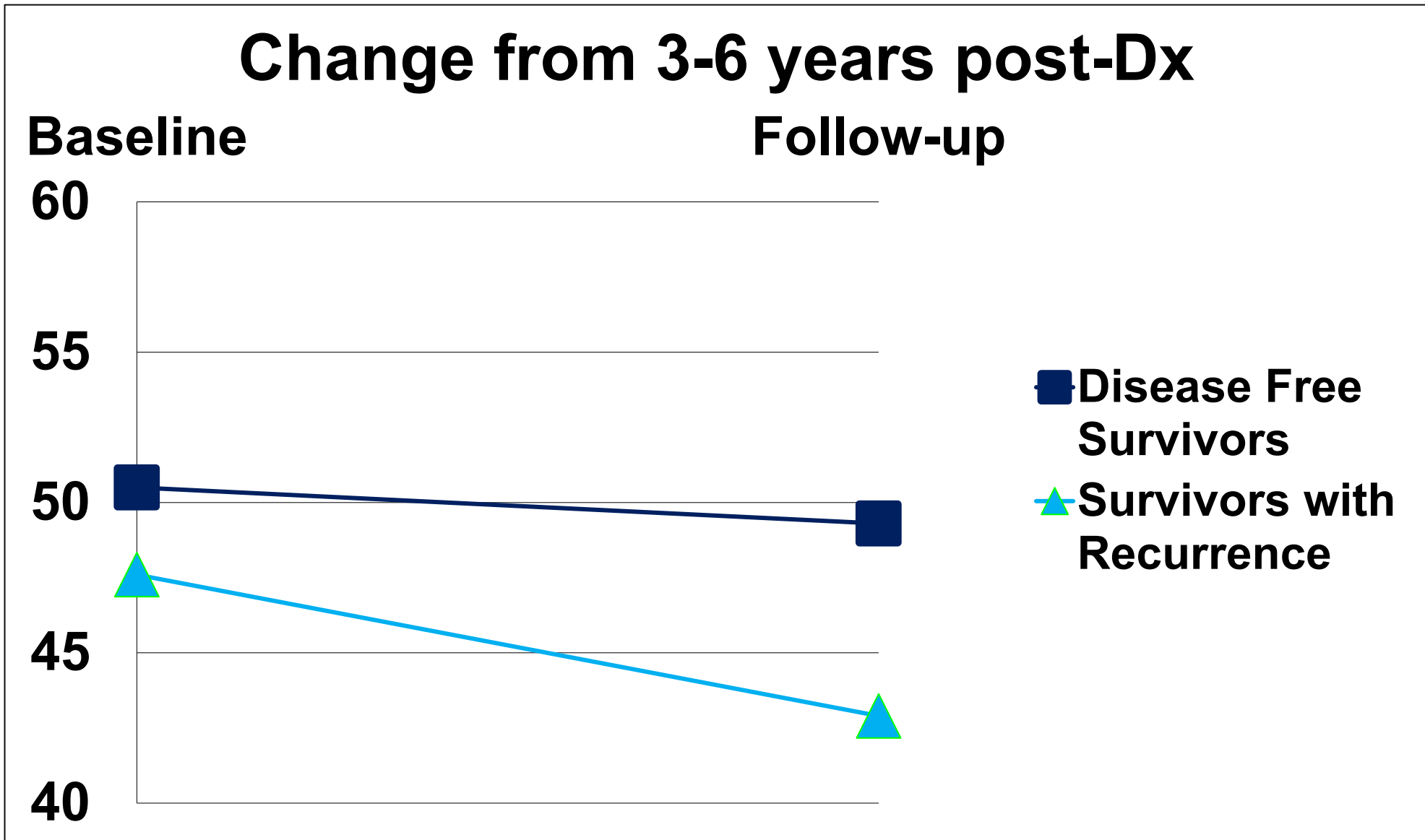
- Comparison of 54 breast cancer survivors with a recurrence at follow-up to a matched sample of 54 women who remained disease-free.
- Women with a recurrence reported significantly poorer functioning on various QOL domains compared to women who remained disease-free.
- Differences were largely due to the poorer QOL of women with metastatic disease.
- Women with recurrence reported good mood, low stress, and good quality of interpersonal relationships, but significantly higher cancer-specific stress compared to disease-free women at follow-up.

Results from Oh, et al. for Women with Recurrence

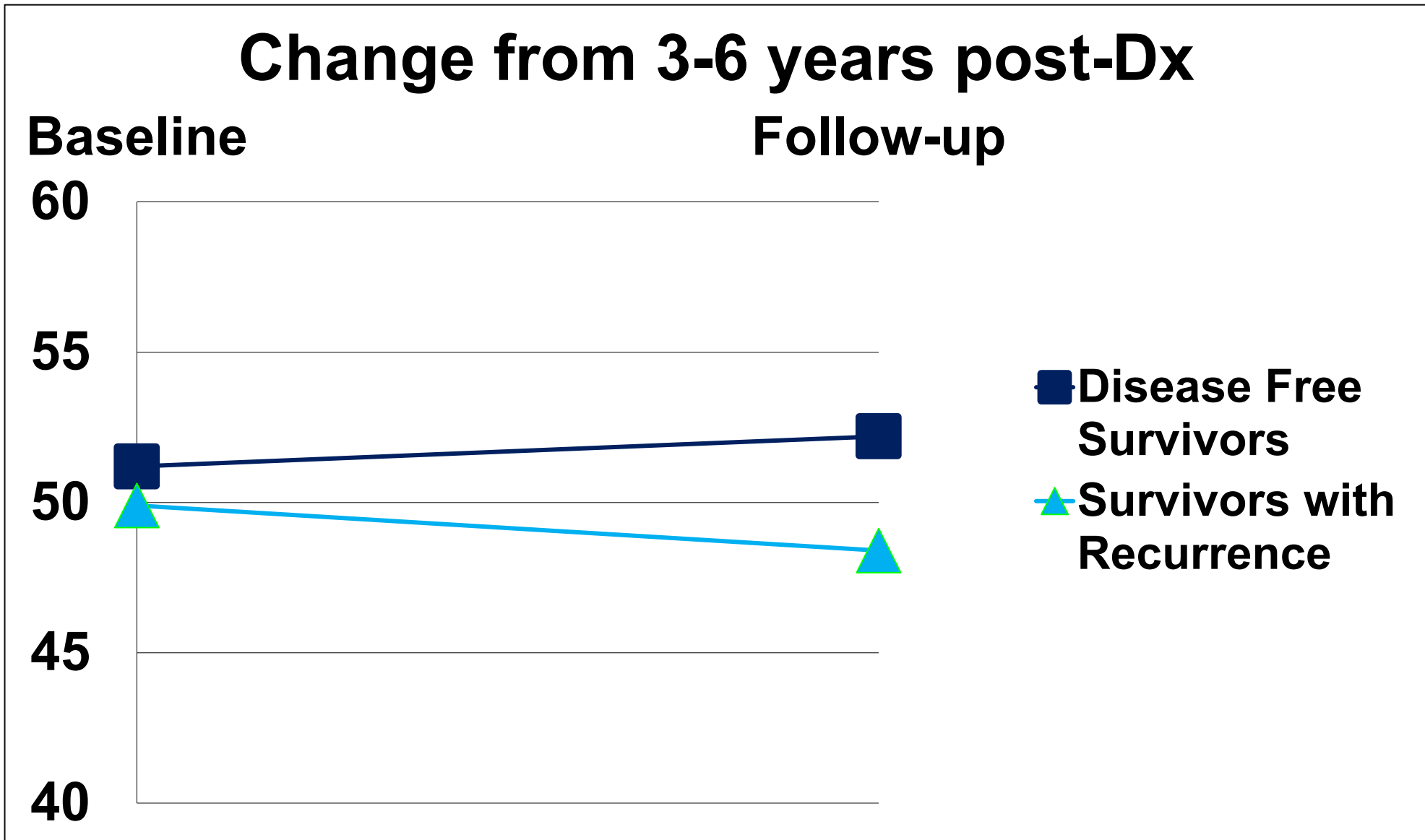
- Change in SF-36 scores between baseline and follow-up surveys for women with recurrent cancer
- RAND SF-36 norms as reference
- Compared to survivors without a recurrence, **statistically significant changes are in physical function, social functioning, general health perceptions**



SF-36 Physical Component Summary Scales



SF-36 Mental Component Summary Scales



Summary: Impact of Recurrence on QOL

- Symptoms are common at recurrence, and improve over 6 months of follow-up
- Patients with metastatic vs. local recurrence experience greater impact on QOL, especially physical functioning
- Measures of mental health/psychological functioning demonstrate resilience, although women with a recurrence have diminished health perceptions and may feel more vulnerable
- Personal observation: Most women with breast cancer recurrence report initial emotional distress; however, they know how to navigate the health care system, and have greater self-efficacy in getting the evaluation and clinical treatments that are needed.

Conclusions

- Most breast cancers today are small; diagnosed with mammographic screening
- Lumpectomy with clear margins is standard of care, usually followed by radiation therapy, of increasingly shorter duration
- Local breast symptoms after surgery are minimal with little impact on QOL
- Cancer recurrence is associated with decline in physical and social function, as well as poorer health perceptions
- Symptoms associated with recurrence (pain, fatigue, insomnia) primarily occur with distant metastatic disease
- Patients with recurrent breast cancer are generally psychologically resilient, unless there is an underlying history of depression or anxiety



Questions?