

# **Alcohol Consumption and Breast Cancer Hormone Receptors**

**Shelley M. Enger, Ph.D.**

**Research Scientist**

**Kaiser Permanente Medical Care Program**

**Southern California**



**KAISER PERMANENTE®**

# Postdoctoral Fellowship at the University of Southern California School of Medicine

Funded by the California Breast Cancer  
Research Program,  
1995 - 1997



KAISER PERMANENTE®

- ◆ Risk factors for breast cancer
- ◆ Alcohol and breast cancer
- ◆ Breast cancer hormone receptors
- ◆ Alcohol and breast cancer hormone receptors
- ◆ Future research topics



# Breast Cancer Risk Factors

- ◆ Hormonal
- ◆ Genetic
- ◆ Metabolic
- ◆ Other



# ALCOHOL CONSUMPTION



- ◆ Over 70 studies to date
- ◆ Significant and direct relationship
- ◆ Premenopausal and postmenopausal
- ◆ 7-9% increase in breast cancer risk for every 10 grams of alcohol (about  $\frac{3}{4}$  of a drink of alcohol) consumed per day

Howe G et al. Int J Cancer 1991;47:707-710.

Longnecker M. Cancer Causes Control 1994;5:73-82.

Smith-Warner S et al. JAMA 1998;279:535-540.

Singletary K et al. JAMA 2001;286:2143-2151.



KAISER PERMANENTE®

---

Does the type of alcoholic  
beverage matter???

---



# No, any will do.



KAISER PERMANENTE®

# So why does alcohol increase breast cancer risk?



# So why does alcohol increase breast cancer risk?

Several hypotheses:

- ◆ ↑ Circulating estrogens or androgens in premenopausal & postmenopausal women, especially postmenopausal women taking HRT
- ◆ ↑ Breast density
- ◆ ↓ Efficacy of cancer-protective factors (e.g., carotenoids, folate)
- ◆ ↓ Ability to detoxify harmful products of metabolism among people with certain genetic traits
- ◆ ↑ Risk of late stage breast cancer, recurrence and death



# What are hormone receptors and what do they do?

- ◆ They are molecules that can occur in the nucleus of breast cells (and other types of cells).
- ◆ They bind hormones like a lock and key (for example, ER binds estrogen, PR binds progesterone).
- ◆ The bound hormones stimulate the cells to divide and the breast tissue to grow.
- ◆ They are produced in response to the presence of circulating steroid hormones.



# Under what conditions are hormone receptors present in breast cells?

- ◆ They are present during periods of breast cell growth:
  - Puberty
  - Pregnancy and lactation
  - Malignancy
- ◆ Some breast malignancies depend on estrogen to promote breast cell division/tumor growth (ER+ cancers), and estrogen receptors are the target of hormone therapies like Tamoxifen. Some do not depend on estrogen (ER-).



# Why do we study breast cancer risk factors and breast cancer hormone receptors?

- ◆ To better understand how hormone-related risk factors influence breast cancer risk.
- ◆ To gain insight into the role of circulating hormones on breast cancer hormone receptor status
- ◆ To better understand the nature of breast cancer as defined by hormone receptor status – different stages or different diseases?



# Summary of all studies that examined the role of alcohol on breast cancer hormone receptor status

	<u>Number of studies</u>
↑ ER+ risk	5
↑ ER-	1
↑ ER+ and ER-	4
No associations	2

McTiernan et al. (1986); Cooper et al. (1989); Nasca et al. (1994); Potter et al. (1995); Yoo et al. (1997); Baumgartner et al. (2002); Britton et al. (2002); Sellers et al. (2002); Li et al. (2003); Cotterichio et al. (2003); Colditz et al. (2004); McDonald et al. (2004).



# Study Design

## Original studies:

Two population-based case-control studies of breast cancer: 55-64 year olds (PI: Ronald K. Ross, MD) and 40 year olds (PI: Leslie Bernstein, PhD)

## Present study:

Alcohol and Risk of Estrogen Receptor Positive Breast Cancer

*Principal Investigator:* Shelley M. Enger, Ph.D.

*Sponsor:* Leslie Bernstein, Ph.D.

*Study funded by California BCRP (1FB-034)*



# Eligibility Criteria (Original Study)

---

## Eligible subjects:

white/Hispanic, English-speaking,  
female residents of Los Angeles County,  
born in U.S., Canada, or Europe

**Cases:** Diagnosed with in situ  
or invasive breast cancer at ages  
55-69 yrs from 03/87-12/89 or at  
<41 yrs of age from 07/83-12/88

**Controls:** Individually  
matched to cases on birthdate  
(+/-3years), parity (younger women  
only), and neighborhood of residence



# Data Collection: Risk Factors (Original Study)

- ◆ Family history, reproductive and breastfeeding histories, height, weight, physical activity, oral contraceptive use, HRT, demographics
- ◆ Alcohol consumption:  
Participants were asked about the number of drinks of beer, wine, and liquor they consumed per day at ages 18, 25, 40 (for ages 55-64) and one year before diagnosis.



# Data Collection: ER/PR Status (Current Study)

- ◆ Los Angeles County Cancer Surveillance Program abstracts reviewed for ER/PR information. If missing, pathology records requested from hospital of diagnosis.
- ◆ Information on ER/PR status was available for about 2/3<sup>rd</sup> of the participants



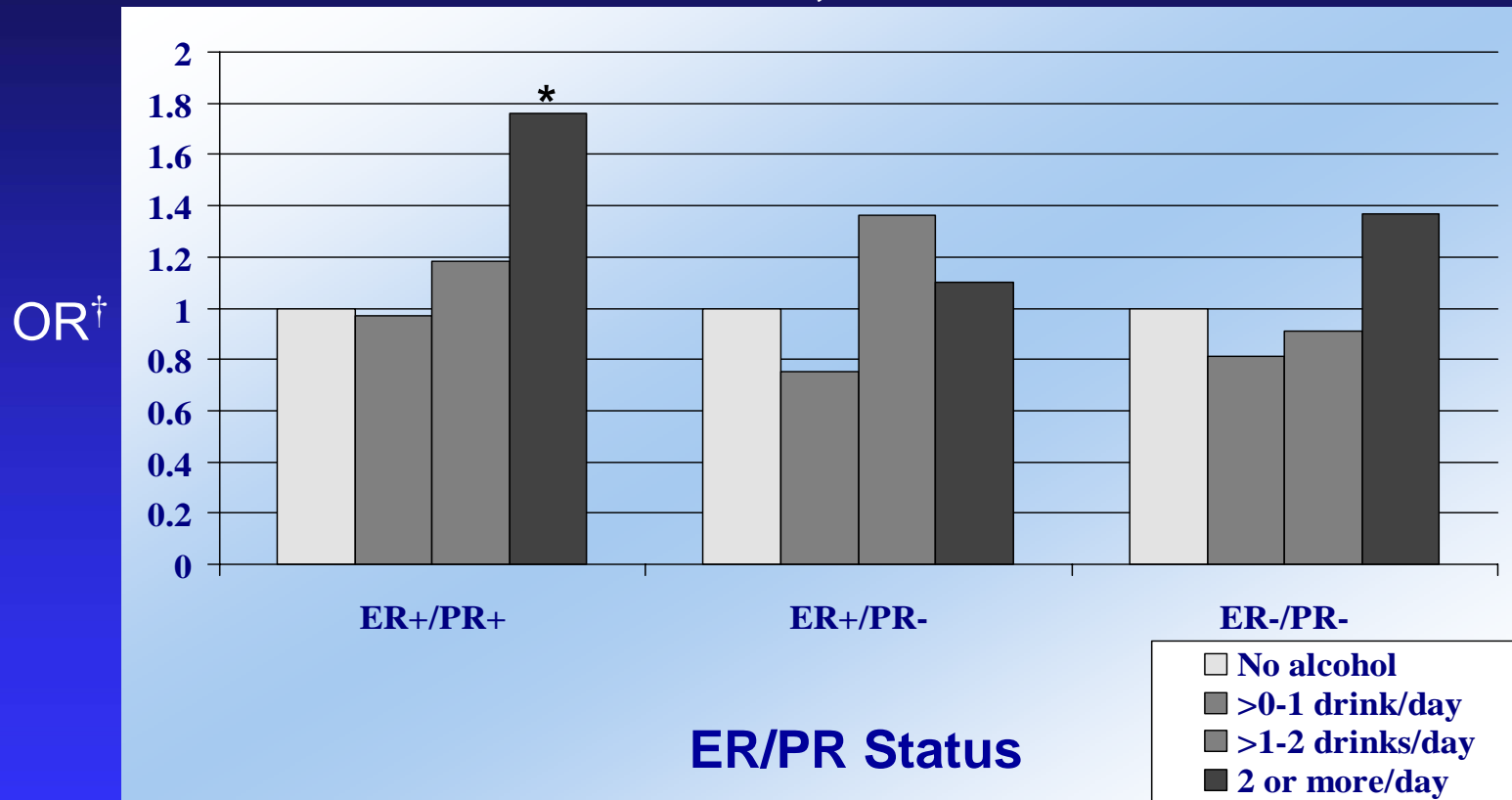
# Data Analysis

- ◆ Logistic regression performed separately by ER/PR group vs controls. There were too few ER-/PR+ tumors for useful analyses.
- ◆ We adjusted for known and suspected breast cancer risk factors
- ◆ Exclusions: For the 55-64 year old women, we included only postmenopausal women who knew their age at menopause. For the women <41 years, we included only those who were still menstruating at the time of their breast cancer diagnosis.



# Alcohol Consumption and Breast Cancer Risk by ER/PR Status (Women aged 55-64 Years)

760 with breast cancer/ 1,091 without breast cancer



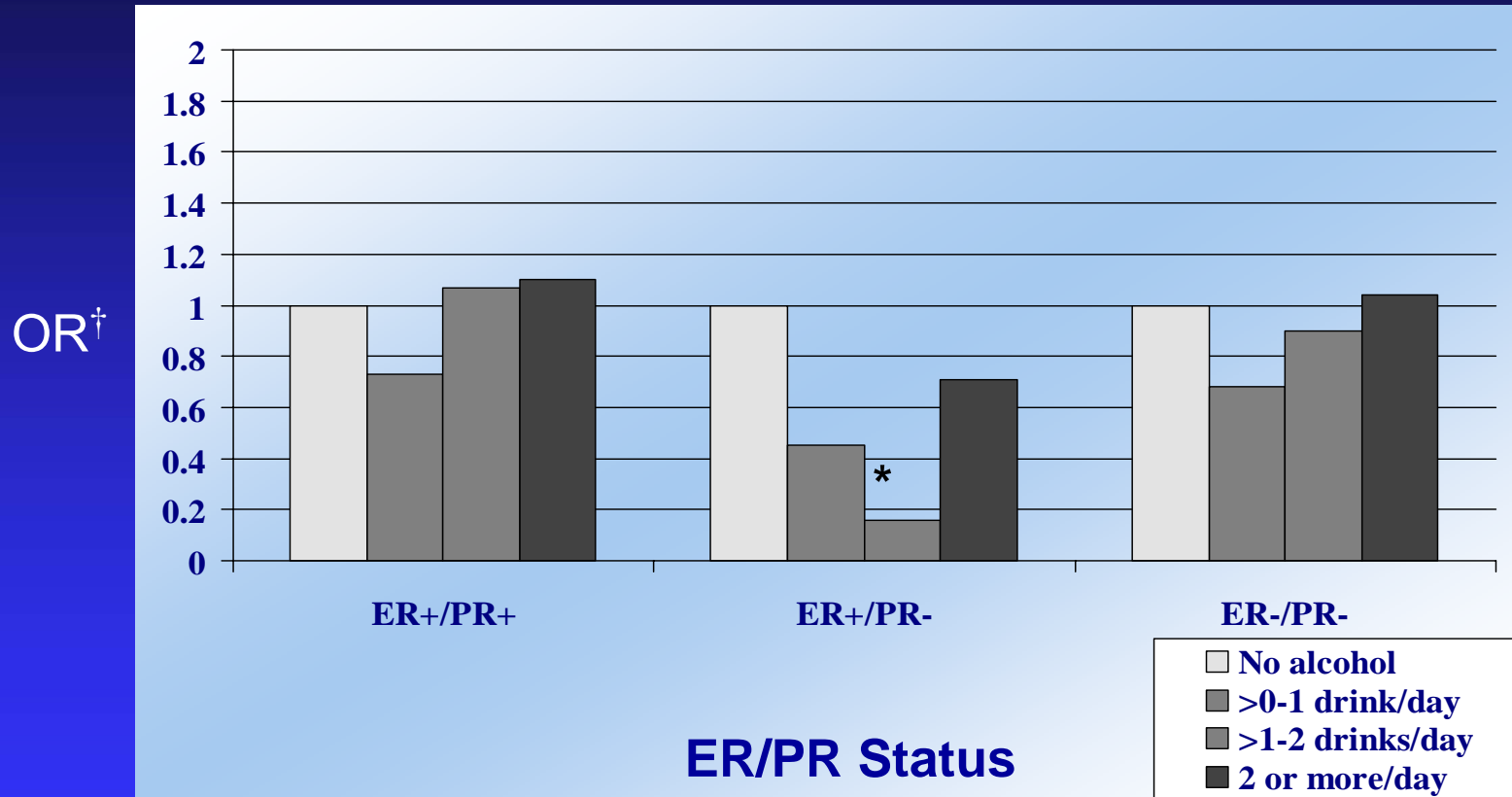
\* Statistically significant (Trend P < 0.05)

†Odds ratios adjusted for age; SES; education; ages at menarche, menopause, and first birth; number of births; breastfeeding; physical activity; body mass index; estrogen replacement therapy use; and family history of breast cancer.



# Alcohol Consumption and Breast Cancer Risk by ER/PR Status (Women aged 40 Years or Younger)

424 with breast cancer/ 714 without breast cancer



\*Very small number of cases (<10 per level of alcohol consumption)

Odds ratios adjusted for age; SES; education; ages at menarche and first birth; number of births; breastfeeding; physical activity; oral contraceptive use; and family history of breast cancer.



No evidence among postmenopausal women that the association of alcohol and hormone receptors differed by body mass index or ERT use.



# What does the sum of the evidence tell us?

Alcohol consumption is:

- 1) associated with increased breast cancer risk
- 2) associated with increased risk of ER+ breast cancer
- 3) rarely associated with ER- breast cancer in the absence of an association with ER+ breast cancer



# So what does this all mean?

- ◆ Results consistent with theory that ER+/ER- cancers represent different diseases.
- ◆ Alcohol's major mechanism of action may be hormonal, given consistent relationship with ER+ cancer; other mechanisms that affect ER-breast cancer development may also play a role.
- ◆ Results also lend evidence to the hypothesis that high circulating hormone levels increase risk of ER+ breast cancer.



# Additional research areas to explore:

