

**Risk Stratification for DCIS
Recurrence: Are There Lessons
in Breast Cancer Screening?**

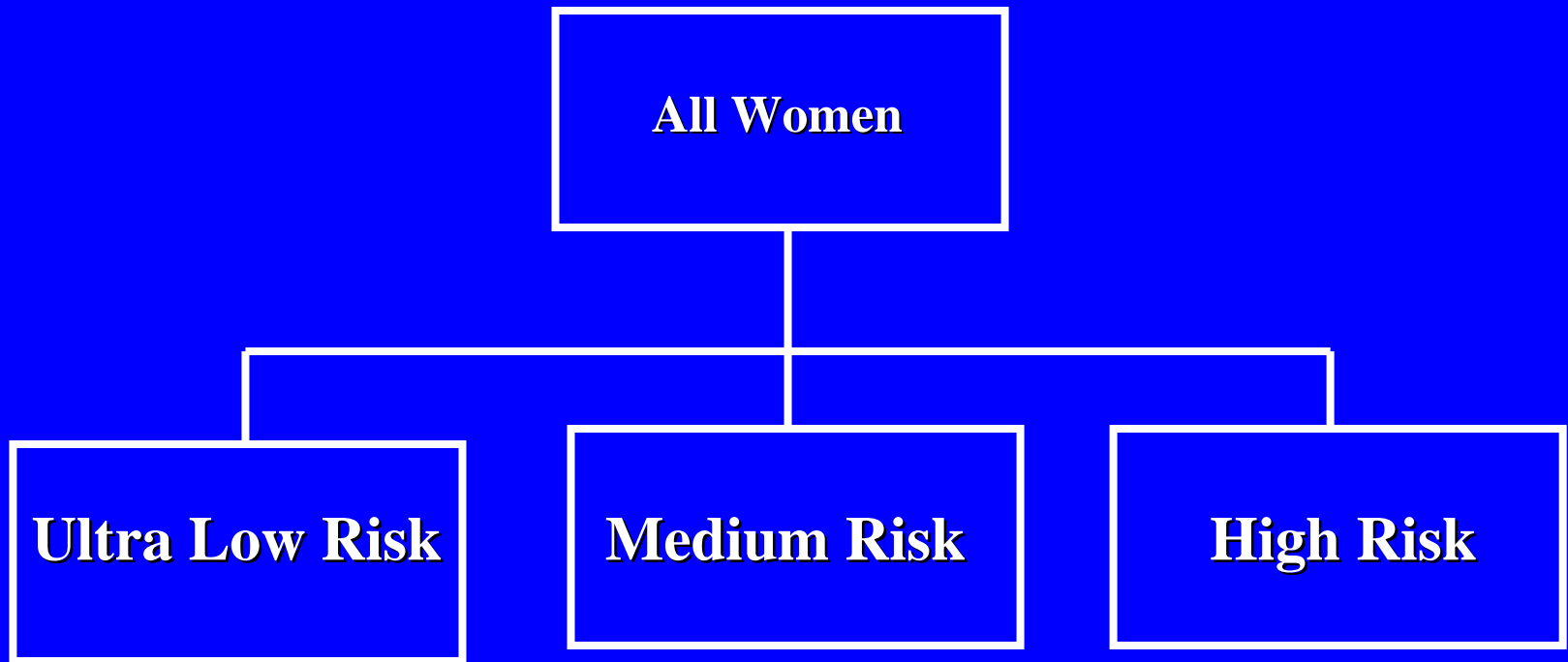
Suzanne W. Fletcher, MD, MSc

DCIS - Prognosis

- Almost all women survive in first 9 years (Ernster et al, 1996)
- Recurrent cancers over 12 years (Fisher et al, 2001)

	<u>All Recurrences</u>	<u>Invasive Recurrences</u>
	%	%
Lumpectomy	31.7	14.1
Lumpectomy & Radiation	15.7	7.8

The Plan





[Calculate Risk for New Patient](#)

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Breast Cancer Risk Assessment Tool

*An interactive tool
to measure a woman's risk
of invasive breast cancer*

Scientists at the National Cancer Institute (NCI) and the National Surgical Adjuvant Breast and Bowel Project (NSABP) Biostatistics Center have developed this Breast Cancer Risk Assessment Tool, a Web tool that allows a health professional to project a woman's individualized estimate of risk for invasive breast cancer over a 5-year period and over her lifetime (to age 90).

This tool uses statistical methods applied to data from the Breast Cancer Detection and Demonstration Project, a mammography screening project conducted in the 1970s.



Gail Model of Breast Cancer Risk for Individuals

- **Developed in 1989; used to estimate expected incidence in Breast Cancer Prevention Trial**
- **Risk factors in model:**
 - age**
 - age at menarche**
 - age at first birth/nulliparity**
 - # of affected first-degree relatives**
 - history of benign breast biopsy/hyperplasia,**

Gail Model Validation in Nurses' Health Study

- **Cohort of 82,109 white women aged 45-71 years in 1992**
- **Observed 1,354 (1.65%) cases of breast cancer over five-year period**
- **Expected/observed ratios:**
 - **total sample: 0.94 (0.89-0.99)**
 - **high-risk subsample: 1.03 (0.96-1.12)**

Individual vs. Group Risk

- Individual woman
Either 0% or 100%
- Groups of women
0% to 100%

Assessing Accuracy of Prediction

- Calibration of model:

The degree to which the percent of the population actually developing disease is similar to the probability estimate of the model. (In the NHS, Model: 1.55%, Observed: 1.65%; E:O = 0.94)

- Discrimination of Model:

The degree to which probabilities are consistently higher for persons who develop disease compared to those who do not.

Assessing Accuracy of Prediction at Individual Level

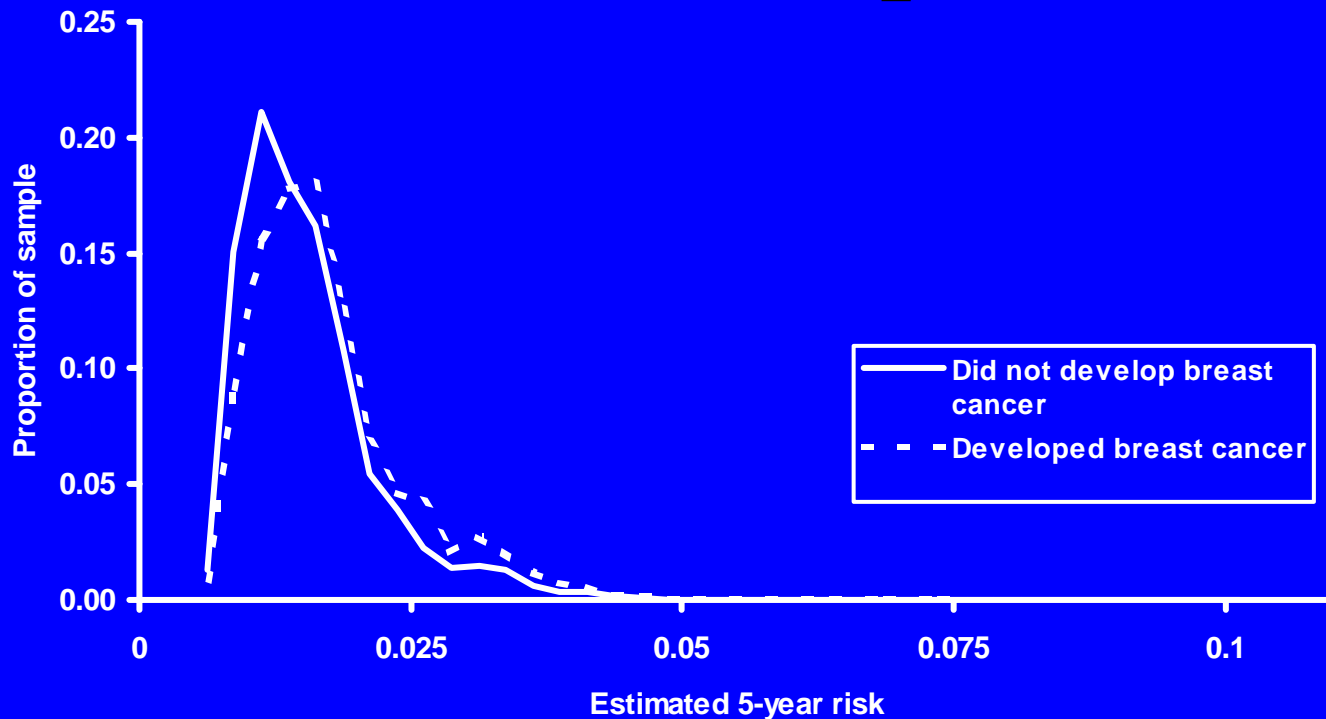
Discriminatory accuracy can be assessed with concordance statistic

- Values range from 0.5 (“coin flip”) to 1.0 (perfect discrimination)**
- Represents probability that, for randomly-selected pair of (diseased, nondiseased) individuals, diseased individual has higher estimated disease probability according to risk factors**

Concordance Statistic for Gail Model in NHS

58%

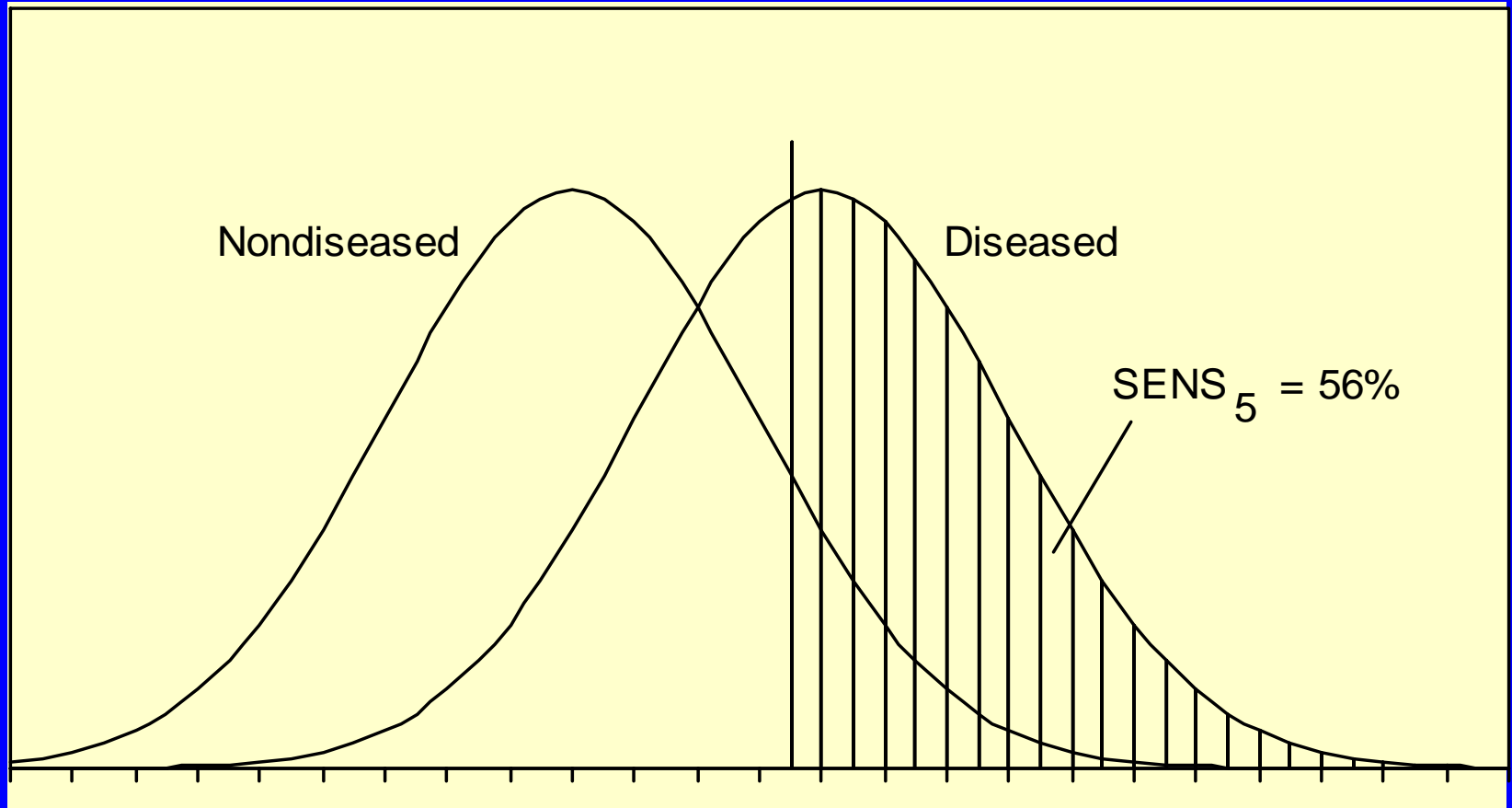
Estimated Five-year Risk of Breast Cancer, According to Breast Cancer Status at End of Follow-up



A large number of people at a small risk may give rise to more cases of disease than the small number who are at high risk. This situation seems to be common, and it limits the utility of the ‘high-risk’ approach to prevention.

Geoffrey Rose, 1985

$$RR_{q1-5} = 200$$



Why Risk Stratification May be Difficult

- **Most risks are too small to differentiate individuals who will and will not develop BC**
- **Many risk factors are spread over the population**
- **Some RR are determined by comparing ends of the spectrum, ignoring women with risks in the middle ranges**

5-Year Risk of Breast Cancer after DCIS

	<u>Any</u>	<u>Invasive</u>
	%	%
Lumpectomy	24	14
Lump & XRT	14	8
Lump & XRT & TAM	9	4
Without DCIS		2

Fisher et al, Semin Oncol 2001
Rockhill et al, JNCI 2001

Risk Factors for Breast Cancer

Major (RR > 3.0)

- **Increasing age** ~ 18 (70 vs 30)
- **Genetic mutation** ~200 (<40)
- **Menopausal hormone therapy** ~ 15 (60s)
- **Atypical hyperplasia** ~ 5
- **Radiation therapy** ~ 5
- **Increased breast density** ~ 4
- **Strong family history** ~ 3-4

Risk Factors for Breast Cancer

Moderate (RR 1.0 – 3.0)

- **Mother or sister with BC**
- **Increased bone density**
- **Older age at first birth**
- **Older age at menopause**
- **Younger age at menarche**
- **Benign breast biopsy**
- **Alcohol**
- **HRT/Contraceptive pills**

Protective Factors against Breast Cancer

- **Oophorectomy before age 35**
- **Breast feeding**
- **Increased parity**
- **Exercise**
- **Lean post-menopausal body mass**

Risk Stratification for Breast Cancer Detection

- **Risk stratification for breast cancer detection may be more difficult than anticipated**
- **Communicating breast cancer risk to women needs as much scientific work as risk stratification.**