

Problems in the Surveillance of Inflammatory Breast Cancer

Paul H. Levine, M.D.

The George Washington University School of
Public Health and Health Services

The Importance of Inflammatory Breast Cancer

- 1) IBC is the hallmark of aggressive breast cancer...to understand IBC is to understand the biology and etiology of aggressive breast cancer
- 2) The risk factors for breast cancer aggressiveness appear to contrast to the risk of developing breast cancer
- 3) Early diagnosis is critical if the patient is to be cured

The SEER Approach to IBC

- Pathologic confirmation is primary (7-1-96—The correct coding for a case with “a clinical diagnosis of inflammatory carcinoma, but there was no mention of invasion of dermal lymphatics on the pathology report,” is 8500/3, Infiltrating duct carcinoma)
- Other options include Extent of Disease and Tumor Size (998)
- Metastatic IBC can be captured as metastatic breast cancer, and metastatic IBC could be missed

IBC studies using SEER data

- 1) Levine et al (1984) used clinical (EOD 50 and 70) and pathologic criteria to identify IBC cases. Three year survival was less than 60% in all categories vs. 90% for all other breast cancer cases.
- Chang et al (1998) only used pathologically confirmed cases and showed a doubling of incidence between 1975-7 and 1990-1992.
- Hance et al (2003) indicated how to separate IBC from locally advanced breast cancer.

Hance KW, Devesa S, Anderson WA, Young
H. and Levine PH, San Antonio 2003

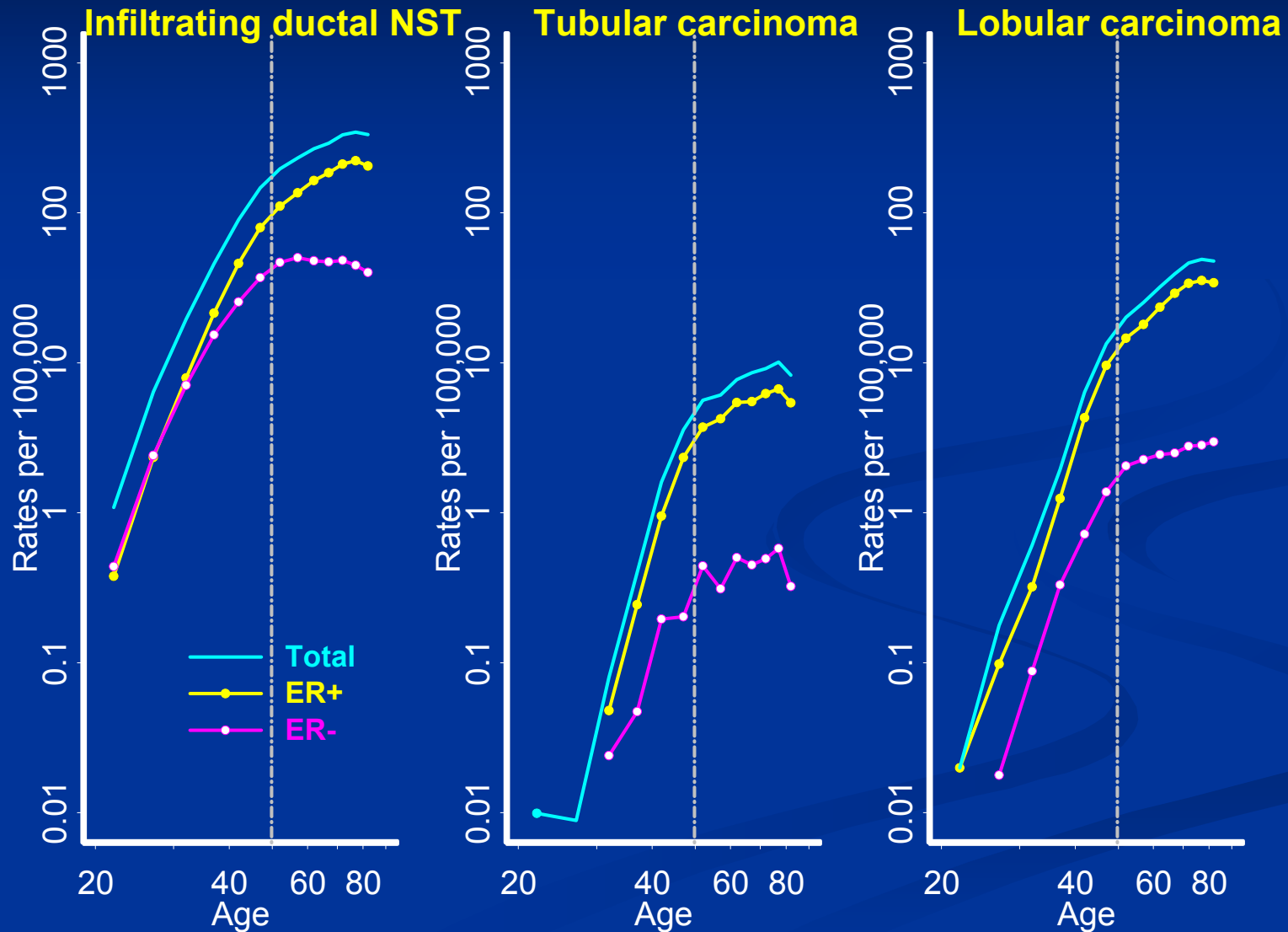
**Trends in Inflammatory Breast Carcinoma
Incidence and Survival: The Surveillance,
Epidemiology, and End Results Program at
the National Cancer Institute**

Hance et al. (1)

SEER Coding Conventions

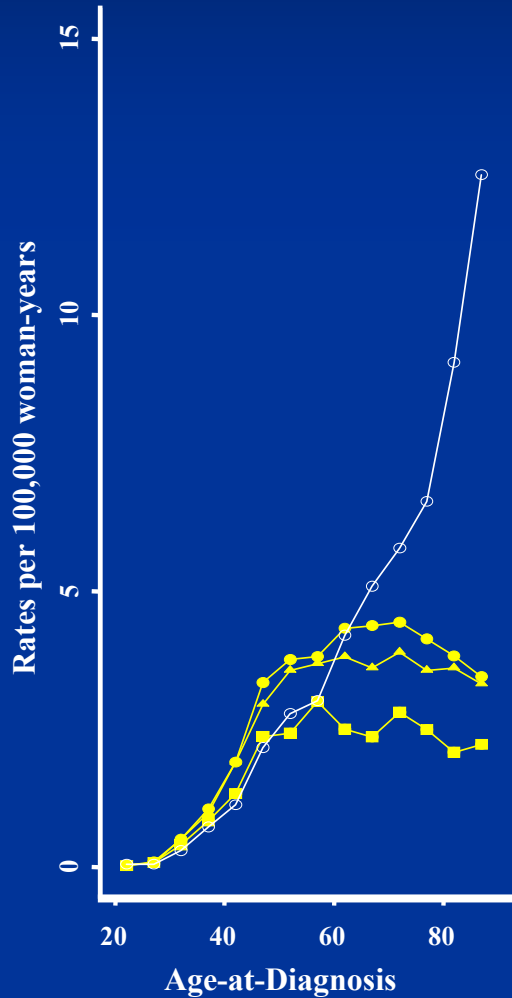
| <u>EOD Code</u> | <u>AJCC</u> | <u>Definition</u> |
|-----------------|-------------|---|
| EOD 10 | T1-3 | “Confined to breast tissue and fat including nipple and/or areola.” |
| EOD 40 | T4a | “Invasion of (or fixation to) chest wall, ribs, intercostals, or serratus anterior muscles.” |
| EOD 50 | T4b | “Extensive skin involvement: skin edema, peau d’orange, “pigskin,” en cuirasse, lenticular nodule(s), inflammation of the skin, erythema, ulceration of skin of breast, satellite nodule(s) in skin of primary breast.” |
| EOD 60 | T4c | EOD 60 = EOD 40 + EOD 50. AJCC T4c = AJCC T4a + AJCC T4b. |
| EOD 70 | T4d | “Inflammatory carcinoma, including diffuse (beyond that directly overlying the tumor) dermal lymphatic permeation or infiltration.” |
| EOD 998 | T4d | “Diffuse; widespread: $\frac{3}{4}$'s or more of breast; inflammatory carcinoma.” |

Results for the 1st rate pattern

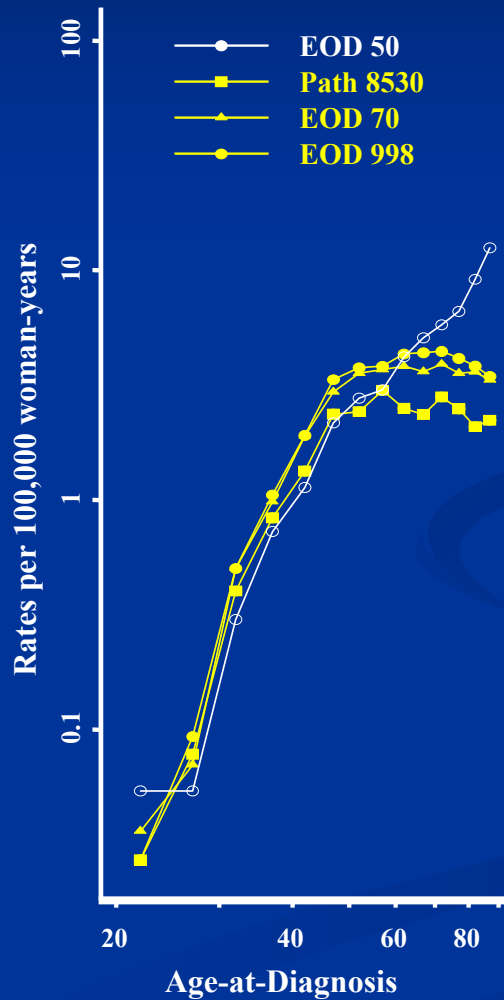


Hance et al. (2)

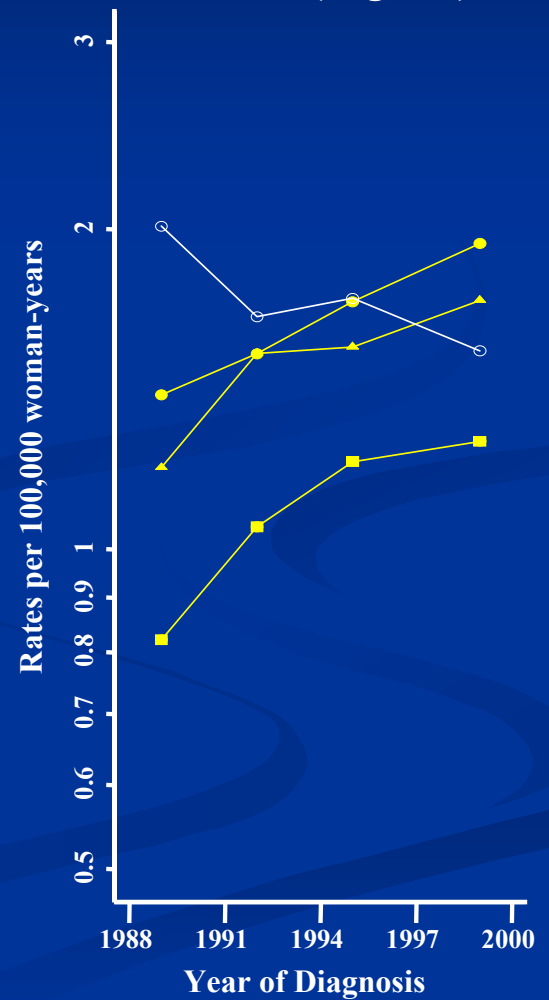
A. Age-Specific Incidence Rates (Linear Scale)



B. Age-Specific Incidence Rates (Log-Log Plot)

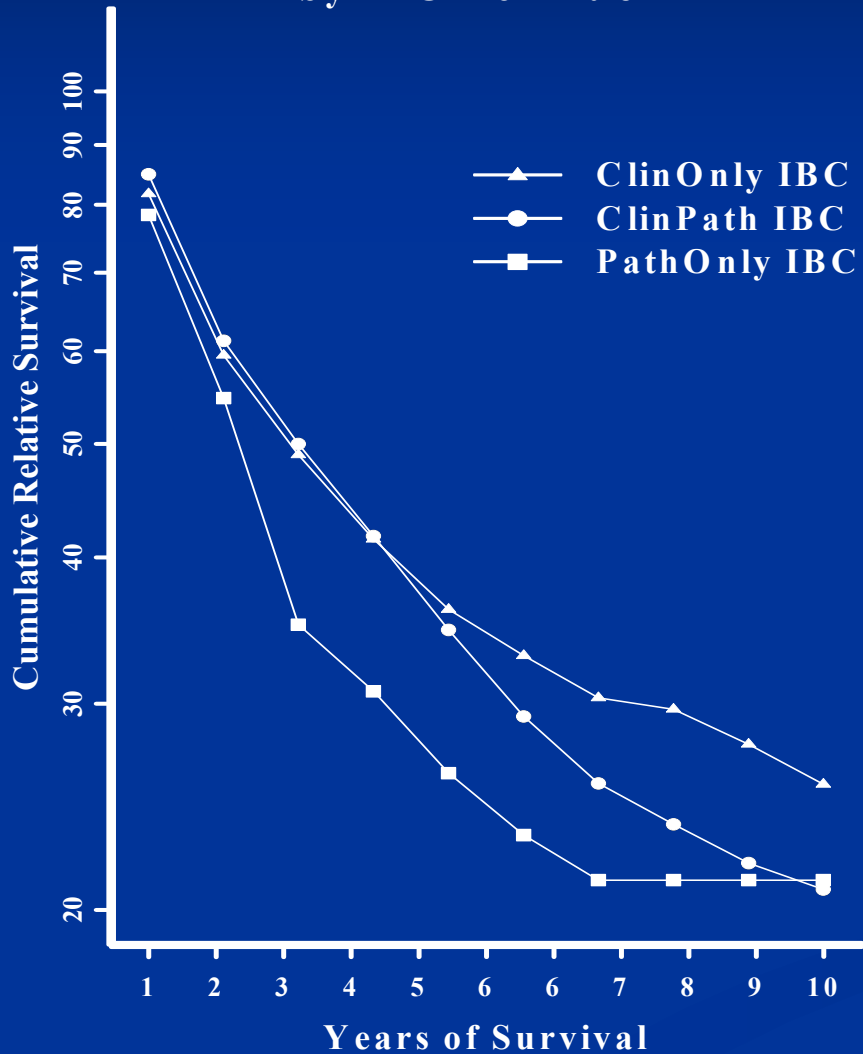


C. Age-Adjusted Incidence Rate Trends (Log Plot)

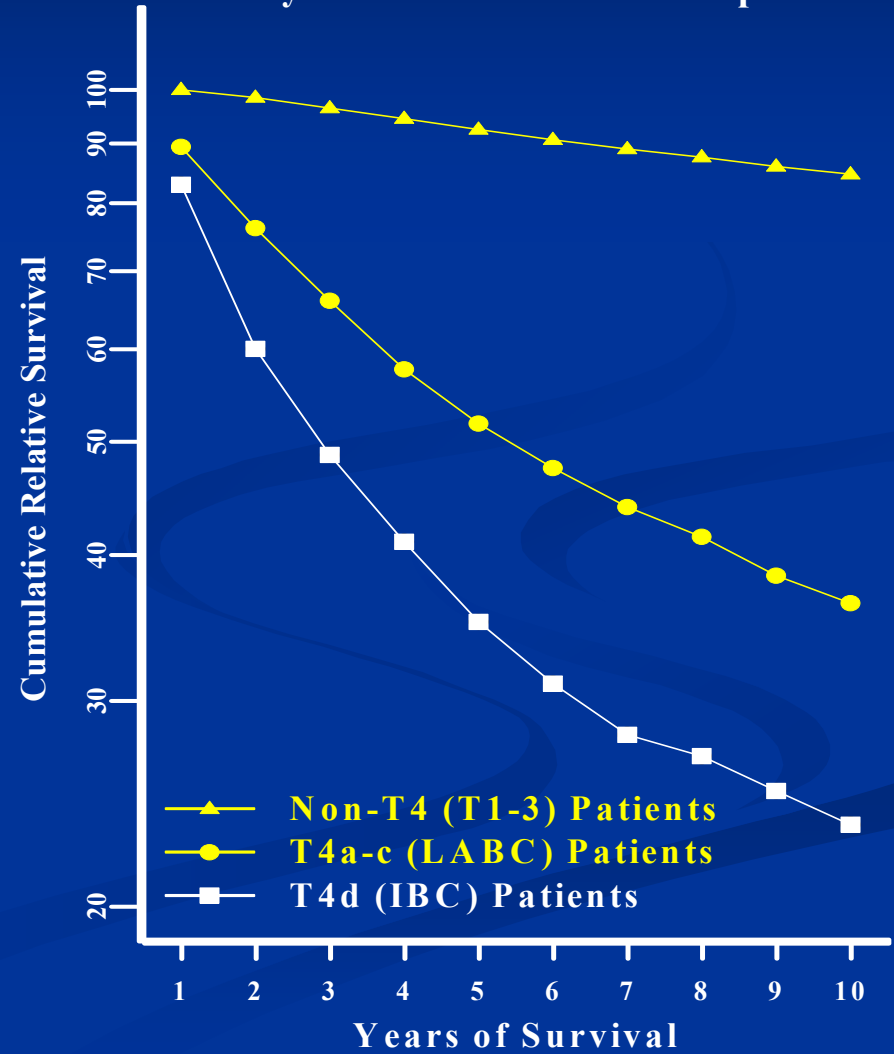


Hance et al (3)

Cumulative Relative Survival by IBC Definition



Cumulative Relative Survival by Breast Cancer Group



The Definition of Pousee Evolutive (PEV)

- PEV 1--Rapid growth by history without objective skin changes
- PEV 2--Redness, warmth and edema involving less than half the breast
- PEV 3--Redness, warmth and edema involving more than half the breast

IBC Figure 1



The Inflammatory Breast Cancer Registry (IBCR): Lessons Learned from the First 50 Cases

Paul H. Levine, M.D.

Ladan Zolfaghari, M.D.

Muhannad S. Hafi, M.D.

Heather Young, PhD

The George Washington University

School of Public Health and

Health Services

Purpose of the IBCR

- To collect standardized clinical and epidemiologic information on patients with IBC diagnosed in the United States and Canada
- To collect biospecimens from these patients to determine whether the molecular patterns correlate with the clinical patterns of disease.

Methods

- Patients identified by referral through web sites focusing on supporting IBC patients and through physician and patient referral.
- All patients interviewed by PHL and detailed history of clinical onset obtained.
- Patients classified by clinical and pathologic features into one of 7 subgroups (Table 1)

Table 1

Seven Categories for IBC

- Group 1: Classical history and physical findings, pathological confirmation
- Group 2: Classical history and physical findings, no pathological confirmation
- Group 3: Incomplete findings of IBC, with pathological confirmation
- Group 4: Incomplete findings of IBC, without pathological confirmation
- Group 5: Pathological findings without clinical features
- Group 6: Secondary IBC
- Group 7: IBC vs. neglected breast cancer
- Group 8: Apparent neglected breast cancer

Results I

- 120 total patients enrolled as of 11/1/03
- Of the first 50 patients, 46 contacted us through the Internet and four were referred by GW physicians.
- Patients were diagnosed and treated in 23 different states and 2 Canadian provinces.
- Geographic characteristics of patients were widespread very rural as well as urban areas.

Results II

| <u>Categories</u> | <u>N</u> | <u>%</u> |
|-------------------|----------|----------|
| CAT 1 | 15 | 30% |
| CAT 2 | 7 | 14% |
| CAT 3 | 12 | 24% |
| CAT 4 | 14 | 28% |
| CAT 5 | 2 | 4% |

Conclusions

- The AJCC criteria for IBC are too extreme and miss a significant percentage of cases
- There should be more uniformity between SEER and AJCC (why is 998 more than $\frac{3}{4}$ of the breast with the AJCC definition more than $\frac{1}{2}$ the breast?)

Inter-Registry Issues

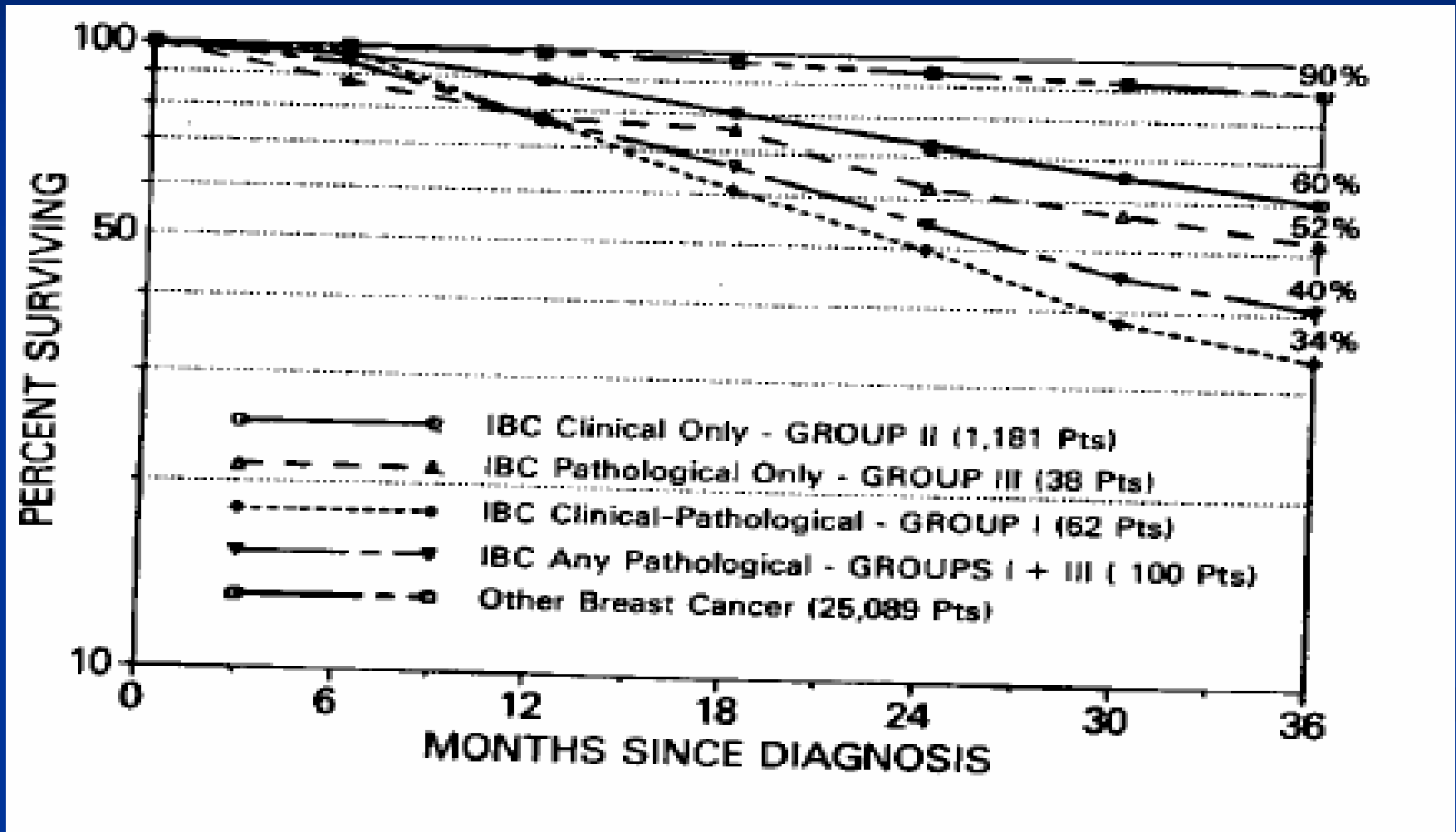
- Using EOD code 998 (clinical IBC involving more than $\frac{3}{4}$ of the breast) 0.4% of 34,469 Connecticut cases had IBC vs. 2.2% of 45,884 Los Angeles cases
- Using 8530 code (pathologically confirmed), 0.5% of 36,837 metropolitan Detroit cases had IBC vs. 2.0% of 45,884 Los Angeles cases

Are these differences meaningful and worth investigating re differences in diagnostic procedures vs. differences in populations?

Some current Questions

- Does SEER miss the approximately 25% of IBC cases that fit Category 4 in our Registry (equivalent to PEV2)?
- Is IBC increasing in incidence?
- Are the Inter-Registry differences in IBC incidence significant and worthy of follow-up?
- What are the risk factors for IBC?
- What laboratory studies are most important to characterize IBC and its relationship to aggressive breast cancer without clinical signs of IBC?

Percent relative Survival Rate by months since Diagnosis



The Castro Valley IBC Cluster

- Three women in the same office developed well documented IBC within one year
- Concerns re mammography unit, MRI unit, ventilation problems
- Detailed interviews suggest importance of family history, exogenous hormones, obesity, exposure to herbicides/pesticides
- Three additional IBC patients reported in same time period in nearby office complex
- California SEER Registries meeting reveals problems in diagnosis of IBC, GIS

Hance et al. (3)

Case Definitions

IBC Cases:

- 1) Clinical and Pathological Features:
(ICD-O-2 8530/3 + EOD 70 and/or EOD 998)
- 2) Pathological Features Only:
(ICD-O-2 8530/3 only)
- 3) Clinical Features Only:
(EOD 70 and/or EOD 998 only)

LABC Cases:

- 1) AJCC T4a-c:
(EOD 40-60)

Non-T4 (T1-3) Cases:

- 1) AJCC Non-T4 (T1-3):
(EOD 10)

Hance et al. (4)

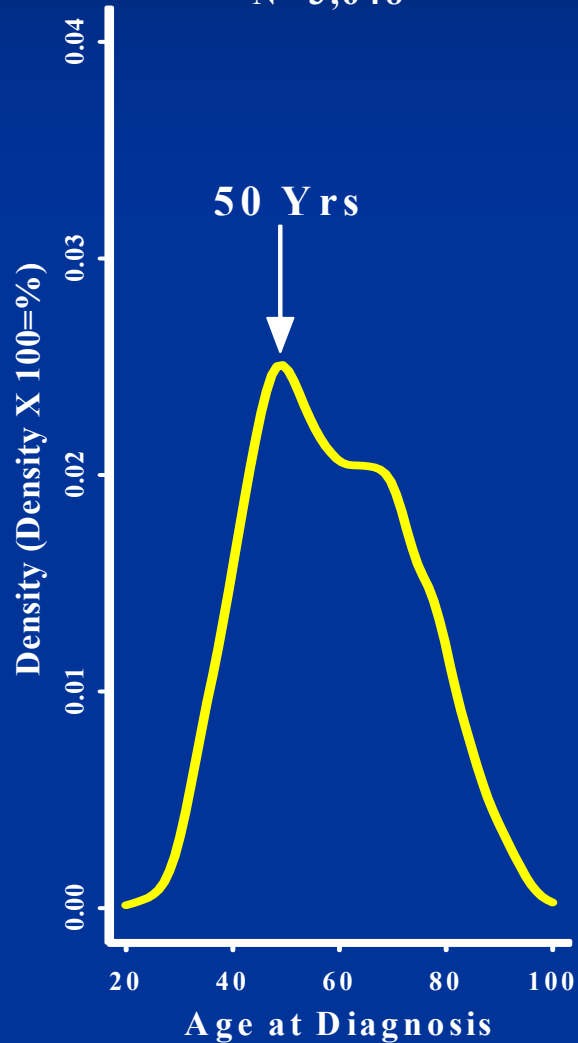
Case Selection

| <u>Case Description</u> | <u>N</u> |
|--|----------|
| All Breast Cancer Cases Diagnosed Between 1988-2000: | 258,777 |
| Female Cases Only: | 257,157 |
| Microscopically Confirmed Cases Only: | 253,768 |
| Malignant Breast Cancer Cases Only: | 214,677 |
| AJCC T4d (IBC) Cases: | 3,648 |
| AJCC T4a-c Cases: | 3,636 |
| AJCC Non-T4 (T1-3): | 172,940 |
| Other or Unknown Cases: | 34,453 |

Hance et al. (6)

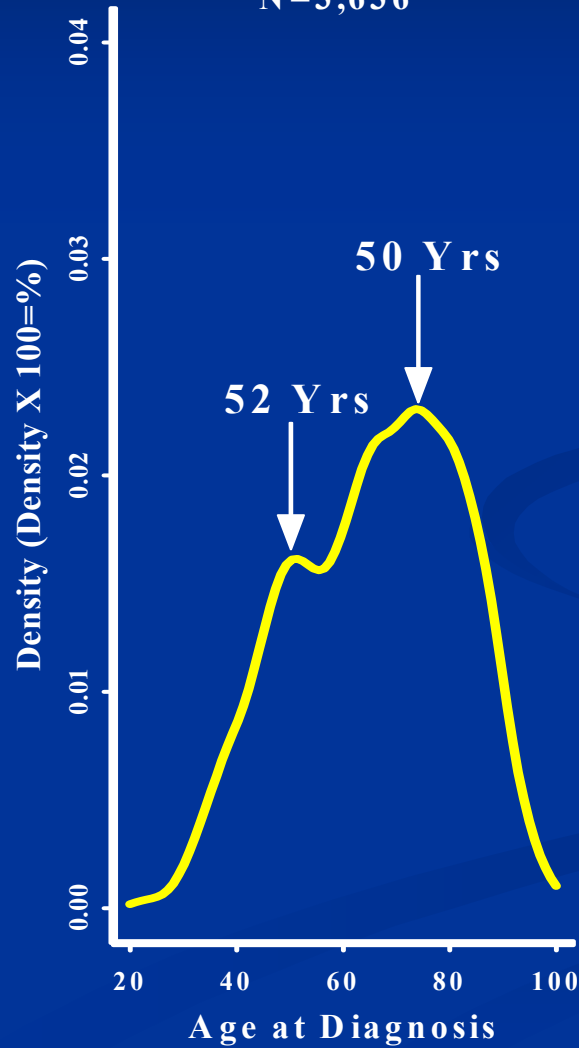
A. T4d (IBC) Patients

N=3,648



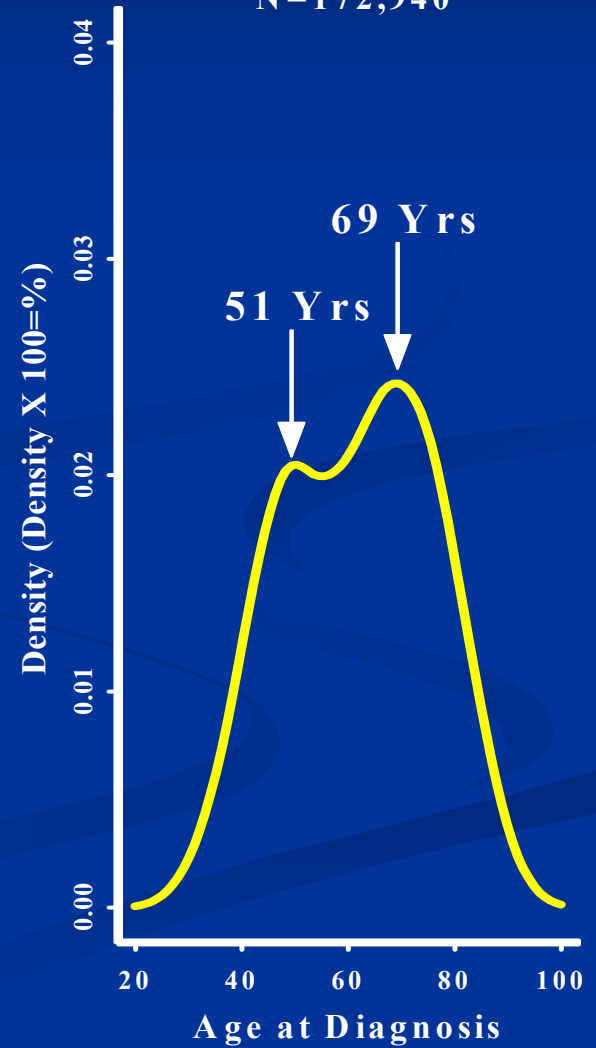
B. T4a-c (LABC) Patients

N=3,636



C. Non-T4 (T1-3) Patients

N=172,940



Hance et al (9)

Trends in Survival

Table 4A: Trends in T4d (IBC) Survival by 3-Year Interval

| 3-Yr interval | Median Survival (Yrs.) | Log Rank Test |
|----------------------|-------------------------------|----------------------|
| 1988-1990 | 2.23 | Reference |
| 1991-1993 | 2.76 | p = 0.0338 |
| 1994-1996 | 2.68 | p = 0.0092 |
| 1997-1999 | 2.93 | p = 0.0005 |

Table 4B: Trends in T4d (IBC) Survival by Race

| Race | Median Survival (Yrs.) | Log Rank Test |
|-------------------|-------------------------------|----------------------|
| Caucasians | 2.77 | Reference |
| African-Americans | 1.92 | p < 0.0001 |
| Other | 2.90 | p = 0.1775 |

Hance et al (10)

Conclusions

- These findings are consistent with the pernicious nature of IBC.
- IBC incidence increased by 25% between 1988-1999.
- A large number of cases that were defined by clinical features of IBC without the pathologic confirmation of dermal lymphatic invasion (N=1,910).
- IBC survival increased after the 1988-1990 interval
- Significant racial disparities exist in both IBC and LABC

Figure 1

IBC Cases in US and Canada

Number of Cases by States:

Arizona (2)
Arkansas (1)
California (5)
Connecticut (1)
Florida (1)
Illinois (2)
Indiana (2)
Louisiana (1)
Maryland (2)
Massachusetts (3)
Michigan (2)
Montana (1)
New Hampshire (1)
New Jersey (2)
New York (1)
Ohio (4)
Oklahoma (1)
Oregon (1)
Pennsylvania (1)
South Carolina (1)
Texas (2)
Virginia (3)
Washington (4)
District of Columbia (3)
Canada (3)

