# Behaviour of DCIS (in the older population)

Sarah E Pinder
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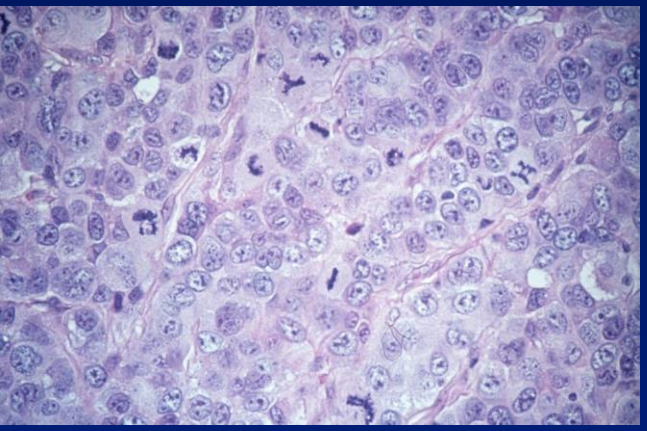
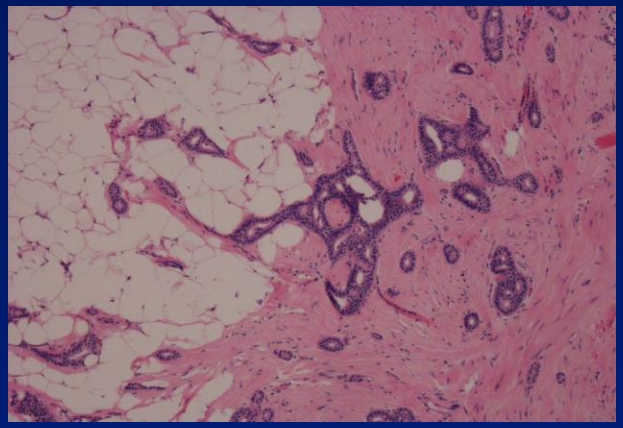
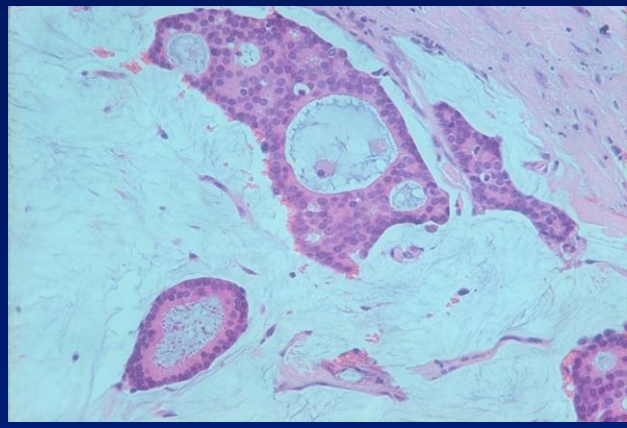
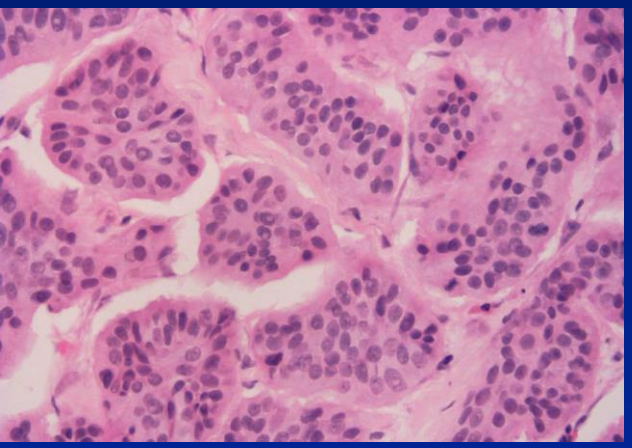
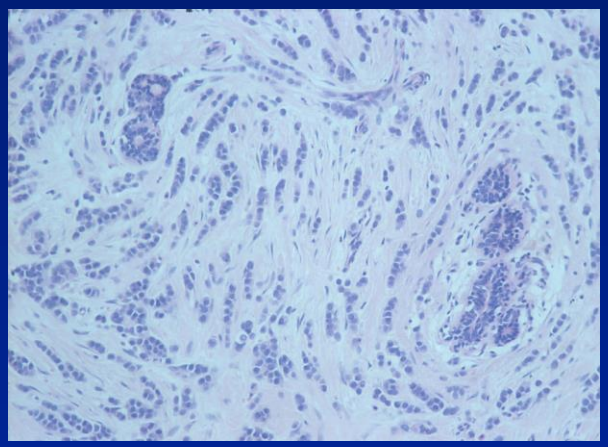
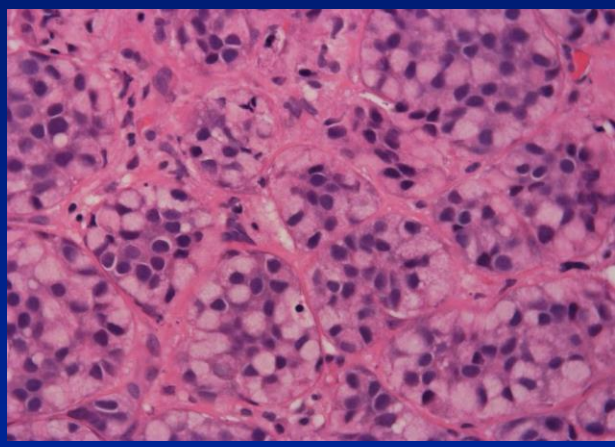
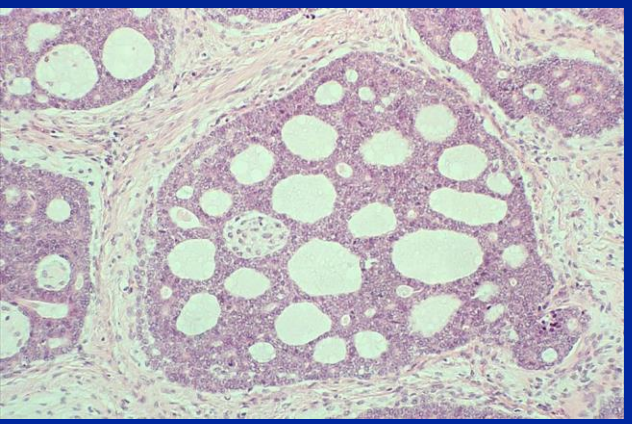
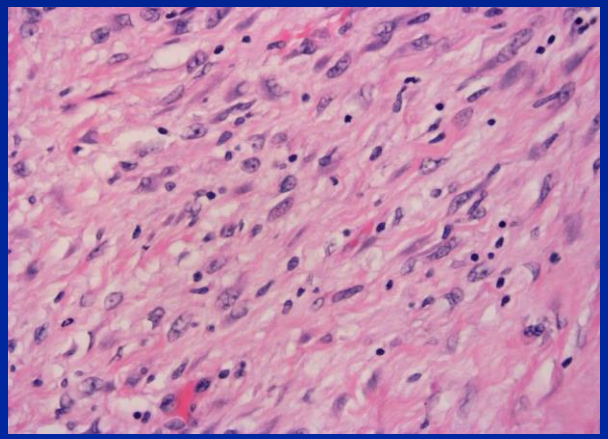
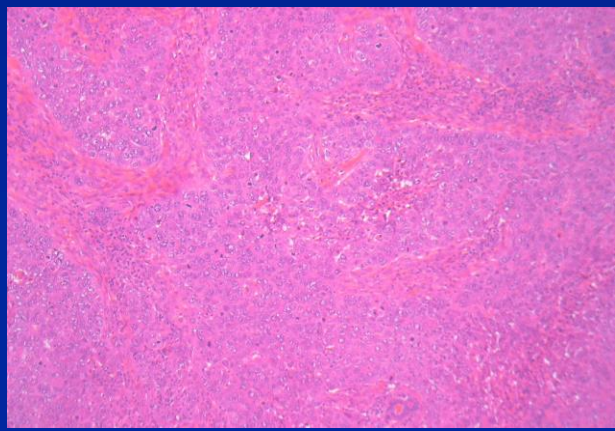
King's College London

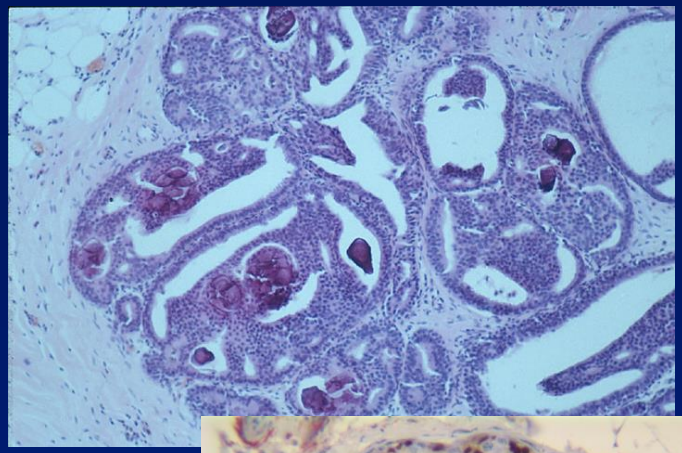
# Invasive breast cancer - histological types

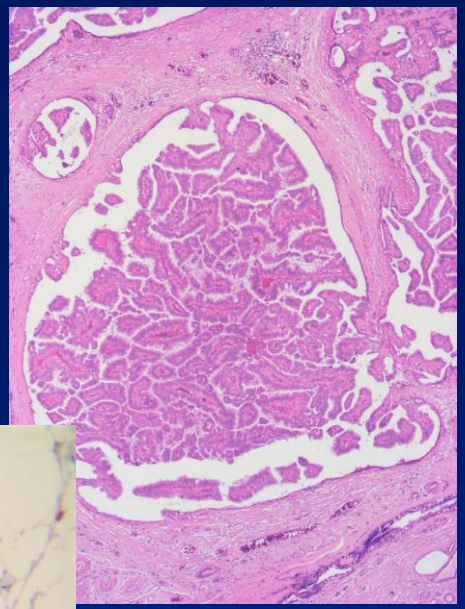










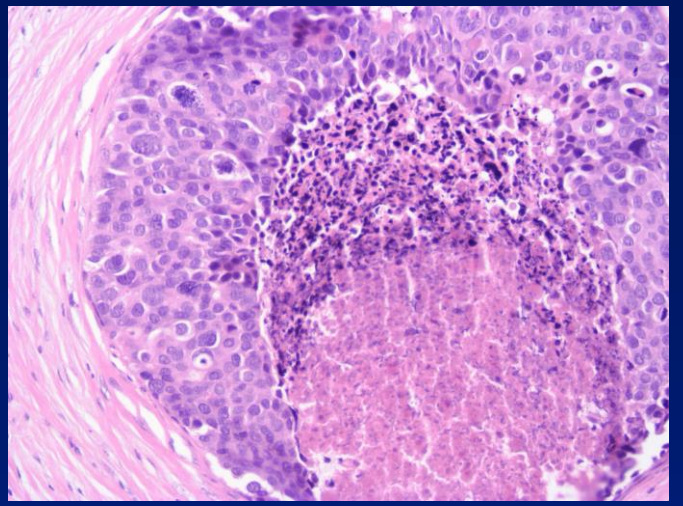
# Invasive Cancer
# Intrinsic Sub-groups - age

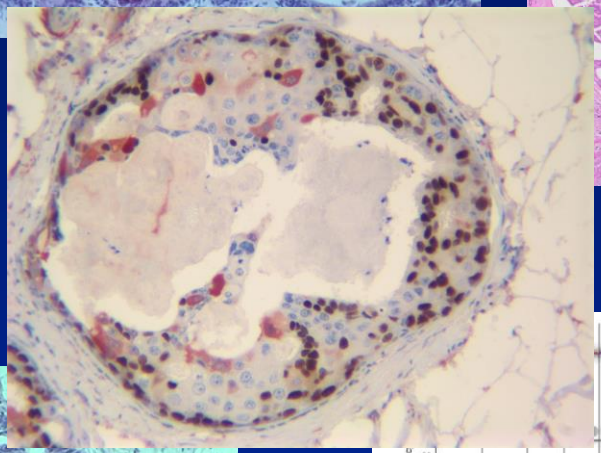
- 3,947 patients from publicly available clinical & gene expression microarray data sets
- Incidence of luminal (A, B, and A+B) tumours increased with age, basal-like tumours decreased
- Among patients 70 years & older, luminal B (32%), HER2-enriched (11%) & basal-like tumours (9%)
- After controlling for sub-type, treatment, tumour size, nodal status, grade, increasing age had no impact on RFS or DSS

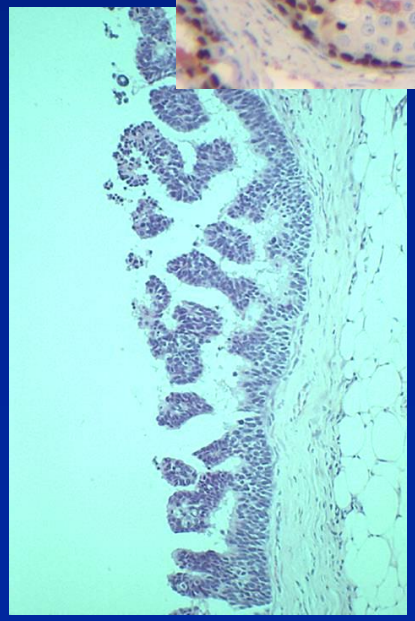
Jenkins EO et al. Oncologist. 2014;19:1076-83

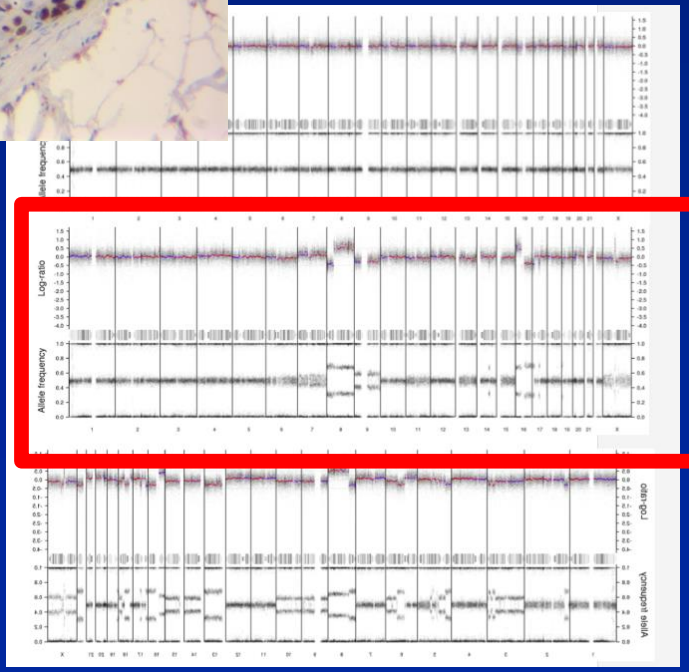


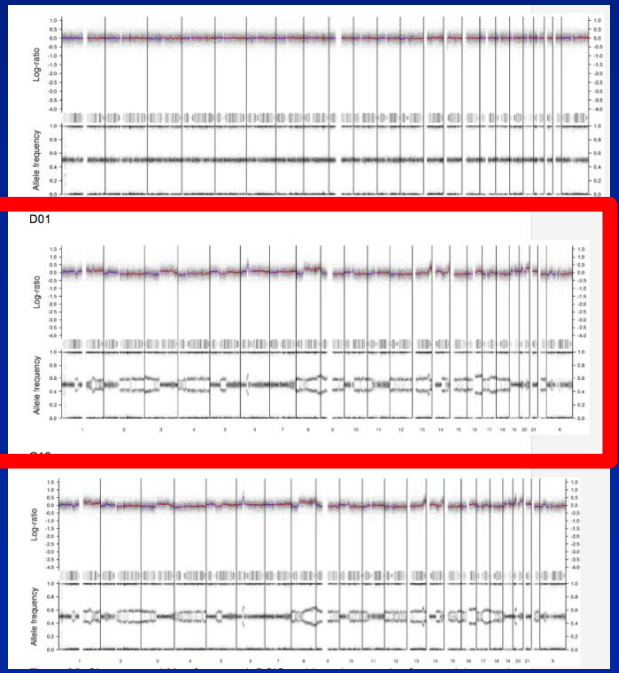








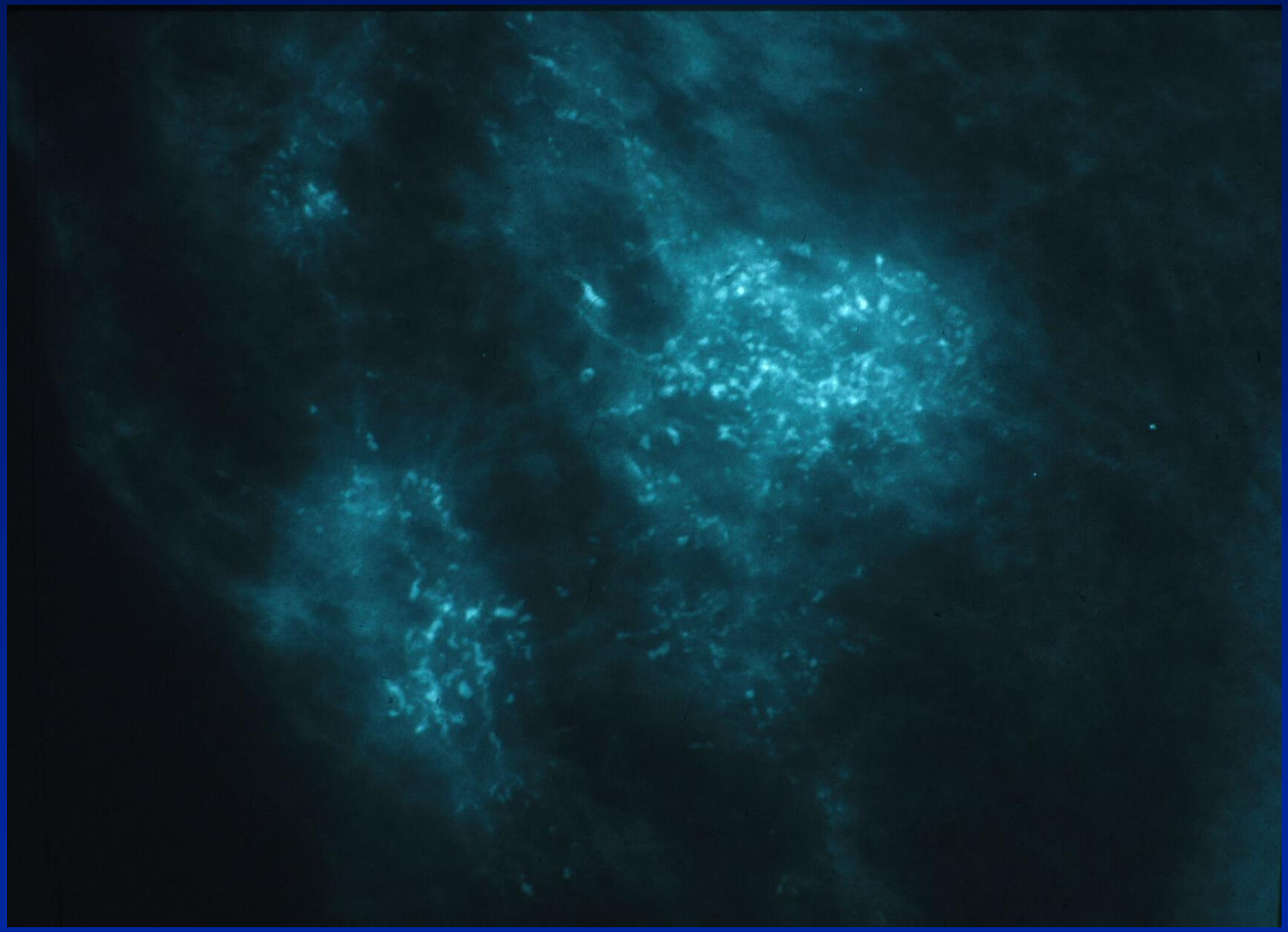

Log-ratio
Allele frequency


Log-ratio
Allele frequency
D01

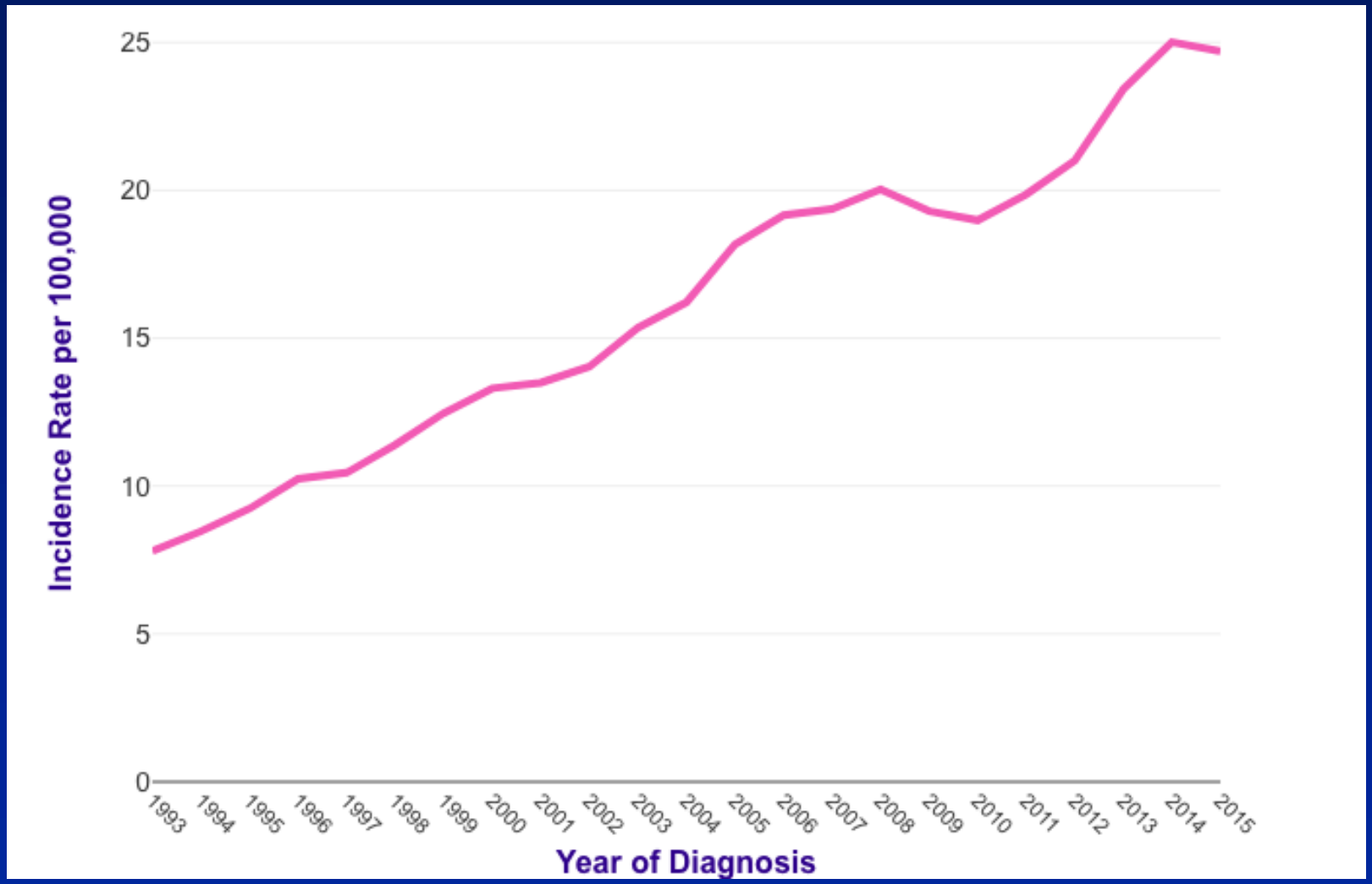
# Age and DCIS – Literature Review

- DCIS in younger patients more frequently has adverse prognostic pathological factors and more extensive than in older patients
- In series with adequate follow-up, younger patients treated with WLE & RT had significantly higher rate of LR, especially invasive LR
- "Successful treatment of younger patients with DCIS with lumpectomy & RT requires careful attention to patient evaluation, selection, and surgical technique. When this is done, age at diagnosis should not be a contraindication to breast-conserving therapy"

  Vicini FA & Recht A. J Clin Oncol. 2002;20:2736-4

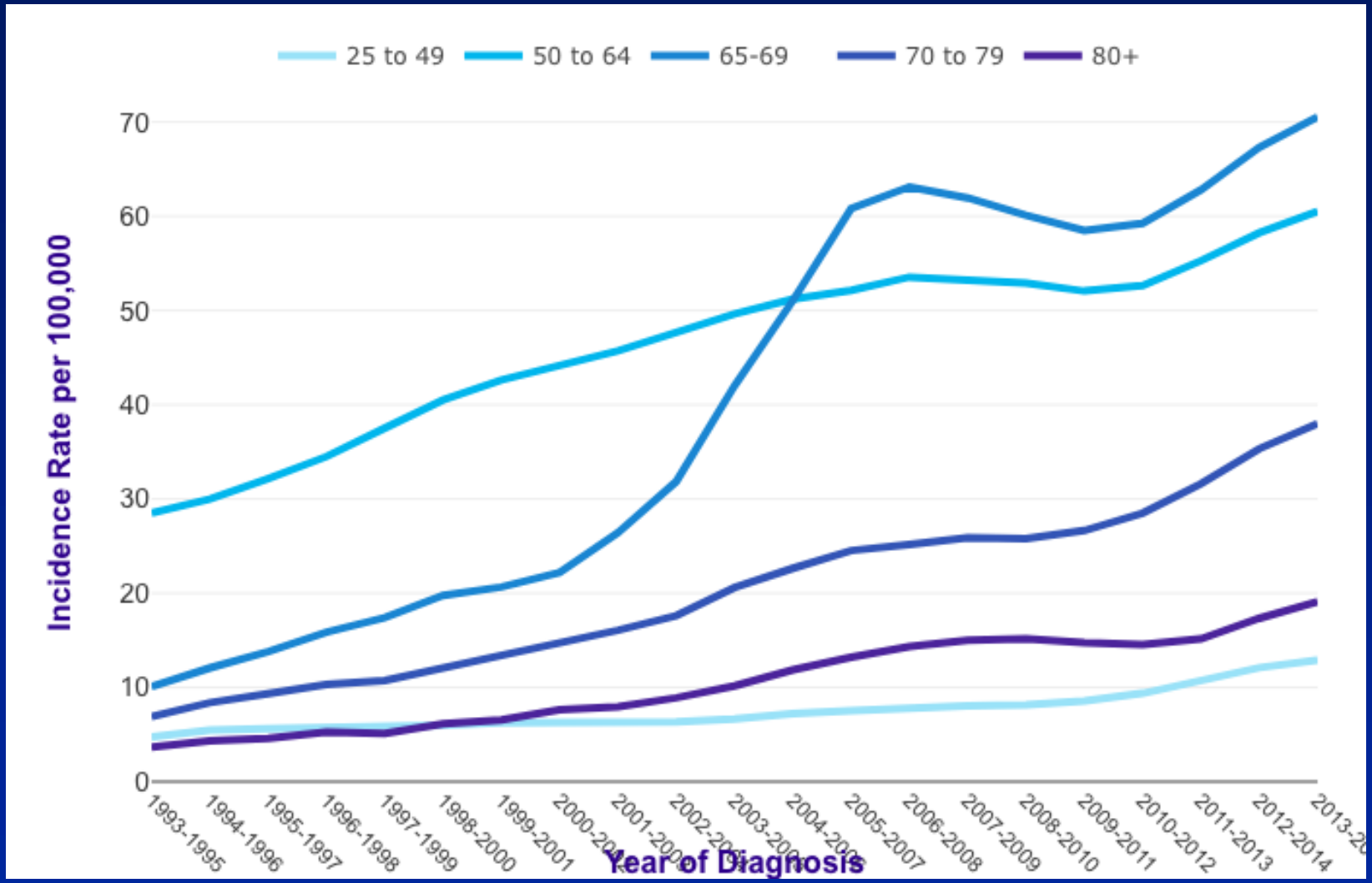


# Breast Carcinoma In Situ (D05), European Age-Standardised Incidence Rates, Females, UK, 1993-2015




https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer/incidence-in-situ#heading-Two

# Breast Carcinoma In Situ (D05), European Age-Standardised Incidence Rates, By Age, Females, UK, 1993-2015



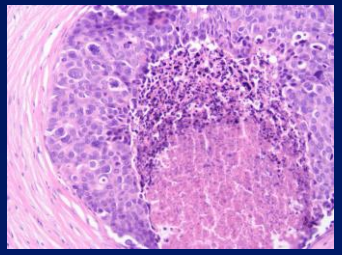

https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer/incidence-in-situ#heading-Two

Cancer Epidemiology, Biomarkers & Prevention

*Short Communication*

# Age-Specific Incidence Rates of *In situ* Breast Carcinomas by Histologic Type, 1980 to 2001

Christopher I. Li, Janet R. Daling, and Kathleen E. Malone



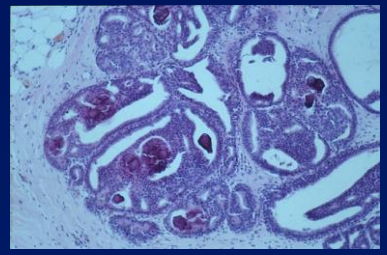


**Table 1. Overall and age-specific proportional changes in *in situ* carcinoma incidence rates from 1980 to 2001, 1992 to 2001, and 1997 to 2001, by histologic type**

| Age (y) | Proportional change (95% CI)* | | | |
|---|---|---|---|---|
| | DCIS, overall | DCIS, noncomedo | DCIS, comedo | LCIS |
| All ages | | | | |
| 1980-2001 | 7.2 (6.8-7.7)† | 6.1 (5.7-6.5)† | 15.7 (13.5-18.4)† | 2.6 (2.3-2.9)† |
| 1992-2001 | 1.8 (1.7-1.9)† | 2.1 (2.0-2.3)† | 0.9 (0.9-1.0)† | 1.3 (1.2-1.5)† |
| 1997-2001 | 1.1 (1.0-1.2)† | 1.2 (1.1-1.2)† | 0.8 (0.8-0.9)† | 1.1 (1.0-1.3)† |
| 30-39 | | | | |
| 1980-2001 | 3.7 (3.1-4.5)† | 2.9 (2.4-3.6)† | 8.8 (5.6-13.6)† | 0.9 (0.6-1.3) |
| 1992-2001 | 1.4 (1.2-1.7)† | 1.8 (1.5-2.3)† | 0.7 (0.5-1.0)† | 1.2 (0.7-2.0)† |
| 1997-2001 | 0.9 (0.7-1.2) | 1.1 (0.8-1.4) | 0.6 (0.3-0.9)† | 0.5 (0.3-1.0)† |
| 40-49 | | | | |
| 1980-2001 | 5.8 (5.1-6.6)† | 5.1 (4.4-5.8)† | 10.9 (7.7-15.4) | 1.4 (1.2-1.8)† |
| 1992-2001 | 1.6 (1.5-1.8)† | 2.0 (1.8-2.2)† | 0.8 (0.7-1.0)† | 1.1 (0.9-1.3) |
| 1997-2001 | 1.0 (0.9-1.1) | 1.1 (0.8-1.4) | 0.7 (0.6-0.9)† | 1.0 (0.8-1.3) |
| 50-59 | | | | |
| 1980-2001 | 9.2 (8.0-10.6)† | 7.8 (6.7-9.0)† | 19.3 (13.6-27.2)† | 3.5 (2.8-4.4)† |
| 1992-2001 | 1.8 (1.6-2.0)† | 2.2 (2.0-2.5)† | 0.8 (0.7-1.0)† | 1.4 (1.2-1.7)† |
| 1997-2001 | 1.1 (1.0-1.2) | 1.1 (1.0-1.3)† | 0.7 (0.6-0.9)† | 1.3 (1.0-1.6)† |
| 60-69 | | | | |
| 1980-2001 | 9.2 (8.0-10.6)† | 7.7 (6.6-8.9)† | 22.0 (15.6-30.9)† | 4.8 (3.7-6.4)† |
| 1992-2001 | 1.9 (1.7-2.1)† | 2.2 (2.0-2.5)† | 1.0 (0.9-1.2) | 1.6 (1.2-2.2)† |
| 1997-2001 | 1.2 (1.1-1.3)† | 1.2 (1.1-1.4)† | 1.0 (0.8-1.3) | 1.4 (1.0-1.9)† |
| 70-79 | | | | |
| 1980-2001 | 7.5 (6.5-8.5)† | 6.4 (5.5-7.4)† | 16.0 (11.3-22.7)† | 4.2 (3.0-5.9)† |
| 1992-2001 | 1.9 (1.7-2.1)† | 2.2 (1.9-2.5)† | 1.2 (1.0-1.5) | 1.4 (1.0-2.1)† |
| 1997-2001 | 1.2 (1.0-1.4)† | 1.2 (1.0-1.3)† | 1.1 (0.8-1.4) | 1.2 (0.7-1.8) |
| ≥80 | | | | |
| 1980-2001 | 6.3 (5.3-7.6)† | 5.5 (4.5-6.7)† | 15.3 (9.1-25.9)† | 4.3 (2.0-9.0)† |
| 1992-2001 | 1.9 (1.6-5.2)† | 2.1 (1.7-2.5)† | 1.3 (0.9-1.8) | 3.0 (1.3-6.9)† |
| 1997-2001 | 1.2 (1.0-1.5)† | 1.3 (1.0-1.6)† | 1.0 (0.7-1.6) | 1.8 (0.7-4.7) |

*Proportional changes estimated using negative binomial regression and adjusted for age at diagnosis, race, and SEER registry.
†$P < 0.05$.

The Breast 20 (2011) 71–77

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Original article

# The effect of age in the outcome and treatment of older women with ductal carcinoma in situ

Alice Ho[a,*], Anuj Goenka[a], Nicole Ishill[b], Kimberly Van Zee[c], Amanda McLane[a], Anne Marie Gonzales[a], Lee Tan[d], Hiram Cody[c], Simon Powell[a], Beryl McCormick[a]

- 646 women
- ≥ 60 years old (2000 - 2007) with DCIS

**Table 2**
Patient and tumor characteristics.

| | Number | % |
|---|---|---|
| **Age (years)** | | |
| 60–69 | 401 | 62.1 |
| 70–79 | 191 | 29.6 |
| ≥80 | 54 | 8.4 |

Ho A et al. Breast 2011;20:71-7

| | 60–69 Years ($n$=407) | | 70–79 Years ($n$=192) | | ≥80 Years ($n$=55) | | $P$ value |
|---|---|---|---|---|---|---|---|
| | Number | % | Number | % | Number | % | |
| **Ethnicity** | | | | | | | |
| Caucasian | 328 | 81% | 183 | 85% | 48 | 87% | 0.35 |
| Hispanic | 20 | 5% | 8 | 4% | 4 | 7% | |
| African-American | 38 | 9% | 16 | 8% | 3 | 5% | |
| Other | 21 | 5% | 5 | 3% | 0 | 0% | |
| **Grade** | | | | | | | |
| Low | 58 | 14% | 42 | 22% | 9 | 16% | 0.28 |
| Intermediate | 204 | 50% | 84 | 44% | 24 | 44% | |
| High | 143 | 35% | 64 | 33% | 22 | 40% | |
| Unknown | 2 | 0% | 2 | 1% | 0 | 0% | |
| **Necrosis** | | | | | | | |
| None | 85 | 21% | 45 | 23% | 12 | 22% | 0.39 |
| Focal | 95 | 23% | 54 | 28% | 18 | 33% | |
| Moderate | 132 | 32% | 52 | 27% | 11 | 20% | |
| Extensive | 61 | 15% | 29 | 15% | 7 | 13% | |
| Unknown | 34 | 8% | 12 | 6% | 7 | 13% | |
| **Margin status** | | | | | | | |
| Negative | 351 | 86% | 154 | 80% | 41 | 75% | 0.2 |
| Positive | 12 | 3% | 8 | 4% | 2 | 4% | |
| Close (≤2 mm) | 43 | 11% | 30 | 16% | 12 | 22% | |
| Unknown | 1 | 0% | 0 | 0% | 0 | 0% | |

Ho A et al. Breast 2011;20:71-7

| | | |
|---|---|---|
| **Grade** | | |
| Low | 109 | 16.7 |
| Intermediate | 312 | 47.7 |
| High | 229 | 35.0 |
| Unknown | 4 | 0.6 |

**UK Screen-detected DCIS; mean 60 yrs (range 46-87):**

| | |
|---|---|
| **750** | **(10.7%)** |
| **2227** | **(31.8%)** |
| **4020** | **(57.4%)** |
| **10** | **(0.1%)** |

**Ho A et al. Breast 2011;20:71-7**

## Differences in the Pathologic and Molecular Features of Intraductal Breast Carcinoma between Younger and Older Women

**Rodrigues NA et al. Cancer 2003; 97**

TABLE 5
Differences in Tumor Marker Characteristics with Respect to Age

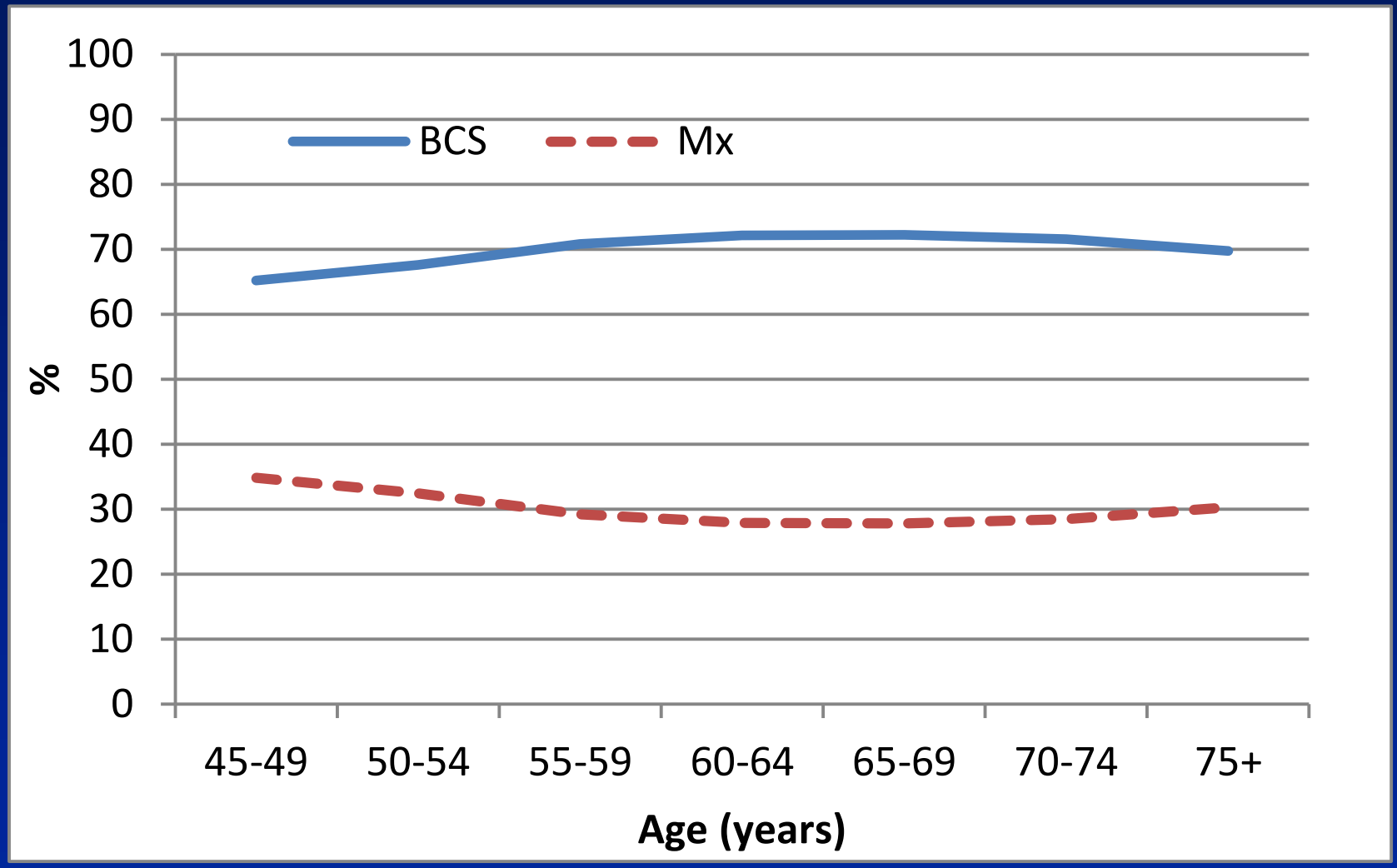
| | Young patients <42 years | | Older patients >60 years | | |
|---|---|---|---|---|---|
| Biologic marker | No. positive[a] | Percent positive | No. positive[a] | Percent positive | *P* value |
| ER | 18/20 | 90.0 | 27/34 | 79.4 | 0.31 |
| PR | 16/20 | 80.0 | 23/33 | 69.7 | 0.41 |
| p53 | 3/19 | 15.8 | 6/34 | 17.6 | 0.86 |
| HER-2/*neu* | 13/20 | 65.0 | 13/34 | 38.2 | 0.06 |
| ki-67 | 8/20 | 40.0 | 9/34 | 26.5 | 0.30 |
| cyclin D1 | 14/20 | 70.0 | 16/34 | 47.1 | 0.10 |
| *bcl*-2 | 11/20 | 55.0 | 16/33 | 48.5 | 0.65 |

- 2037 patients (1996 – 2009) with pure DCIS
- 6.5 % <40, 83 % 40-70, 10.5 % >70 yrs
- No differences in ER status, necrosis or DCIS size
  Alvarado R et al. Ann Surg Oncol 2012;19:3777-84

- **Overall, no convincing evidence that DCIS in older women is any different biologically from that in younger women**

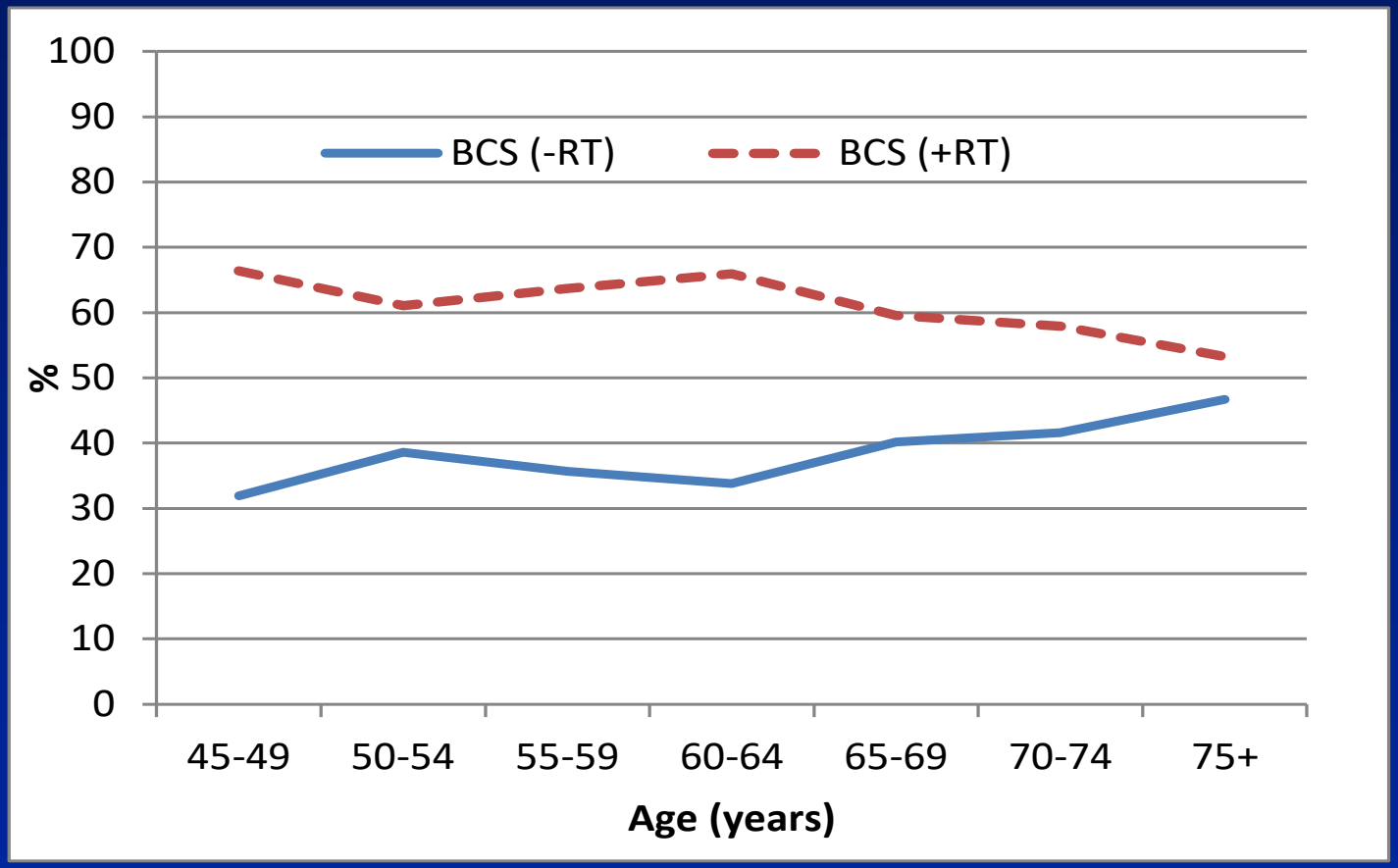
- **Management?**
- **Behaviour / outcome?**

# Sloane Project




**Variation in breast conserving therapy (BCS) and mastectomy (Mx) rates with age at 1st surgery**

# Sloane Project - Variation in use of RT in patients receiving breast conserving therapy (BCS) by age at first surgery




**Women aged 70 years + less likely to have RT than those aged 50-70 years (p = 0.006)**

# RT in Older Women

- **"For older women with DCIS, radiation therapy appears to confer a substantial benefit that remains meaningful even among low-risk patients"**

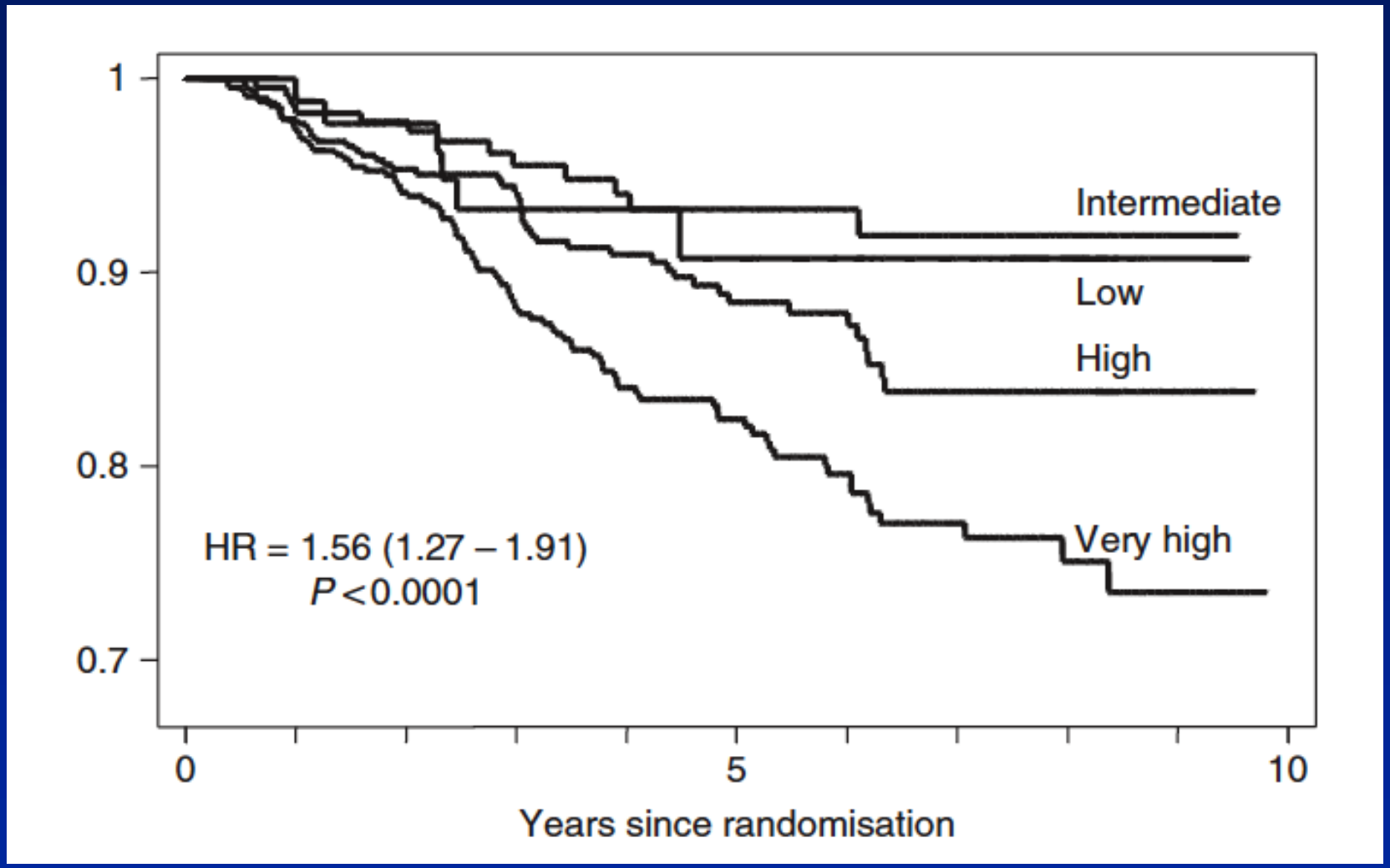
  **Smith BD et al. J Natl Cancer Inst 2006;98:1302-10**

- **"It is possible to identify older women with DCIS in whom the risk of recurrence is acceptably low after WLE alone. WLE alone may be a viable treatment option for select older women with DCIS"**

  **Ho A et al. Breast 2011;20:71-7**

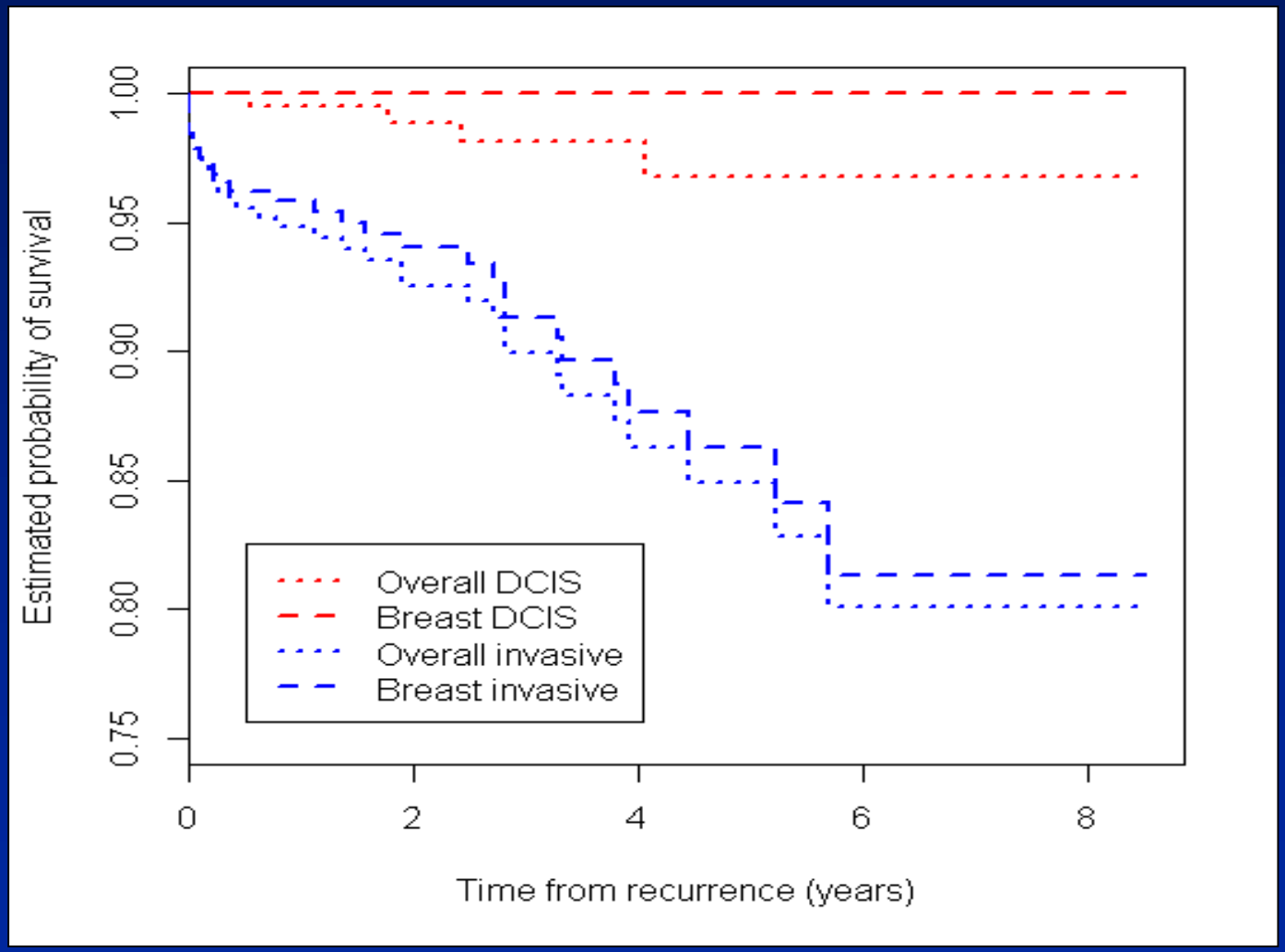
**Reasons for differing views?**

# Ipsilateral Recurrence – significance?




Pinder SE et al. Br J Cancer. 2010;103:94-100

# Overall & breast cancer specific survival in women treated with BCS with recurrent DCIS or invasive disease. (Survival from time of recurrence)




N = 226

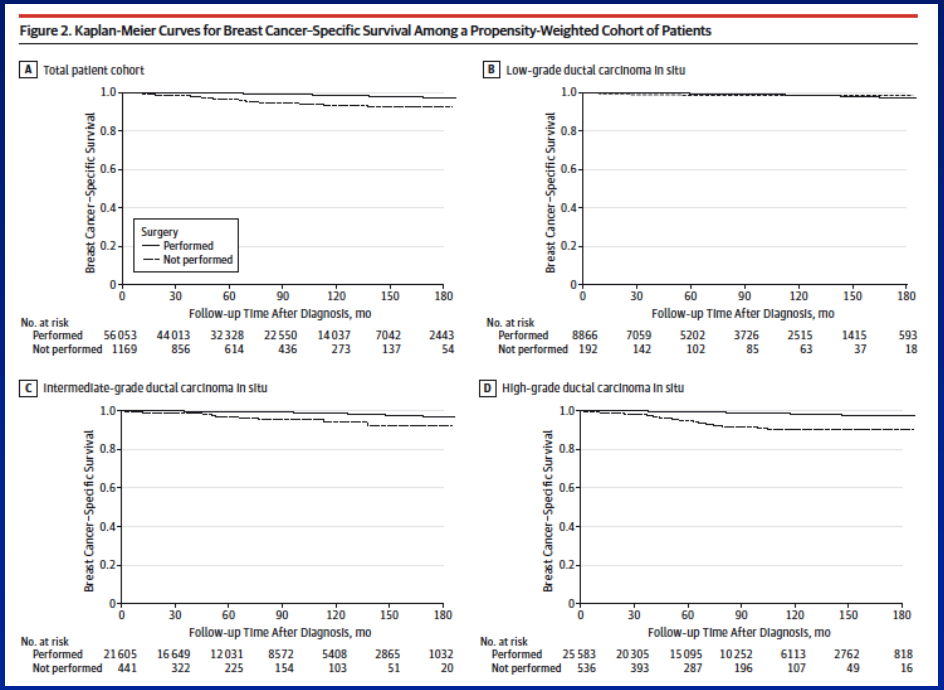
N=332

*A.M. Thompson et al. / European Journal of Cancer 101 (2018) 210–219*

Original Investigation

# Survival Benefit of Breast Surgery for Low-Grade Ductal Carcinoma In Situ
## A Population-Based Cohort Study

Yasuaki Sagara, MD; Melissa Anne Mallory, MD; Stephanie Wong, MD; Fatih Aydogan, MD; Stephen DeSantis, BS; William T. Barry, PhD; Mehra Golshan, MD

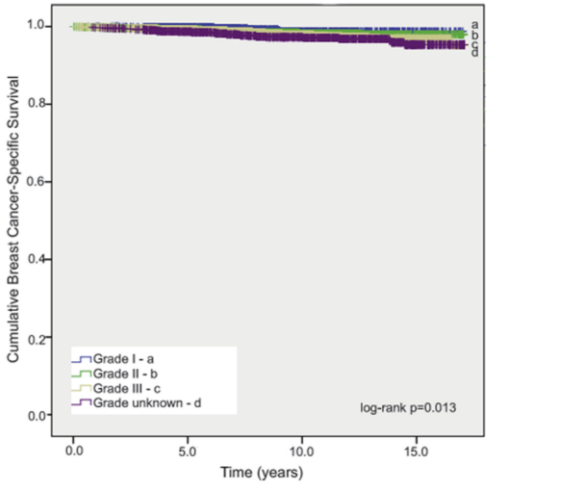



**JAMA Surg 2015;150:739-45**

Original Research

# Breast cancer–related deaths according to grade in ductal carcinoma in situ: A Dutch population–based study on patients diagnosed between 1999 and 2012

M.C. van Maaren [a,b,*,1], M. Lagendijk [c,1], M.M.A. Tilanus-Linthorst [c], L. de Munck [a,d], R.M. Pijnappel [e], M.K. Schmidt [f,g], J. Wesseling [f], L.B. Koppert [c], S. Siesling [a,b]




| Grade | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| I | 1,507 | 1,493 | 1,480 | 1,307 | 1,102 | 898 | 732 | 606 | 472 | 363 | 286 | 190 | 133 | 92 | 55 | 21 | 1 |
| II | 3,653 | 3,626 | 3,595 | 3,084 | 2,576 | 2,082 | 1,704 | 1,406 | 1,116 | 861 | 632 | 457 | 314 | 210 | 133 | 49 | 4 |
| III | 6,030 | 5,973 | 5,928 | 5,179 | 4,419 | 3,703 | 3,127 | 2,580 | 2,060 | 1,574 | 1,196 | 885 | 611 | 419 | 224 | 114 | 8 |
| Unknown | 1,003 | 989 | 976 | 906 | 842 | 778 | 705 | 633 | 572 | 498 | 431 | 341 | 270 | 201 | 118 | 59 | 13 |

Fig. 4. Kaplan–Meier curves for breast cancer–specific survival of all included DCIS patients diagnosed between 1999 and 2012 in the Netherlands, stratified for grade. DCIS, ductal carcinoma in situ.

European Journal of Cancer 101 (2018) 134–142

Original Investigation

# Breast Cancer Mortality After a Diagnosis of Ductal Carcinoma In Situ

Steven A. Narod, MD, FRCPC; Javaid Iqbal, MD; Vasily Giannakeas, MPH; Victoria Sopik, MSc; Ping Sun, PhD

*JAMA Oncol*. 2015;1(7):888-896. doi:10.1001/jamaoncol.2015.2510

**Table 1. Standardized Mortality Ratios (SMRs) of Breast Cancer Following a Diagnosis of Ductal Carcinoma In Situ, by Age at Diagnosis**

| Age at Diagnosis, y | Person-years | Follow-up, Mean (SD), y | Deaths, No. | | SMR (95% CI) |
|---|---|---|---|---|---|
| | | | Observed | Expected | |
| 30-34 | 8830.1 | 9.0 (6.2) | 22 | 1.3 | 17.0 (10.9-25.3) |
| 35-39 | 35 503.3 | 8.9 (6.0) | 62 | 8.5 | 7.3 (5.6-9.3) |
| 40-44 | 103 719.2 | 8.0 (5.7) | 112 | 35.7 | 3.1 (2.6-3.8) |
| 45-49 | 142 083.6 | 7.7 (5.5) | 144 | 67.4 | 2.1 (1.8-2.5) |
| 50-54 | 149 541.9 | 7.5 (5.4) | 157 | 91.7 | 1.7 (1.4-2.0) |
| 55-59 | 138 475.9 | 7.3 (5.2) | 145 | 103.9 | 1.4 (1.2-1.6) |
| 60-64 | 120 619.5 | 7.1 (5.3) | 138 | 107.3 | 1.3 (1.1-1.5) |
| 65-69 | 113 118.3 | 7.3 (5.3) | 162 | 118.0 | 1.4 (1.2-1.6) |
| All | 811 891.8 | 7.5 (5.4) | 942 | 533.8 | 1.8 (1.7-1.9) |

REPORT

BJC

British Journal of Cancer (2013) 108, 2205–2240 | doi: 10.1038/bjc.2013.177

# The benefits and harms of breast cancer screening: an independent review

*A report jointly commissioned by Cancer Research UK and the Department of Health (England) October 2012.*

M G Marmot*[,1], D G Altman[2], D A Cameron[3], J A Dewar[4], S G Thompson[5], M Wilcox[6] – The Independent UK Panel on Breast Cancer Screening

- **. ……the relevant question is not whether DCIS progresses to invasive cancer (it can), but whether it might have progressed to an invasive cancer that causes symptoms within the lifetime of the women concerned. ….**

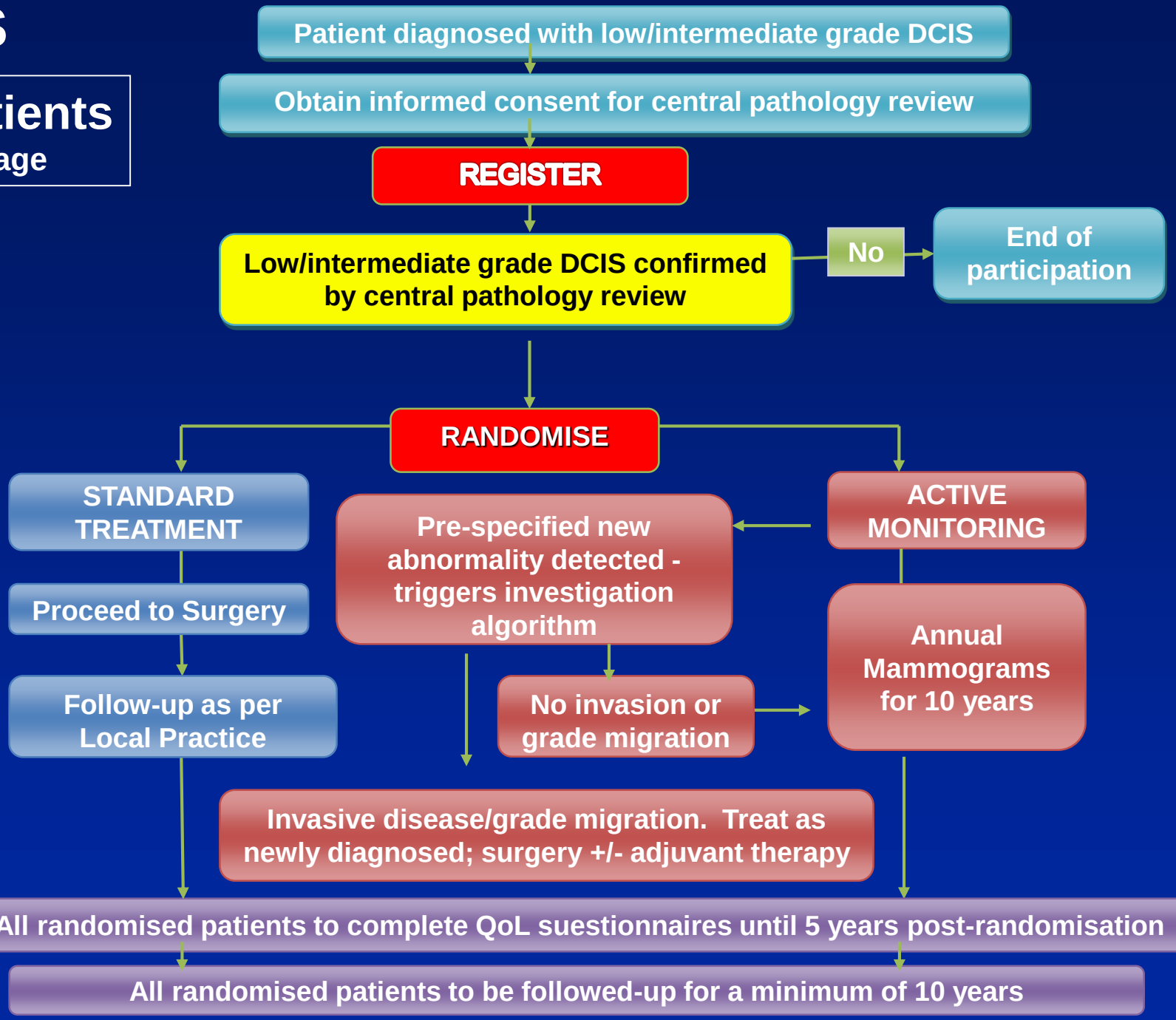
# Natural History of Low Grade DCIS

- 45 women with low-grade DCIS treated by biopsy only
- 16 (36%) invasive carcinoma, same breast & quadrant
- 11 invasive carcinomas within 10 years of DCIS biopsy; subsequent cases at 12, 23, 25, 29 and 42 years
- 7 (including 1 who developed invasive cancer 29 years after DCIS biopsy) developed distant metastasis, resulting in death 1-7 years post-diagnosis of invasive disease
- "The natural history of low-grade ductal carcinoma in situ may extend more than four decades…. Protracted natural history differs markedly from that of patients with high-grade ductal carcinoma ……..balancing recurrence risk with possible treatment-related morbidity for older women"

  Sanders ME et al. Mod Pathol 2015;28:662-9

# LORIS

**932 patients**
>45 years age



# Newsletter

October 2018

**A Phase III Trial of Surgery versus Active Monitoring for Low Risk Ductal Carcinoma in Situ (DCIS)**

## ***Statement from the Independent Data and Safety Monitoring Committee about LORIS***

**Following a recent Data and Safety Monitoring Committee meeting in July this year, the committee released the following statement to be issued to the LORIS participating centres:**

**"The DMC has reviewed the accumulating LORIS data including patient demographics, surgical details, pathology of surgical samples, additional assessments/treatments, long term follow up and adverse events. No safety concerns were identified"**

# Risk factors for the development of invasive cancer in unresected ductal carcinoma in situ

Anthony J. Maxwell [a, b, *], Karen Clements [c], Bridget Hilton [c], David J. Dodwell [d], Andrew Evans [e], Olive Kearins [c], Sarah E. Pinder [f], Jeremy Thomas [g], Matthew G. Wallis [h], Alastair M. Thompson [i], for the Sloane Project Steering Group

European Journal of Surgical Oncology 44 (2018) 429–435

- 89 women with DCIS
- Median age at diagnosis 75 (range 44-94) years
- 44 had endocrine therapy, 1 also received RT
- Median follow-up (to death, invasive disease or last review) 59 (12-180) months
- 29 women (33%) developed invasive cancer after median interval of 45 (12-144) months
- 14/29 (48%) high grade, 10/31 (32%) intermediate grade and 3/17 (18%) low grade DCIS developed invasive cancer after median intervals of 38, 60 and 51 months
- Cumulative incidence of invasion significantly higher in high grade DCIS than other grades

**Table 2**
Invasive carcinoma type and histological grade and the cytonuclear grade of the original DCIS, where known.

| Original DCIS grade | IDC grade 1 | IDC grade 2 | IDC grade 3 | Other invasive cancer | Not known | Total |
|---|---|---|---|---|---|---|
| High | 0 | 2 | 6 | 1 invasive lobular carcinoma grade 2 | 5 | 14 |
| Intermediate | 2 | 3 | 0 | 1 mixed carcinoma | 4 | 10 |
| Low | 1 | 1 | 0 | 0 | 1 | 3 |
| Not known | 0 | 0 | 0 | 1 invasive lobular carcinoma grade 2; 1 invasive papillary carcinoma | 0 | 2 |
| Total | 3 | 6 | 6 | 4 | 10 | 29 |

IDC—Invasive ductal carcinoma.

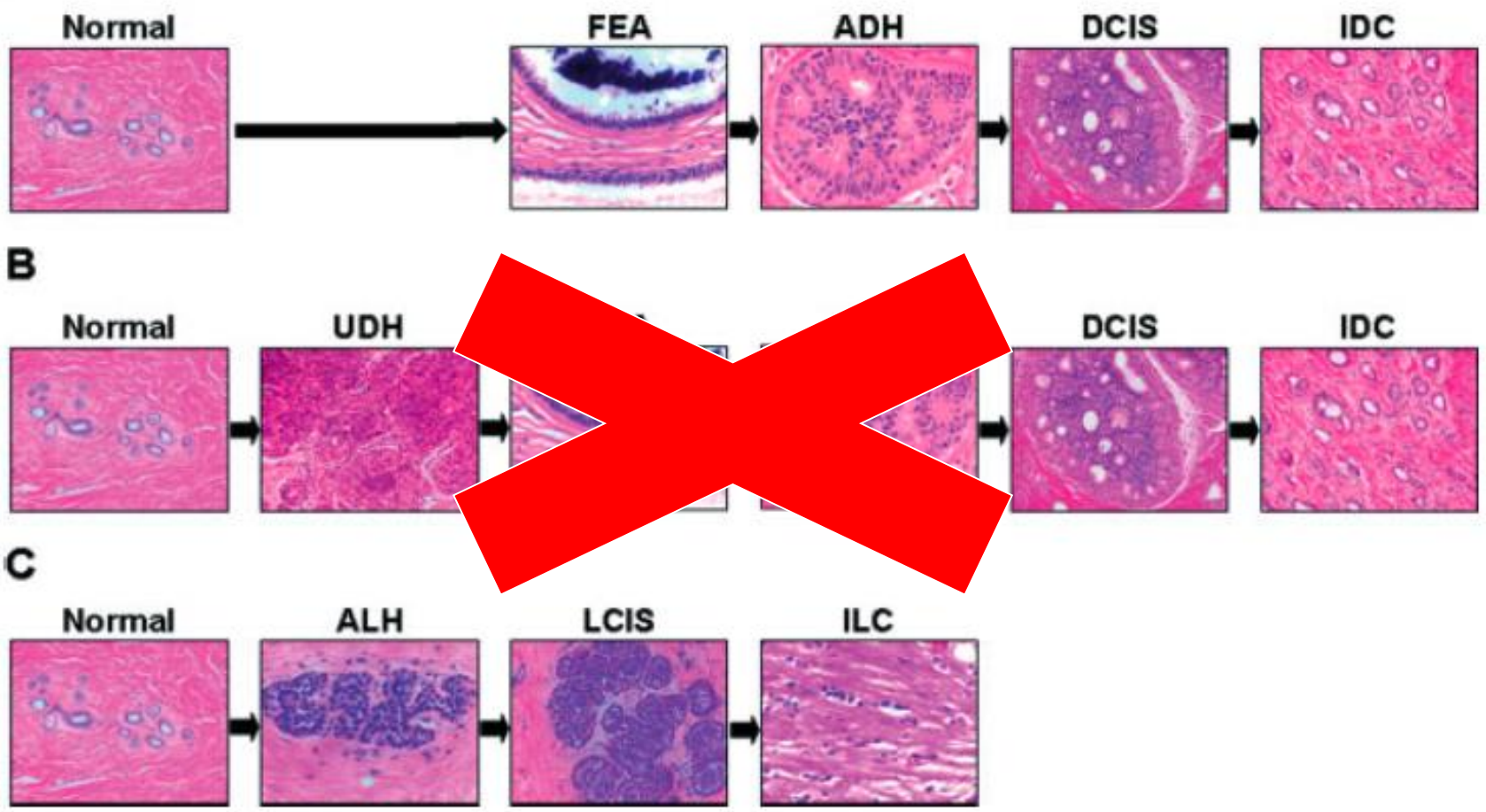
European Journal of Surgical Oncology 44 (2018) 429–435

Journal of Pathology
*J Pathol* 2011; **223**: 307–317
Published online 16 November 2010 in Wiley Online Library
(wileyonlinelibrary.com) DOI: 10.1002/path.2808

INVITED REVIEW

# The molecular pathology of breast cancer progression

Alessandro Bombonati[1] and Dennis C Sgroi[1,2]*



# Summary

- Whilst there is no good evidence that the pattern of heterogeneity of DCIS is different in the older population, the relevance of the differing biology (e.g. low vs high grade, ?ER positive vs ER negative) may be particularly relevant in management


STOP
WRONG WAY
DO NOT ENTER