



diseases of the breast - insurance issues

- benign breast disease
- breast cancer risk factors
- breast cancer screening
- early breast cancer - breast cancer in situ

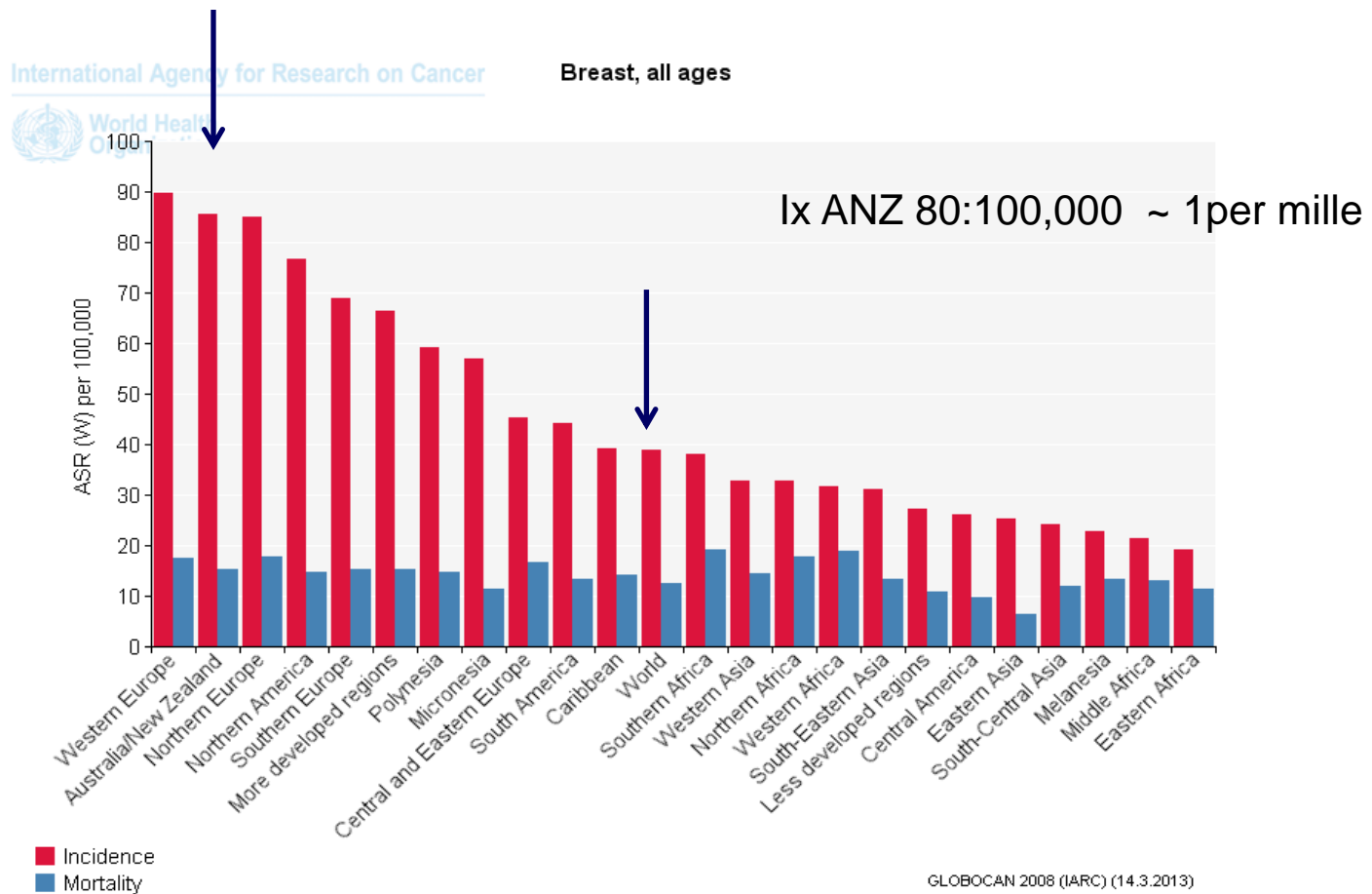
Dr Paul R Davis FRACP

Medical Director

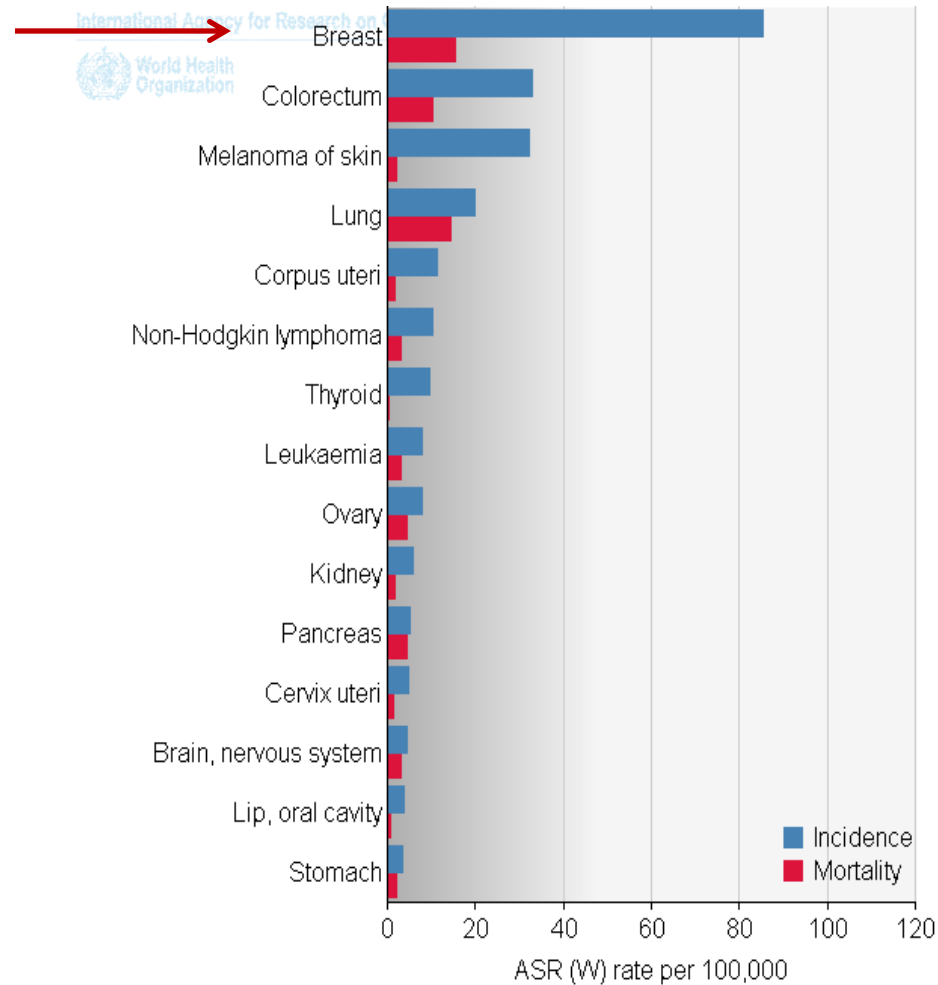
RGA International

December 2013

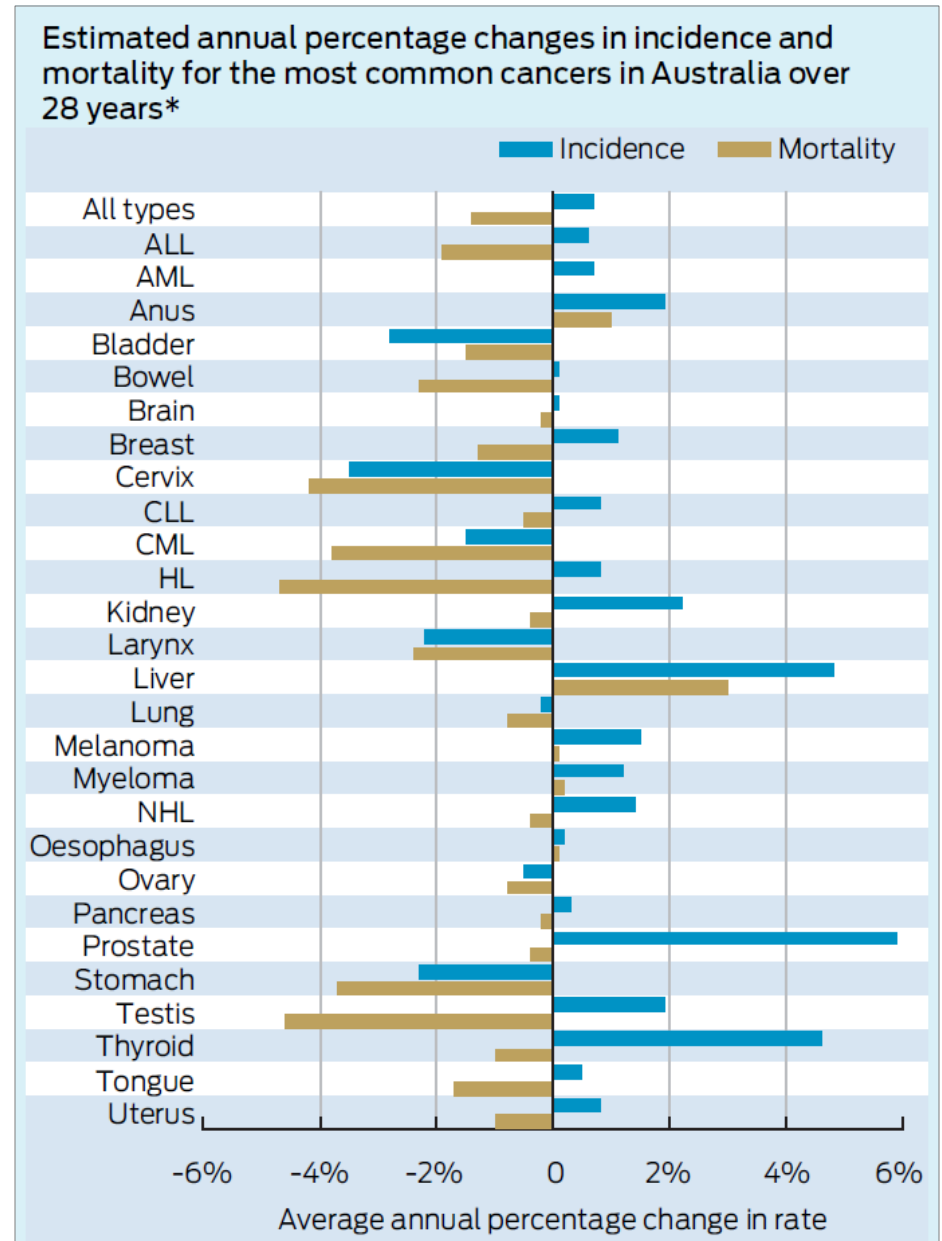
breast cancer WHO - global incidence and mortality



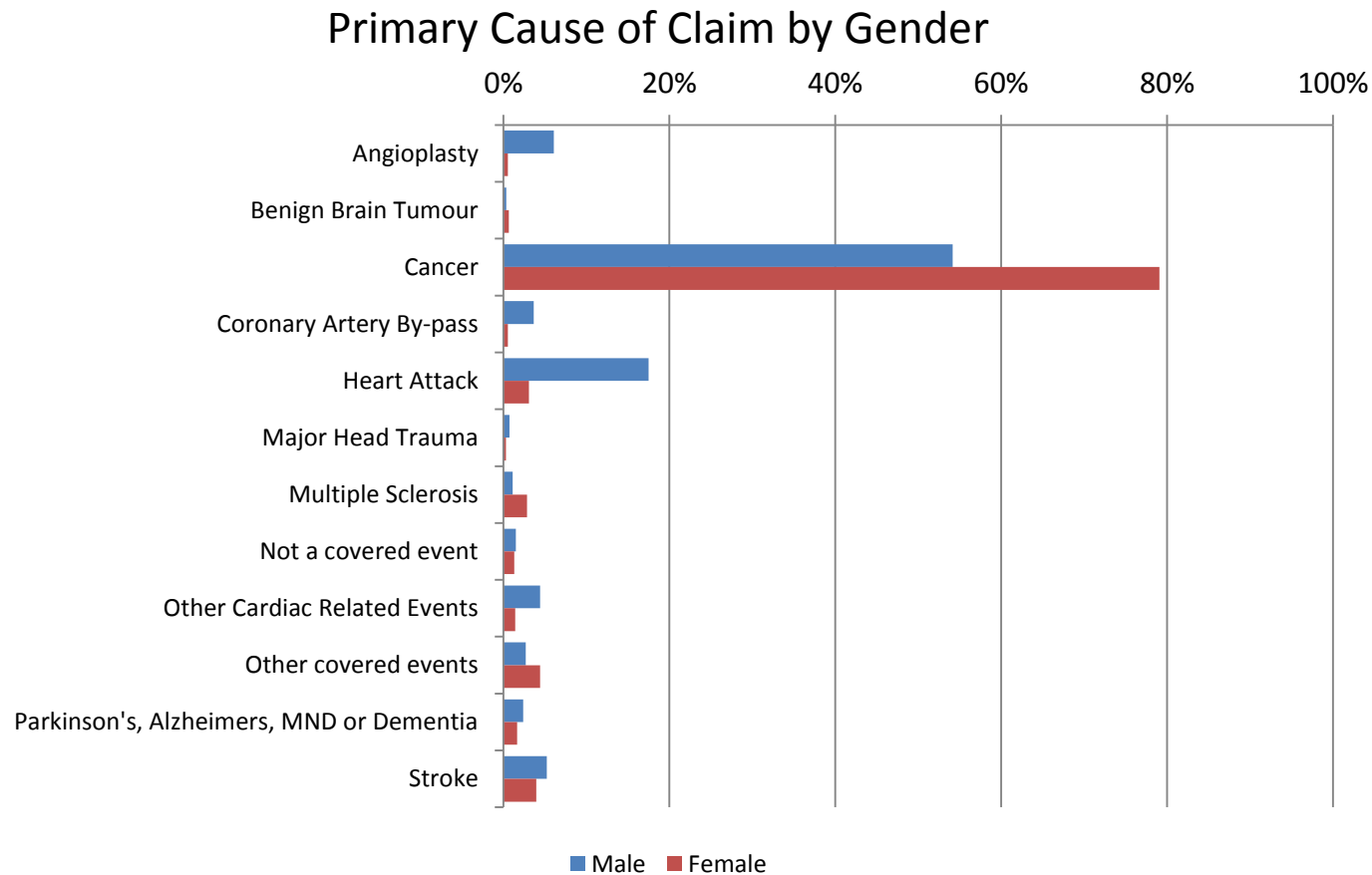
cancer ANZ - females 2008 Globocan



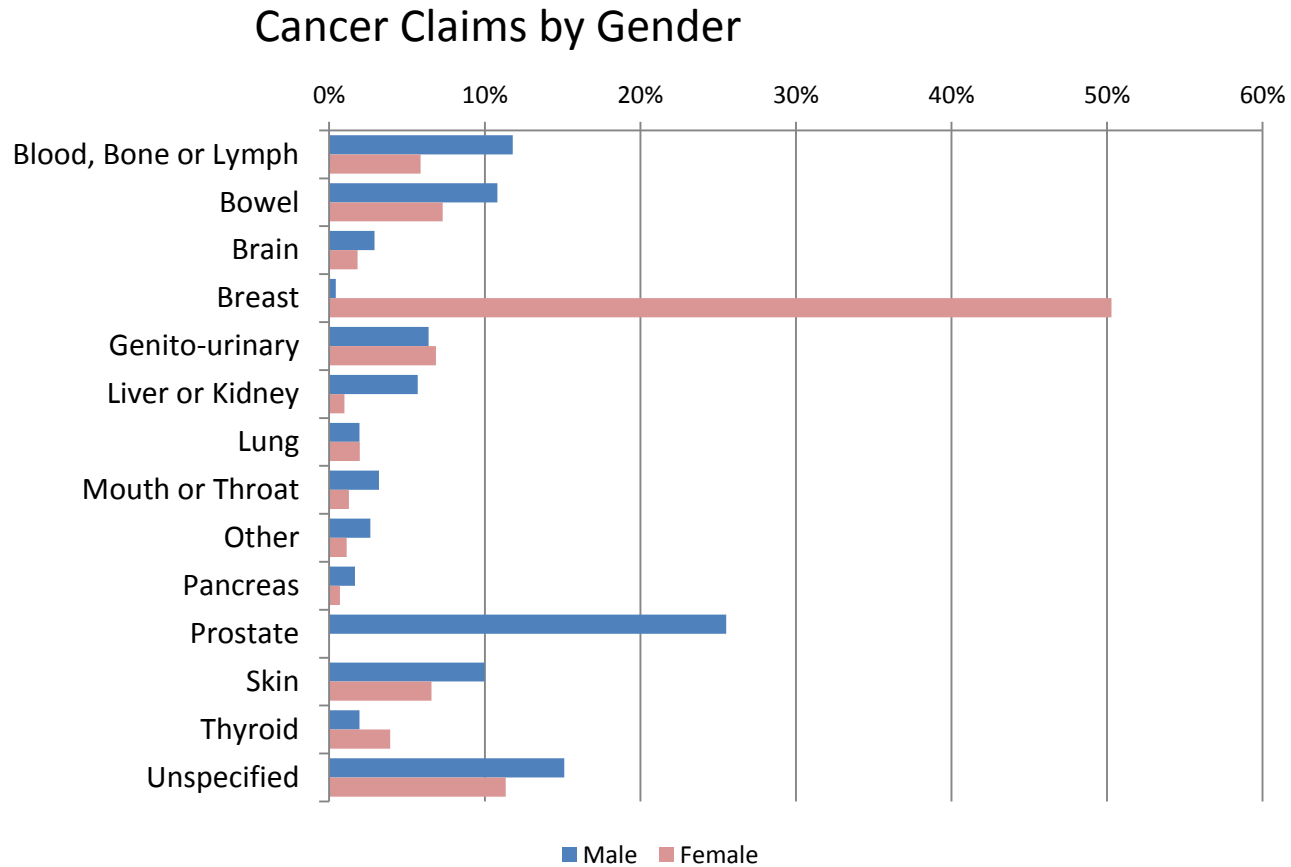
cancer trends - Australia



critical illness - RGA claims experience



critical illness - RGA cancer claims experience



breast cancer - the facts

- incidence 1.25:1000 per annum (SEER 2005 - 2009)
- incidence 0.8:1000 per annum ANZ
- lifetime risk 1:8 for women born today
- incidence increasing 1 - 2 % pa
- invasive cancers begin as CIS in milk ducts or milk lobules
 - ductal cancer ~ 85%
 - lobular cancer ~ 15%
- early detection influences mortality

digital mammography screening programs

- DCIS 1:1300 mammograms
- breast cancer 4:1000 mammograms
- reduction in tumours > 2cms - 45%
- reduction in node positive tumours
- reduction in mortality - 30%



breast cancer screening - mortality benefit

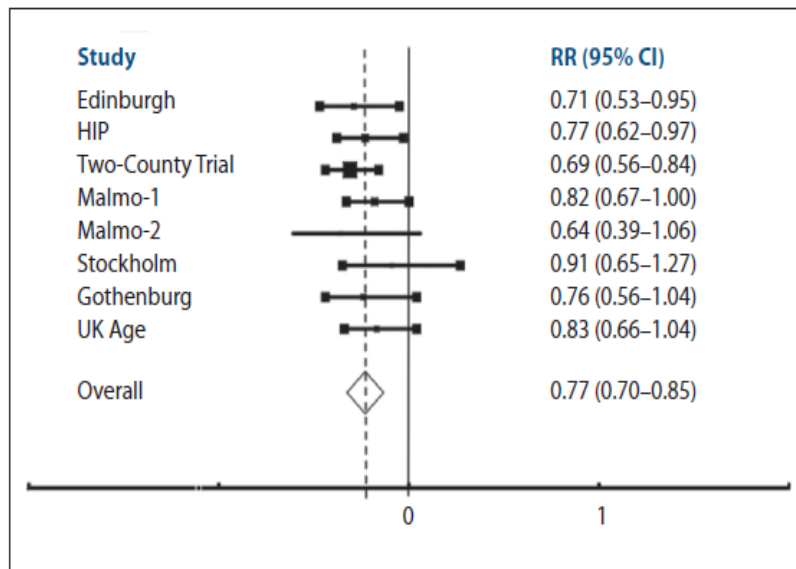


Figure 3a: Relative risks of breast cancer mortality—The group invited to screening is compared with the group receiving usual care in the population-based screening trials.

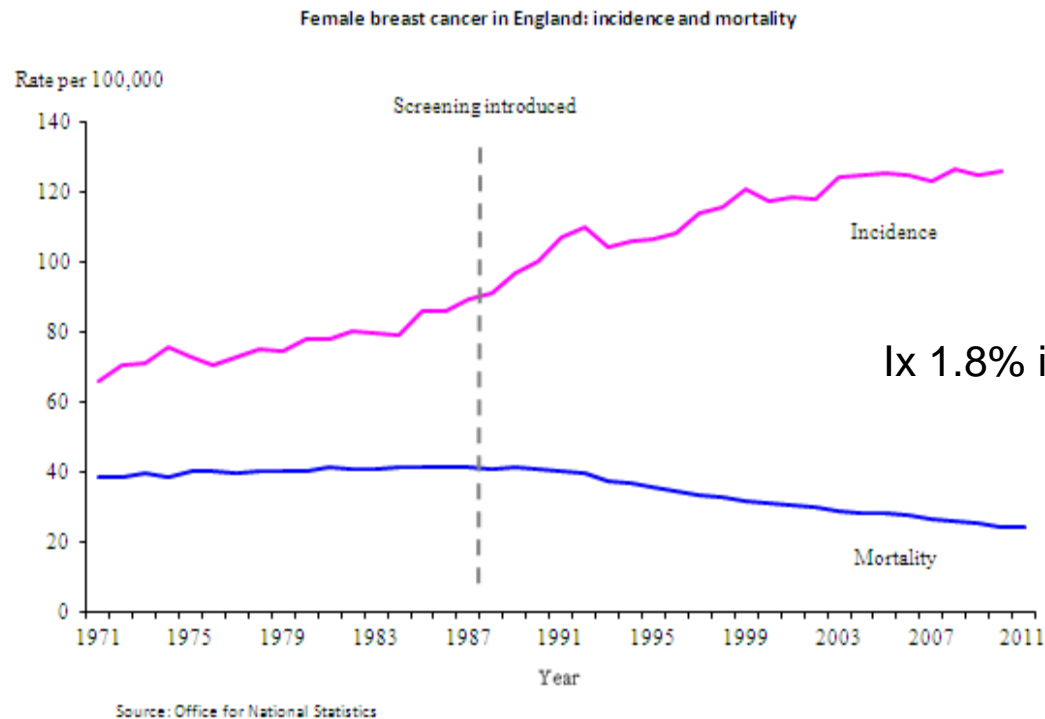
TABLE 1. BENEFIT OF SCREENING MAMMOGRAPHY ACCORDING TO AGE.*

STUDY	DURATION OF FOLLOW-UP	SCREENING INTERVAL	RELATIVE RISK OF DEATH FROM CANCER (95% CI)†	
			AGE 50-74 YR	AGE 40-49 YR
	yr	mo		
Edinburgh	10	24	0.8 (0.6-1.1)	0.8 (0.5-1.5)
Malmö	12	18-24	0.9 (0.6-1.2)	0.5 (0.2-1.2)
Kopparberg	12	24-33	0.8 (0.5-0.9)	0.8 (0.4-1.4)
Östergötland	12	24-33	0.8 (0.6-1.0)	1.3 (0.8-2.3)
Canada	7	12	1.0 (0.6-1.5)	1.4 (0.8-2.2)
Health Insurance Plan	10	12	0.7 (0.5-1.0)	0.8 (0.5-1.2)
Stockholm	8	28	0.6 (0.4-1.1)	1.0 (0.5-2.0)
Gothenburg	7	18	0.9 (0.5-1.6)	0.7 (0.3-2.0)
Overall	—	—	0.8 (0.7-0.9)	0.9 (0.8-1.1)

Smith RA Oncology May 2012

Hortobagyi GN NEJM 1998

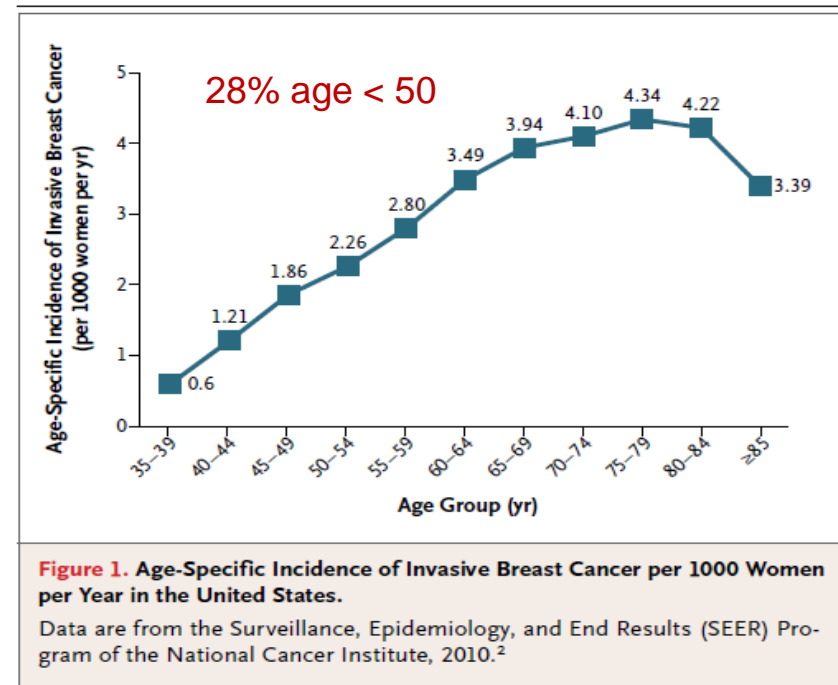
breast cancer screening - mortality benefit UK



breast cancer screening - when should it start

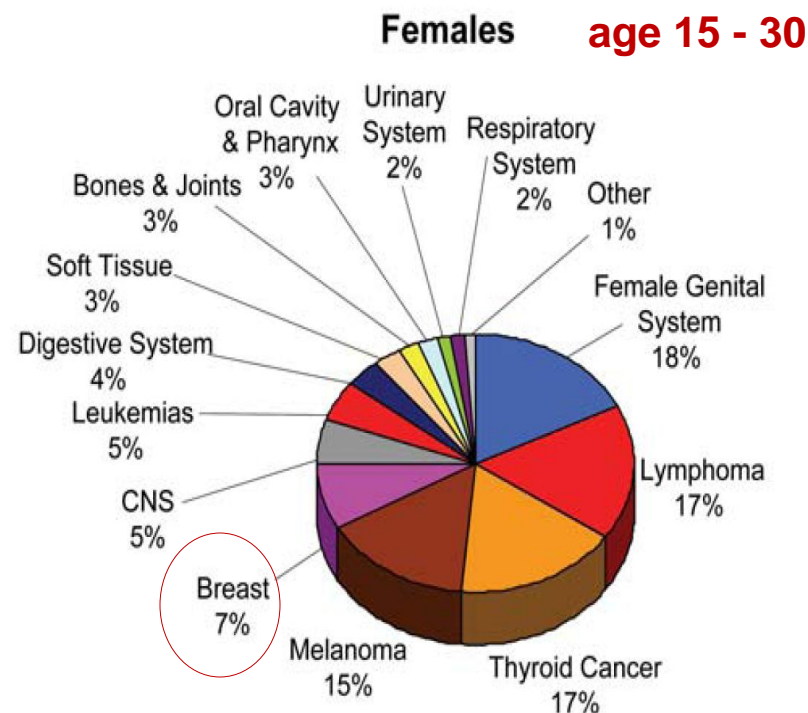
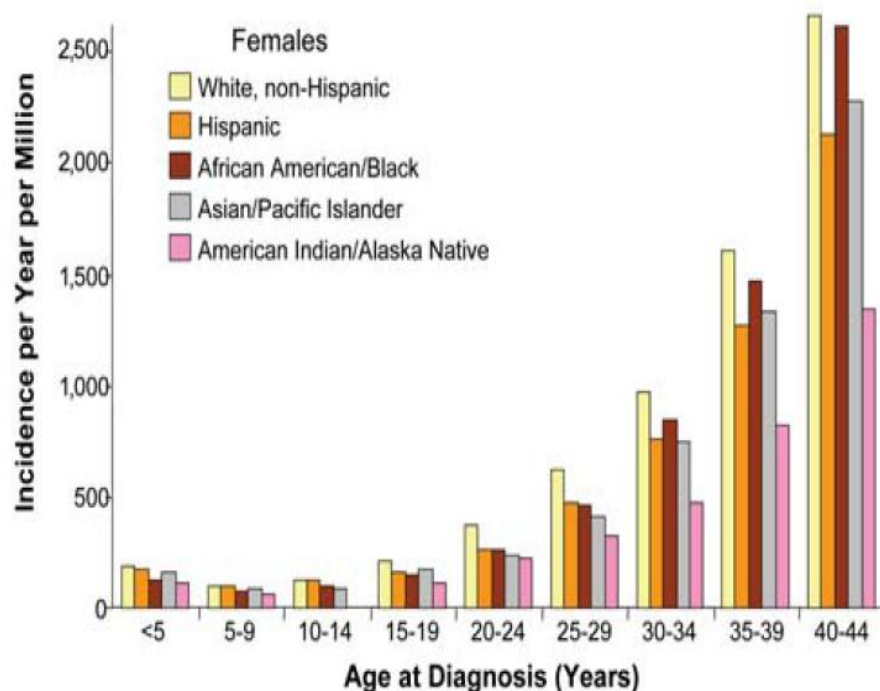
Table 4. Guidelines for Breast-Cancer Screening.*

Organization	Year Guidelines Issued	Mammography
USPSTF	2009	Age 50–74 yr, every 2 yr; age 40–49 yr and age ≥75 yr, individualize the decision (every 2 yr, if performed)
American Cancer Society	2010	Age ≥40 yr, annually†
National Comprehensive Cancer Network	2011	Age ≥40 yr, annually†
National Cancer Institute	2010	Age ≥40 yr, every 1–2 yr†
American College of Physicians	2007	Age 50–74 yr, every 1–2 yr; age 40–49 yr, individualize the decision (every 1–2 yr, if performed)
American College of Obstetricians and Gynecologists	2003	Age 40–49 yr, every 1–2 yr; age ≥50 yr, annually†
American College of Radiology	2008	Age ≥40 yr, annually†
Canadian Task Force on Preventive Health Care	1998–2001	Age 50–69 yr, every 1–2 yr; age 40–49 yr, individualize the decision (every 1–2 yr, if performed)
National Health Service, United Kingdom	2011	Age 47–73 yr, every 3 yr



cancer incidence by age SEER

breast cancer in young people



The Oncologist 2006;11:590–601

ARCHIE BLEYER,^a AARON VINY,^b RONALD BARR^c

screening for disease

- case finding in people who have no symptoms
- apply a test that discriminates between normal and abnormal

ideal test

- 100% sensitive
 - positive in everyone with the disease
 - never negative in anyone with the disease - no false negatives
- 100% specific
 - negative in everyone with no disease
 - never positive in anyone without the disease - no false positives
- no test is 100% sensitive - disease is missed
- no test is 100% specific - disease is diagnosed in people who do not have it
- false negative rates & false positive rates limit a tests utility - predictive value

screening for disease - medical indications

Box 2 | Criteria for establishing and evaluating a screening programme²⁴

- The disease causes a serious risk for the individual and a burden on society
- An effective treatment is available for the disease in question
- The natural course of the disease is understood
- Screening can detect a presymptomatic or early symptomatic stage of disease, and treatment is useful in the early stage
- The screening test has high specificity, high sensitivity, and carries a low risk
- People who test positive on the screening test have access to treatment
- Screening and follow-up is cost effective when balanced with the burden of disease on the individual and on society

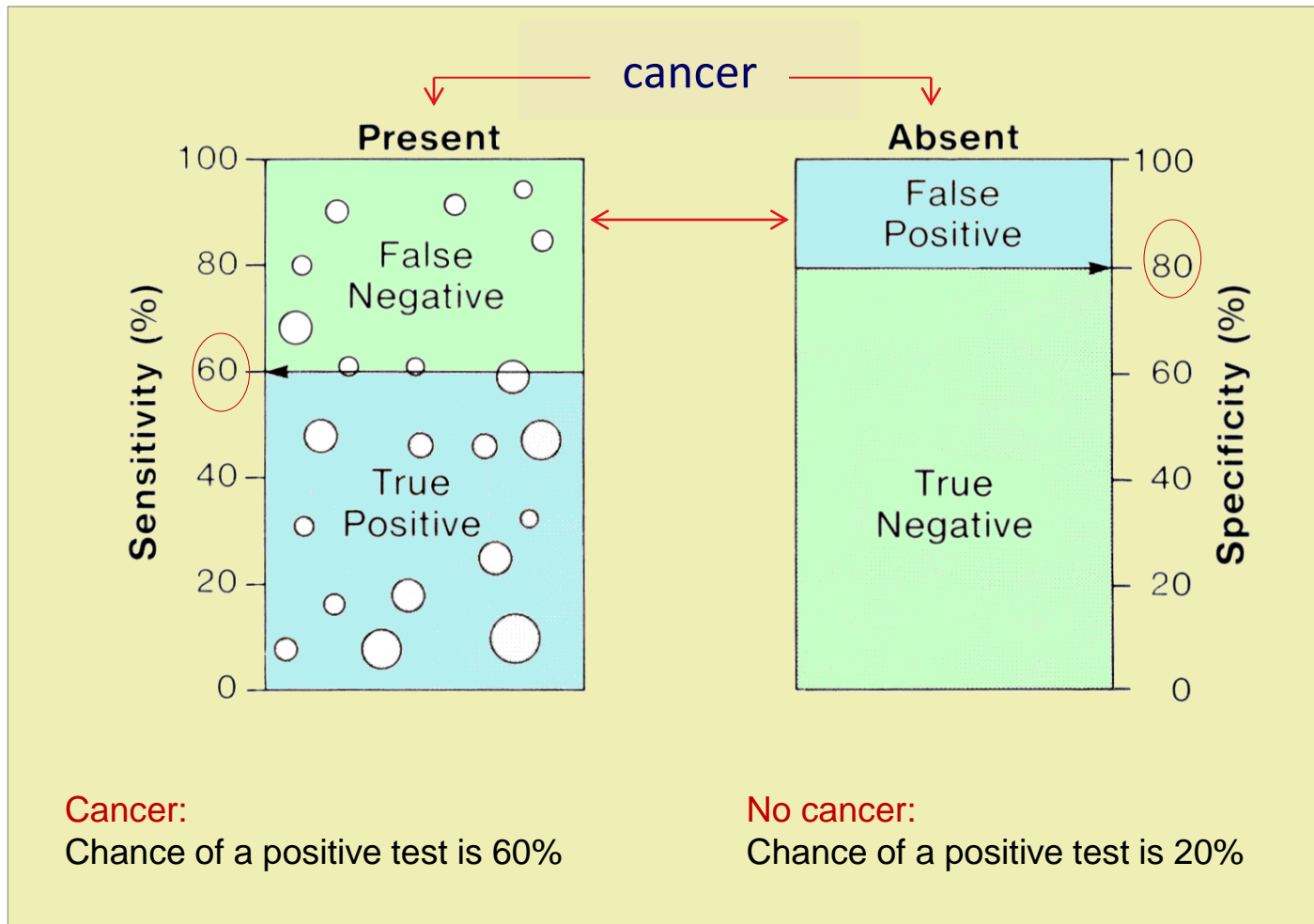
screening for disease - insurance indications

- condition is prevalent in insured population
- impairment must be a claimable
- avoid adverse experience
- preserve profitability
- minimise antiselection
- pricing
- insure future price protection

protection in the absence of screening

- retain capacity to underwrite
- retain capacity to use family history
- choose covered populations carefully
 - disease prevalence
 - disease risk

sensitivity and specificity



sensitivity and specificity - digital mammography

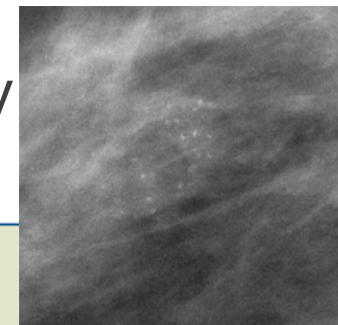


Table 1 Performance Measures for 1,960,150 Screening Mammography Examinations^a Performed in the US From 2002 to 2006 by Age, Based on Breast Cancer Surveillance Consortium Data as of 2009

Age	Sensitivity ^b	Specificity ^c
40-44	73.6%	88.2%
45-49	80.3%	89.0%
50-54	82.4%	90.5%
55-59	84.6%	91.5%
60-64	84.9%	91.9%
65-69	84.6%	92.3%
70-74	84.7%	92.9%
75-89	86.6%	93.4%
Total (40-89)	83.5%	90.9%

- sensitivity 82.4%
 - 84.6% with cancer test positive
 - 15.4% with cancer test negative

- specificity 91.5%
 - 91.5% without cancer test negative
 - 8.5% without cancer test positive

sensitivity and specificity - digital mammography

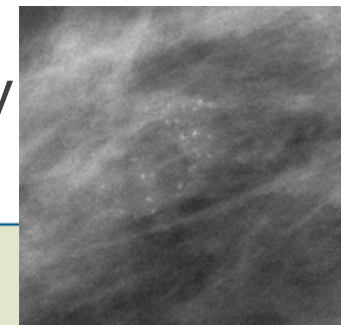


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65-69	84.6%	92.3%
70-74	84.7%	92.9%
75-89	86.6%	93.4%
Total (40-89)	83.5%	90.9%

literature sensitivity ranges 50 - 90%

- sensitivity in dense glandular breasts
 - 50%
- sensitivity in fatty breasts - no glands
 - 98%

sensitivity and specificity - digital mammography

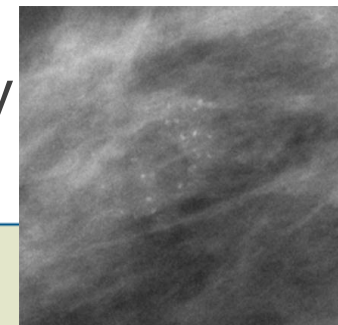


Table 1 Performance Measures for 1,960,150 Screening Mammography Examinations^a Performed in the US From 2002 to 2006 by Age, Based on Breast Cancer Surveillance Consortium Data as of 2009

Age	Sensitivity ^b	Specificity ^c	Recall ^d
40-44	73.6%	88.2%	11.8%
45-49	80.3%	89.0%	11.2%
50-54	82.4%	90.5%	9.7%
55-59	84.6%	91.5%	8.8%
60-64	84.9%	91.9%	8.5%
65-69	84.6%	92.3%	8.0%
70-74	84.7%	92.9%	7.5%
75-89	86.6%	93.4%	7.1%
Total (40-89)	83.5%	90.9%	9.3%

- 10% recall rates
- 10% recalls have biopsy
- screen 1000 → diagnose 4 cancers

sensitivity and specificity - digital mammography

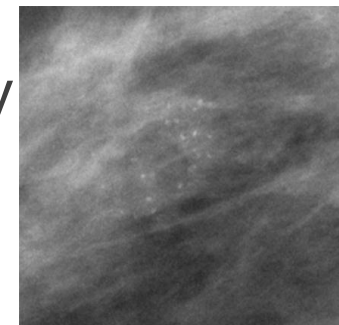


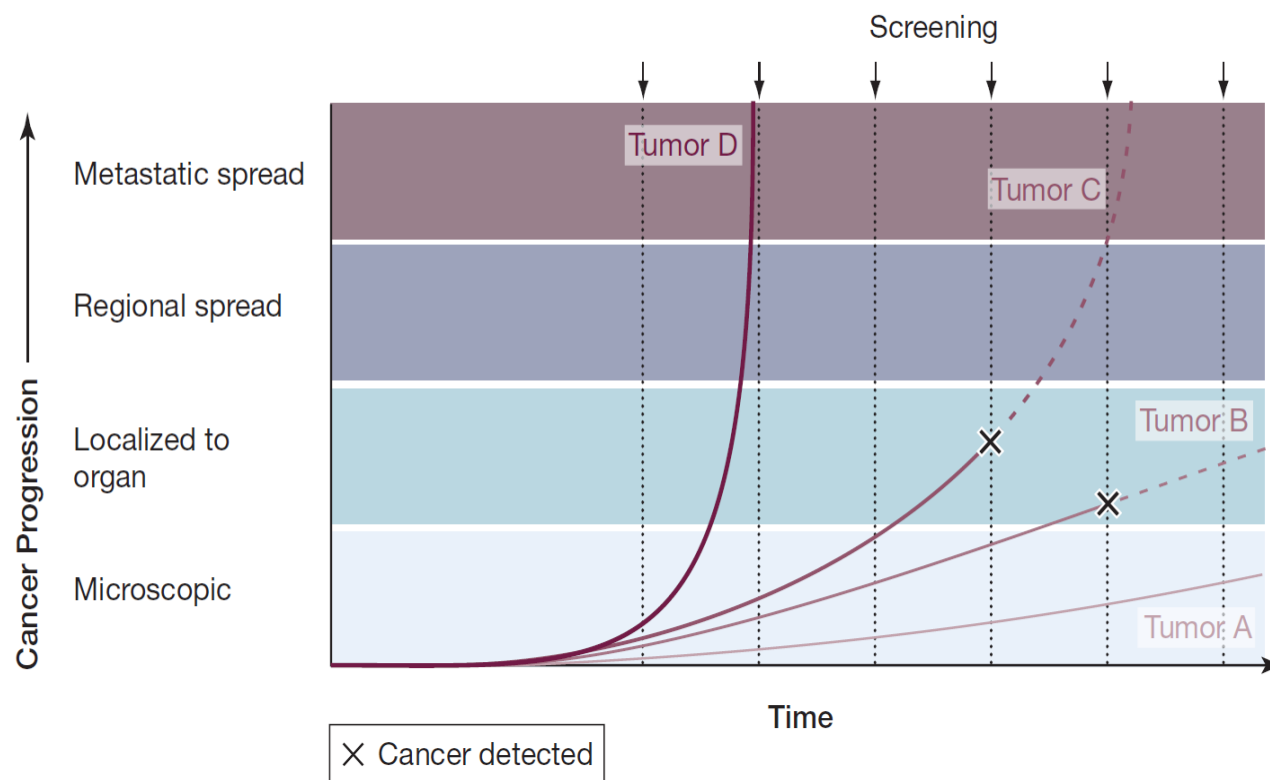
Table 2. Draft balance sheet for screening mammography in 50-year-old women*

Benefits	Harms
One woman will avoid a breast cancer death (36)	Between two and 10 women will be overdiagnosed and treated needlessly Between five and 15 women will be told that they have breast cancer earlier than they would otherwise yet have no effect on their prognosis Between 200 and 500 women will have at least one "false alarm" (50–200 will be biopsied)

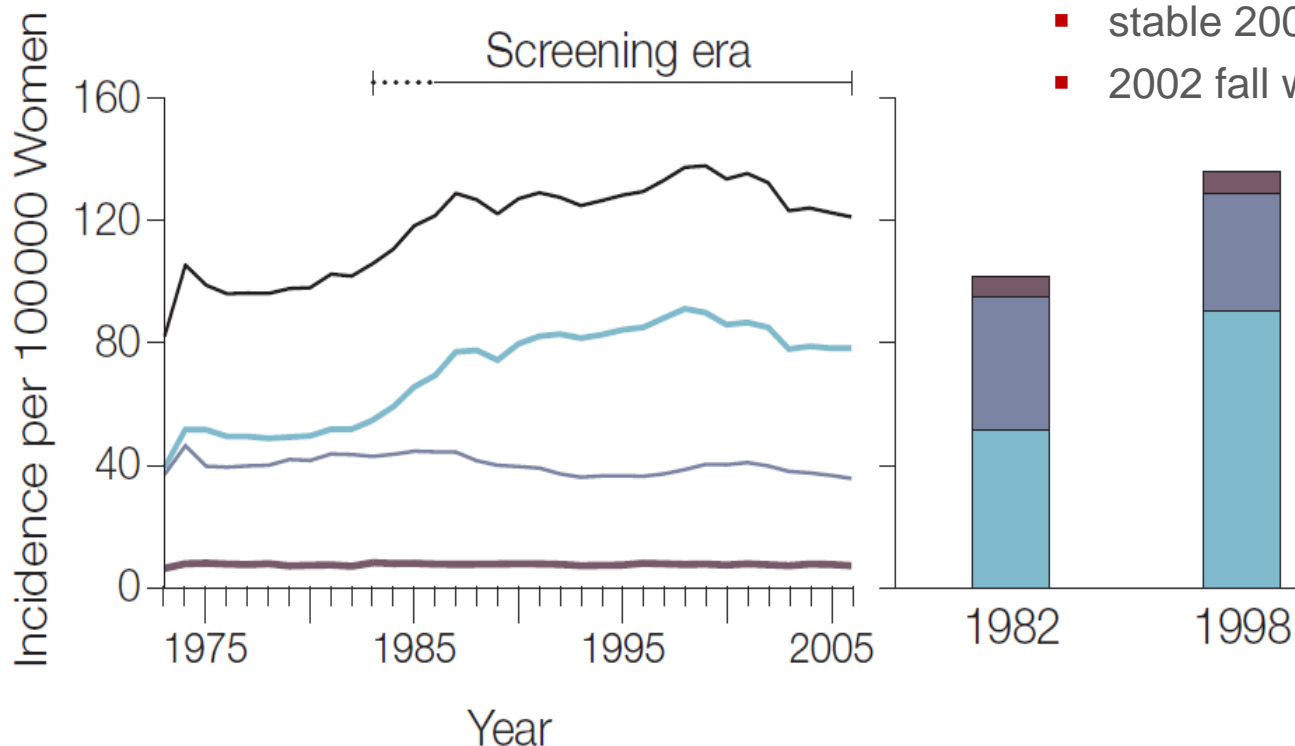
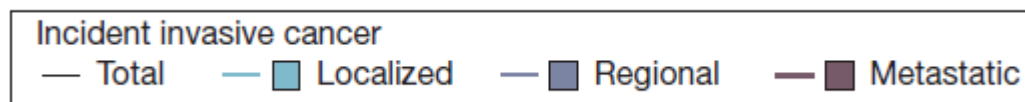
*1000 women with mammography after age 50

tumour behaviour and the utility of screening

Figure 3. Screen Detection Capability Based on Tumor Biology and Growth Rates



screening shortfalls - incident invasive breast cancer



20 years of screening

- DCIS 2% → 30% all cancer
- Ix invasive CA not falling in parallel
- no reduction in aggressive late Δ
- stable 2002 - 2005
- 2002 fall was removal HRT

screening and breast cancer

Effect of Three Decades of Screening Mammography on Breast-Cancer Incidence

Archie Bleyer, M.D., and H. Gilbert Welch, M.D., M.P.H.

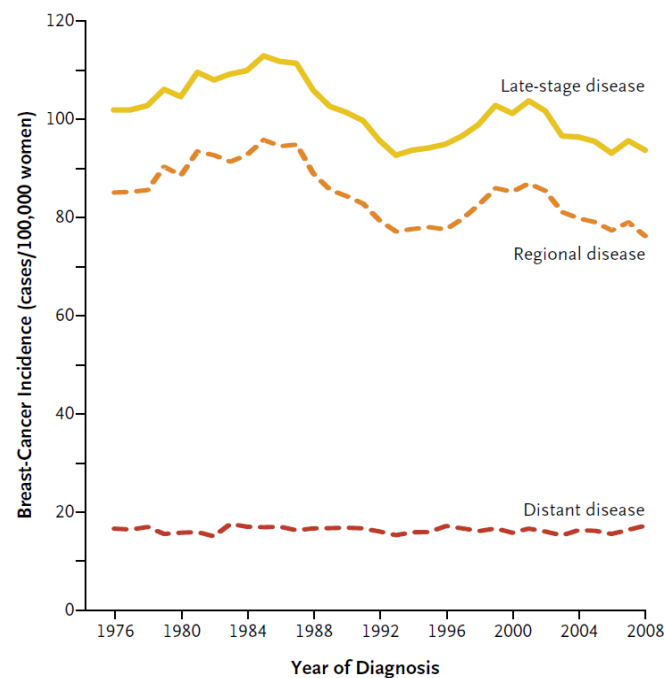
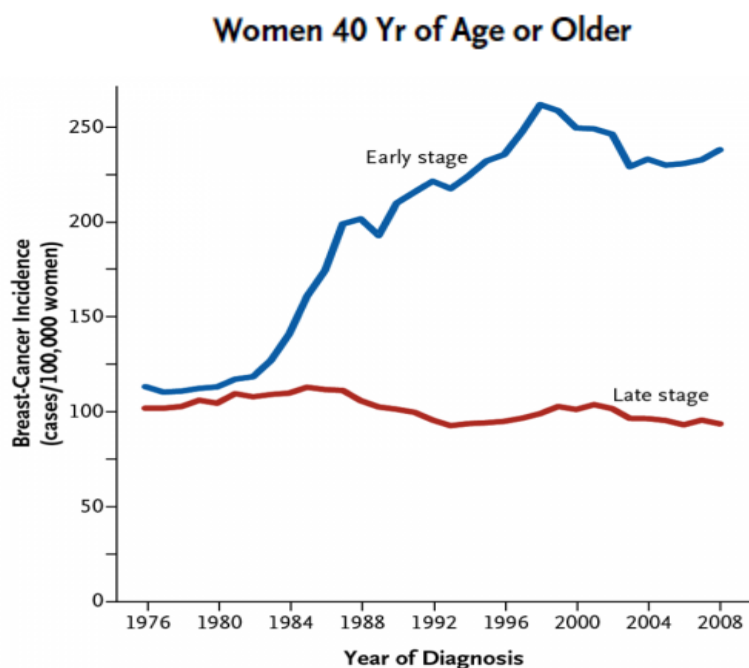


Figure 2. Trends in the Annual Incidence of Late-Stage Breast Cancer and Its Two Components (Regional and Distant Disease) among U.S. Women 40 Years of Age or Older, 1976–2008.

screening and breast cancer

Effect of Three Decades of Screening Mammography on Breast-Cancer Incidence

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Women 40 Yr of Age or Older

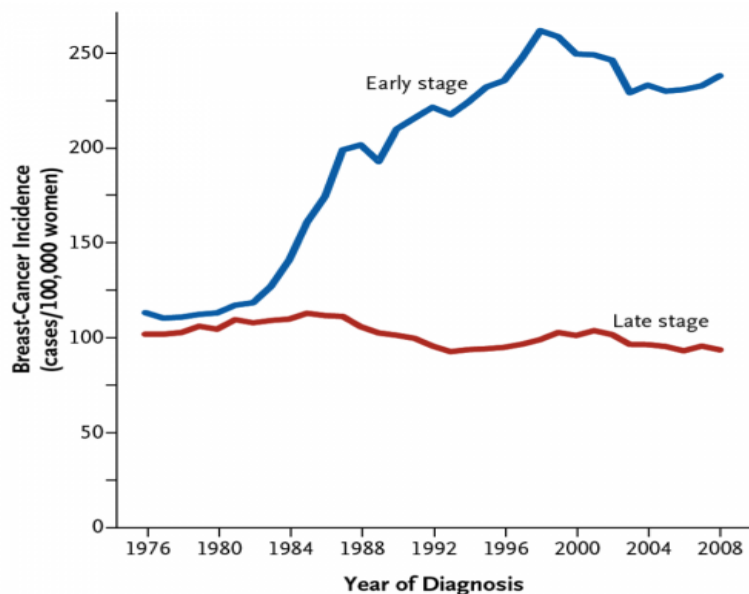


Table 1. Absolute Change in the Incidence of Stage-Specific Breast Cancer among Women 40 Years of Age or Older after the Introduction of Screening Mammography.*

Variable	Annual Breast-Cancer Incidence		
	Before Mammography (1976–1978)	Three Decades Later (2006–2008)	Absolute Change
	<i>number of cases per 100,000 women</i>		
Increase in cases of early-stage breast cancer			
DCIS	7	56	50
Localized disease	105	178	72
Total	112	234	122
Decrease in cases of late-stage breast cancer			
Regional disease	85	78	−8†
Distant disease	17	17	0‡
Total	102	94	−8

breast cancer - screening

digital mammography

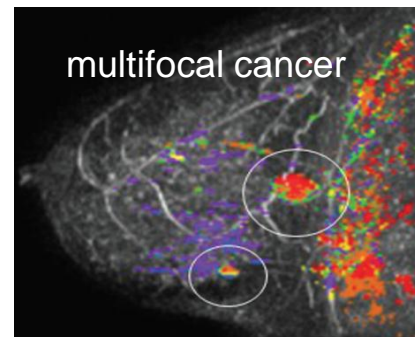
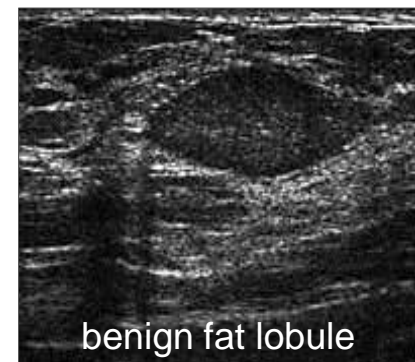
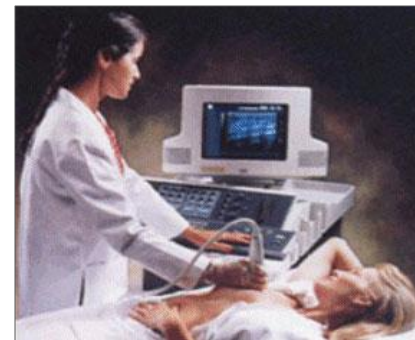
- most appropriate test
- proven to reduce mortality

ultrasound

- unproven as screening tool
- may miss cancer in situ - DCIS and LCIS
- useful adjunct dense breasts - low sensitivity mammogram

MRI

- sensitivity for DCIS 90%
- sensitivity for invasive ductal cancer 90 - 100%
- high false positive rate - over diagnosis
- specificity 40 - 97%
- high cost



breast cancer - screening and harm

radiation induced breast cancer

annual mammography 40 - 55 followed by biennial mammography

- 86 cancers per 100,000 women - 1:1000
- 11 cancer deaths per 100,000 women
- benefit : risk is 4.5 : 1 for lives saved

overdiagnosis of breast cancer

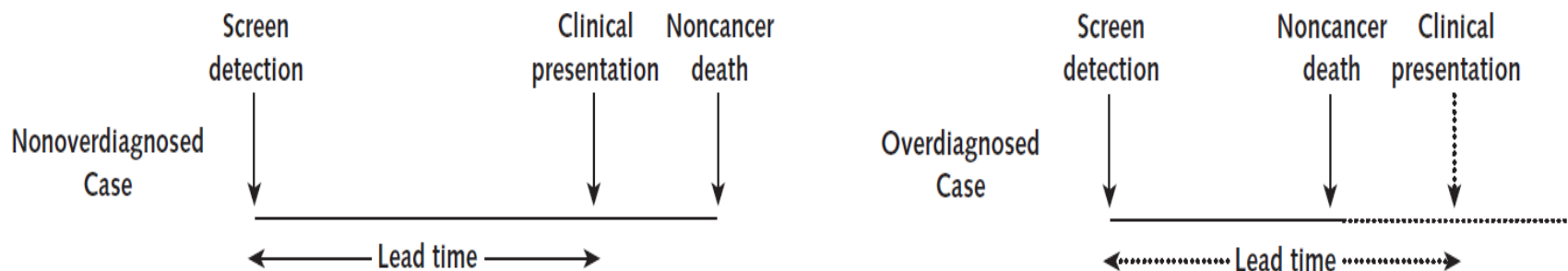
diagnosis that would not have been made in life if screening had not taken place

- overdiagnosed cancer is indistinguishable from potentially progressive Δ
- overdiagnosis rates estimated at 1 - 11%

screening for disease - the concept of overdiagnosis

cancer overdiagnosis

- cancer that would never have presented clinically before death
 - not progressive & death before presentation - slow indolent cancer
 - progressive & death before presentation - cancer in old age
- treatment may cause harm
- treatment generates unwarranted expense
- diagnosis poses an insurance liability



cancer reservoir

Overdiagnosis in Cancer

H. Gilbert Welch, William C. Black

Table 1. Estimated size of the disease reservoir for three cancers, the lifetime risk of death or metastatic disease, and the probability of overdiagnosis where the entire disease reservoir detected

Cancer	Population	% With cancer (disease reservoir) (a)	Lifetime risk of death or metastatic disease* (b), %	Probability of overdiagnosis where entire disease reservoir detected† ($c = [a - b]/a$), %
Prostate	Men older than 60 y	30–70	4	87–94
Thyroid	Adults aged 50–70 y	36–100	0.1	99.7–99.9
Breast	Women aged 40–70 y	7–39	4	43–90

Breast Imaging Reporting And Data System

Table 3. Breast Imaging Reporting and Data System Classification System* and Recommended Management

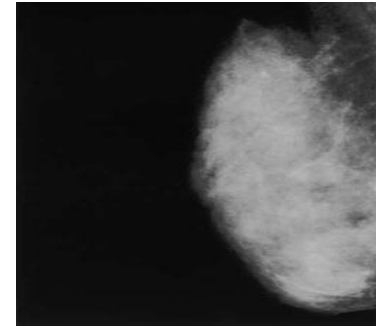
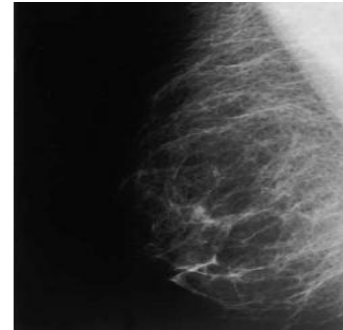
	Description of Result	Management If Study Ordered for Screening	Management If Study Ordered for Clinical Symptom [†]
BI-RADS 1	No abnormal findings	Routine screening imaging in 1–2 y	Consider biopsy or additional work-up
BI-RADS 2	Findings with characteristic benign appearance	Routine screening imaging in 1–2 y	Routine follow-up if concordant; cyst aspiration if symptomatic
BI-RADS 3	Findings present; correlate with less than 2% likelihood of malignancy	Repeat breast imaging every 6 months for 1–2 y to ensure stability	Repeat breast imaging every 6 mo for 2 y to ensure stability or biopsy if clinical concern for malignancy
BI-RADS 4	Suspicious findings; probability of malignancy 2–94%	Biopsy should be considered	Biopsy indicated
BI-RADS 5	Suspicious findings; probability of malignancy 95% or greater	Biopsy indicated	Biopsy indicated
BI-RADS 6	Abnormal findings present correlate with known malignancy	N/A	Ongoing disease treatment
BI-RADS 0	Incomplete study	Further imaging needed	Further imaging needed

Breast Imaging Reporting And Data System

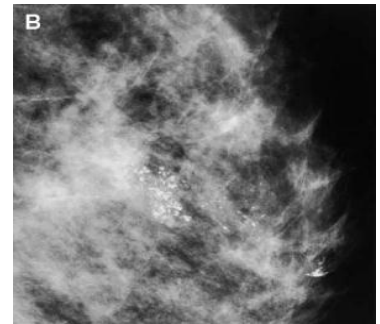
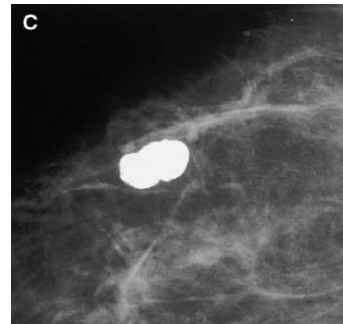
- breast density
- morphological parameters of lesions

	Description of Result
BI-RADS 1	No abnormal findings
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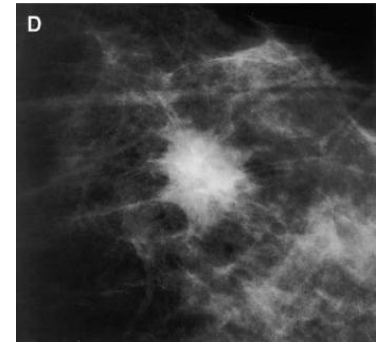
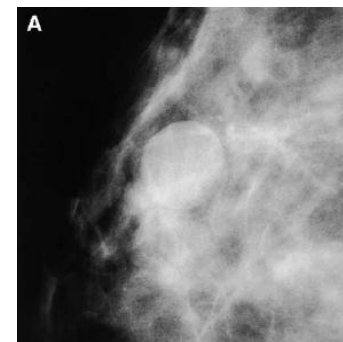
breast density



patterns of calcification



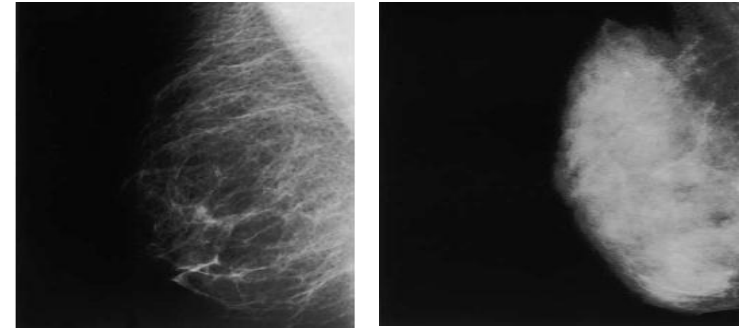
margins of lumps



Breast Imaging Reporting And Data System

- breast density
- morphological parameters of lesions

breast density



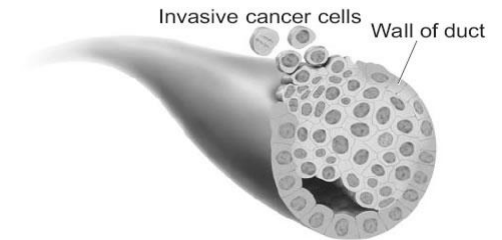
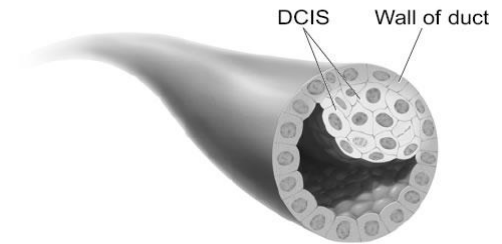
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density

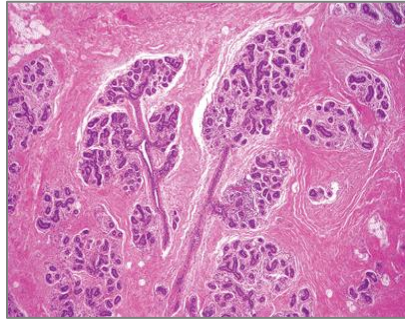
- 1 fatty breast
- 2 25 - 50% glandular
- 3 50 - 75% glandular
- 4 >75% glandular

breast cancer screening - the facts

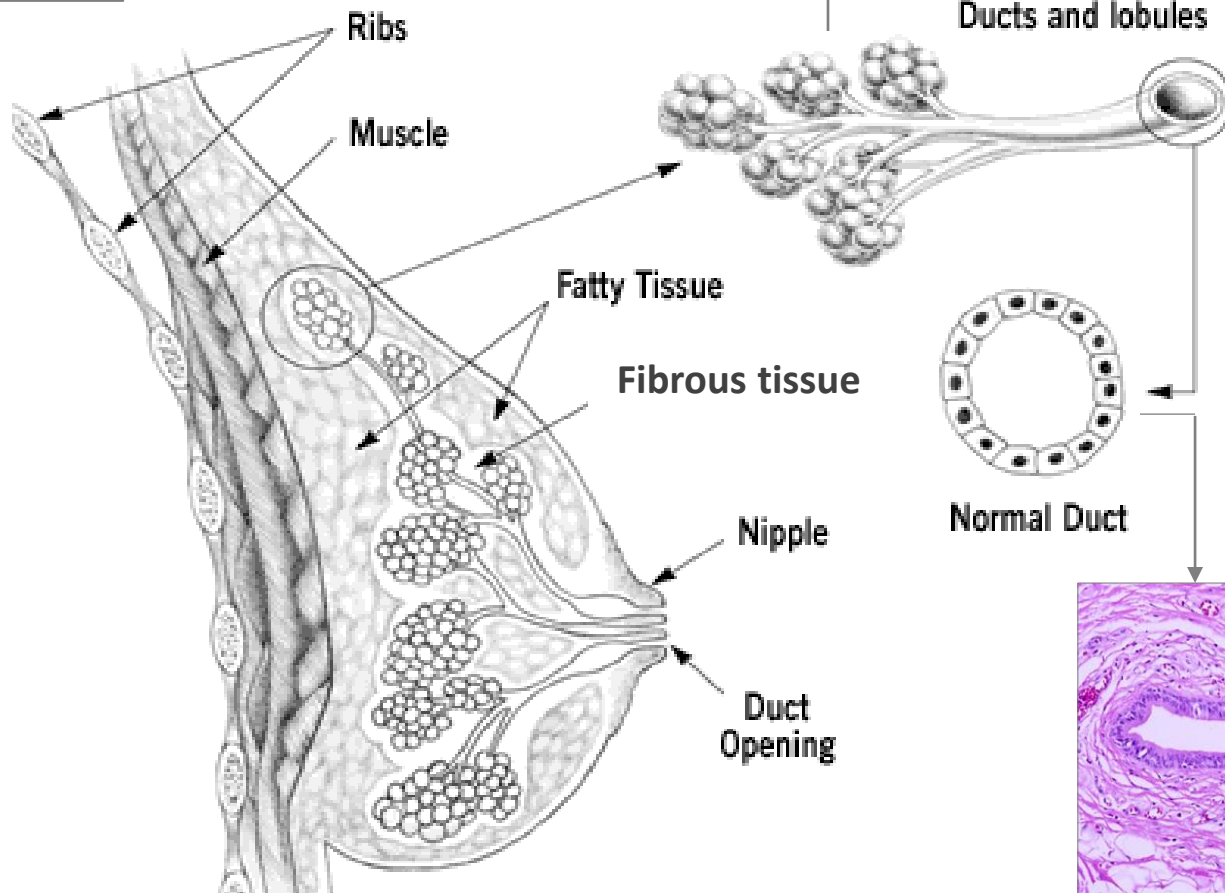
- detect more cancers
- more potentially lethal cancers diagnosed at curable stage
- increasing rates of non invasive cancer - DCIS
 - nearly all invasive cancer begins as DCIS
 - DCIS is heterogeneous
 - 14 - 60% DCIS will invade by 10 yrs (40%)
- more benign disease
- more invasive investigations
- more biopsies, lumpectomies & mastectomies
- overdiagnosis of cancers that would not result in mortality
 - 50% increase in cancers that would not cause death
 - 37% F40 - 45 have undiagnosed DCIS or invasive cancer at autopsy



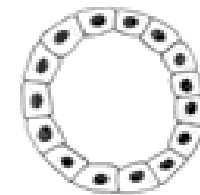
breast anatomy



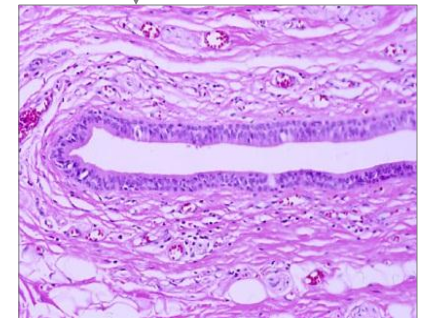
lobule



Ducts and lobules

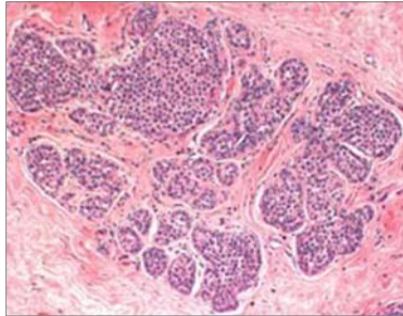


Normal Duct

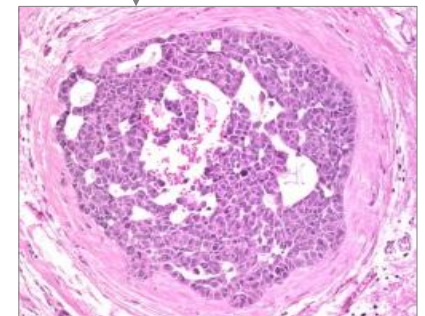
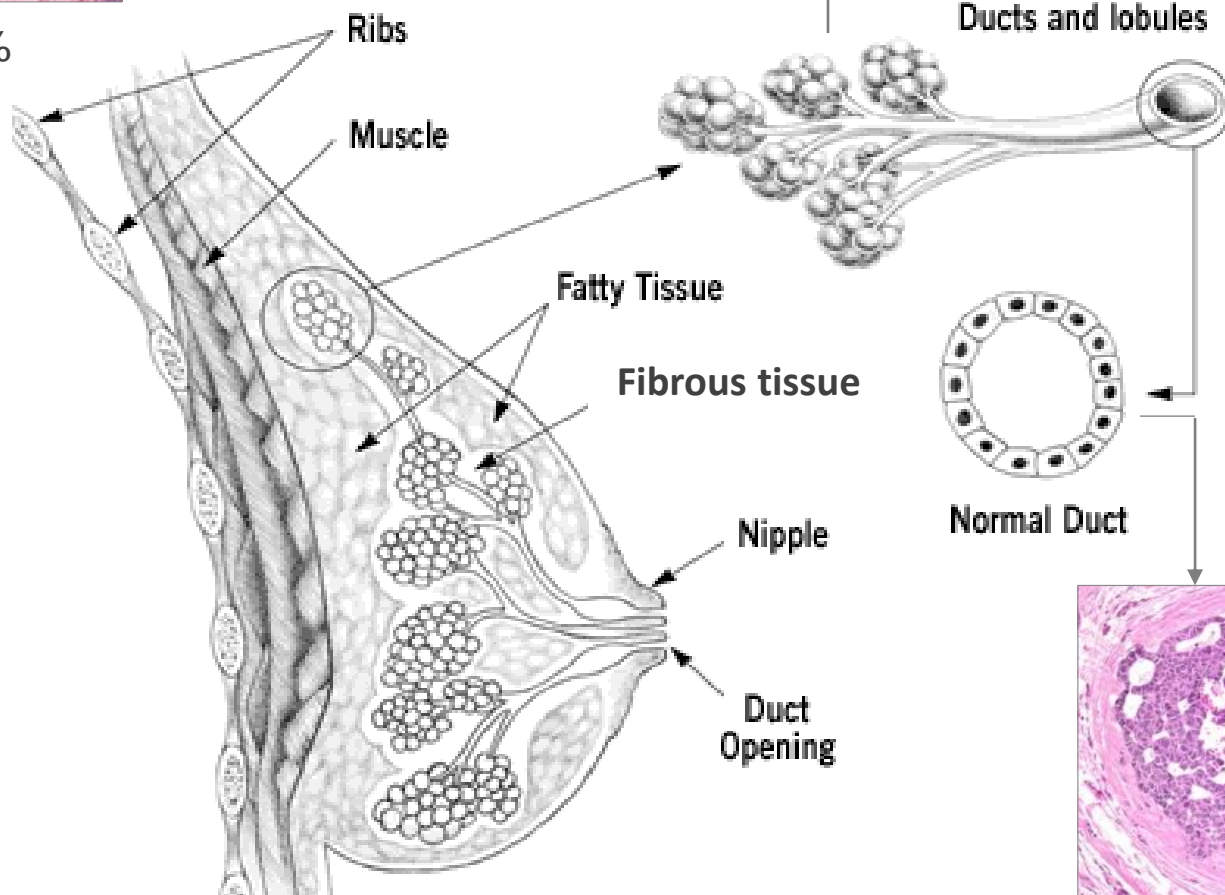


duct

breast cancer in situ

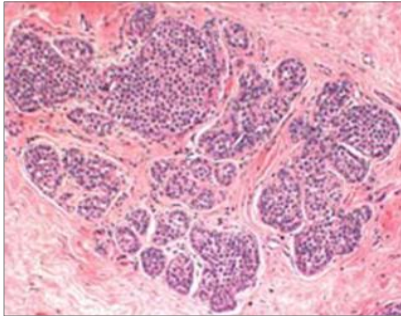


LCIS 5%



DCIS 95%

breast cancer in situ



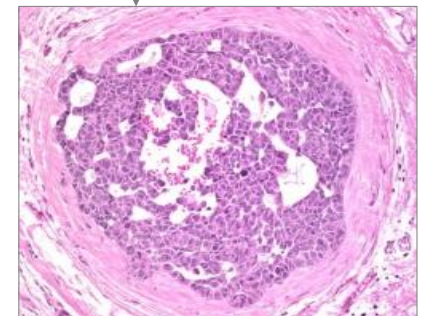
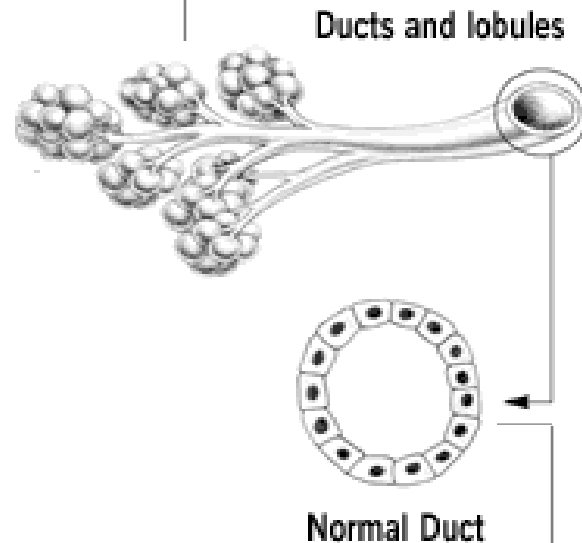
LCIS 5%

LCIS

- not an obligate precursor to invasive cancer
- may be marker for current bilateral cancer
- excised or bilateral mastectomy
- usually no full cancer protocol
- RR future cancer diagnosis 7-18

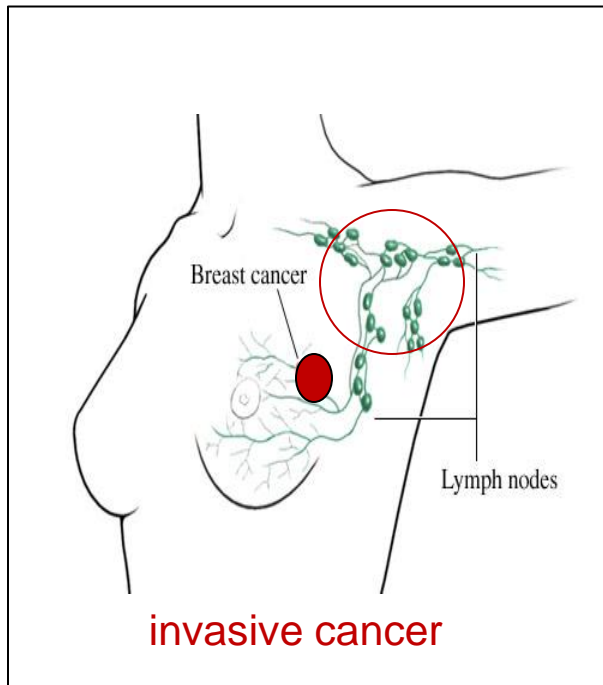
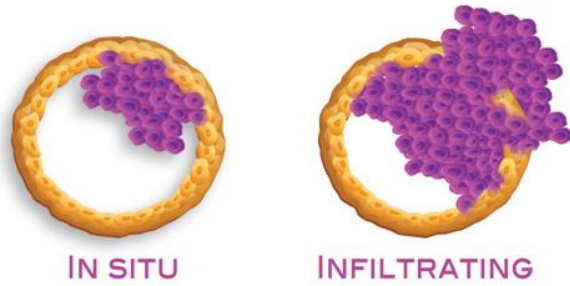
DCIS

- inherent risk of invasion
- majority become invasive - not obligate precursor
- invasive capacity assumed
- full cancer protocol
- RR future cancer diagnosis 2 - 3



DCIS 95%

treatment of cancer in situ & early invasive cancer



carcinoma in situ

- local excision usually adequate
- total mastectomy $\leq 30\%$
- + breast radiotherapy - if no mastectomy
- \pm hormonal therapy - tamoxifen

infiltrating invasive cancer

local excision with removal of nodes

- + breast radiotherapy
- + chemotherapy
- \pm hormonal therapy - tamoxifen

total mastectomy with removal of nodes

- + chemotherapy
- \pm hormonal therapy - tamoxifen

breast cancer risk factors

- average lifetime risk 12%
- OCP does not increase risk (?)
- HRT does increase risk

Table 1. Risk Factors for Breast Cancer.*

Risk Factor	Relative Risk
<i>BRCA1</i> or <i>BRCA2</i> mutation	10.0–32.0
Family history of cancer (no known mutation)†	
1 first-degree relative	1.5–2.0
2 first-degree relatives	3.0
3 or more first-degree relatives	4.0
1 second-degree relative	1.2–1.5
Therapeutic radiation to chest at <30 yr of age‡	7.0–17.0
Hormonal factors	
Late (age >30 yr) parity or nulliparity	1.2–1.7
Early (age <12 yr) menarche or late menopause (age >55 yr)	1.2–1.3
Combined hormone-replacement therapy (e.g., for 10 or more yr)	1.5
Postmenopausal obesity	1.2–1.9
Alcohol consumption (2 drinks/day vs. none)	1.2
Smoking before first live birth	1.2
Sedentary lifestyle	1.1–1.8
White race	1.1–1.5
Breast density (very dense vs. mainly fatty)	5.0
Atypical ductal or lobular hyperplasia or lobular carcinoma in situ on previous breast biopsy	4.0

breast cancer risk factors

- average lifetime risk 12%
- OCP does not increase risk (?)
- HRT does increase risk

Table 1. Breast Cancer Risk Factors

Important Risk Factors for Breast Cancer	Reported Relative Risk
Reproductive	
Early menarche	1.1–1.4
Age of menopause	1.1–1.4 per 5-year increment after age 51
Nulliparity	1.1–1.4
First birth after age 35 (compared with before age 20)	1.5–2.9
Current or past use of menopausal hormone therapy	1.31–1.56
Breast feeding longer than 1 y*	0.7–0.8
Premature menopause (before age 40)*	0.5
Genetic	
Family history of first-degree relative with breast cancer	1.5–2.9
Family history of two first-degree relatives with breast cancer	3.0–6.9
Known <i>BRCA</i> gene mutation	40–85% lifetime risk
High-dose thoracic ionizing radiation	
Especially in young women (younger than age 21)	55.5

Data from Harris Jay R, Lippman ME, Morrow M, Osborne CK. Diseases of the breast. 4th ed. Philadelphia (PA): Lippincott Williams & Wilkins; 2007.

* These items are protective.

population attributable risks for breast cancer in NZ women

modifiable risk factors

- first baby >35 yrs cf <20 yrs RR = 1.4
- alcohol 3 - 5 drinks daily RR = 1.3
- premenopausal obesity RR = 1.0
- post menopausal obesity RR = 1.3
- sedentary vs active* RR = 1.3
- current & recent OC** RR = 1.2
- current HRT*** RR = 1.7
- smoking RR = 1.0

prevalence of modifiable risk factors

- 19% first mothers are aged >35
- 24% Maori, 11% Pacific, 10% European
- 35% all age 51 - 70, 63% Maori obese
- 11% Maori, 15% Pacific, 11% European
- 38% urban & 30% rural current users
- 8.2 % Maori, 21% European

* less than 30 minutes weekly

** risk dissipated after 10 years

*** risk dissipated after 5 years

DCIS - WHO 2012

In 2012 the World Health Organization defined DCIS as “a neoplastic proliferation confined to the mammary ductal-lobular system and characterized by increased epithelial proliferation, subtle to marked cytologic atypia, and an inherent but not necessarily obligate tendency for progression to invasive breast carcinoma.”⁷

DCIS

- DCIS 25% of all new breast cancer diagnoses
- 90% DCIS diagnosed by screening
- 90% + diagnosed as consequence of microcalcification
- DCIS incidence peaks age 65 - 70
- DCIS increase 110% 1991 - 2001 (screening effect)
- DCIS increase 20% 1996 - 2001 (screening effect)

- DCIS per se does not result in mortality - “most DCIS is harmless”
 - microscopic node involvement <3%

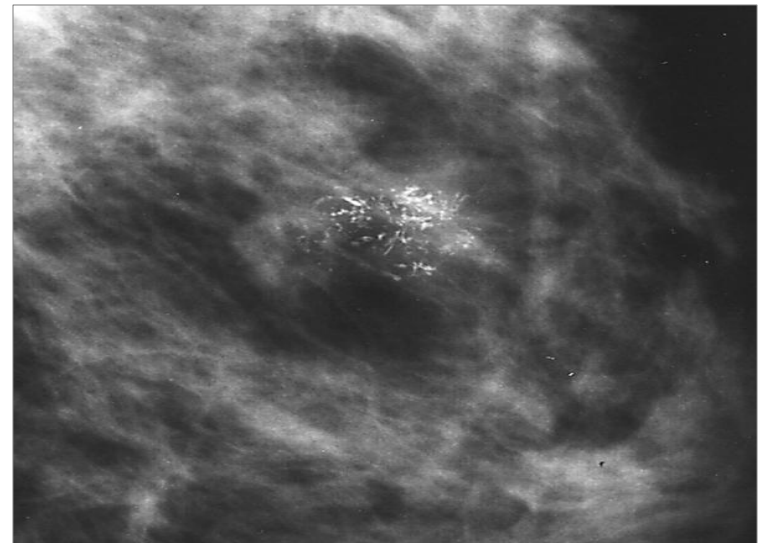
- DCIS full resection with no adjuvant treatment
 - total mastectomy → 98% disease free
 - complete excision → 14% recurrent DCIS near original site
 - complete excision → 7% invasive cancer near original site

DCIS - how does it present

- calcification on mammography 90 - 95%
- lump or nipple discharge 5 - 10%

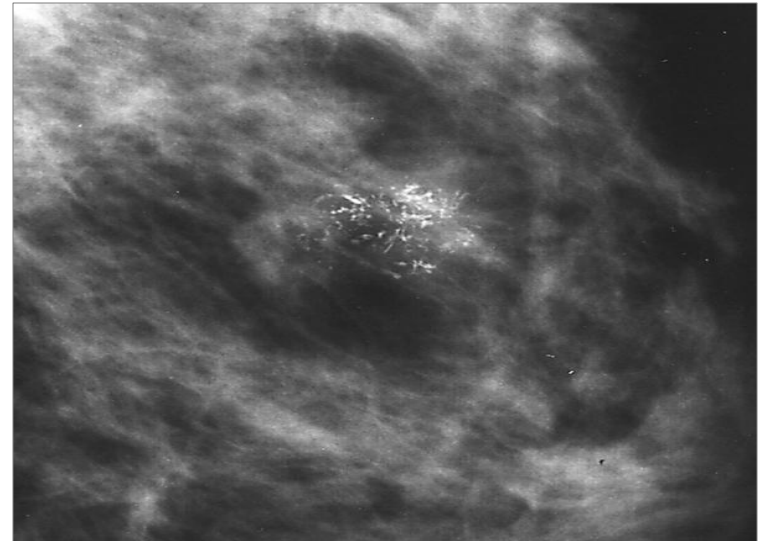
mammogram appearances of biopsy proven DCIS

- 76% microcalcification
- 13% micro calcification + lump
- 11% lump on mammogram



DCIS - mammography and microcalcification

- stage of ductal cancer found by incidental microcalcification on mammography
 - DCIS 65%
 - DCIS with microscopic invasion 32%
 - invasive cancer 4%



DCIS - what happens if you do not treat it

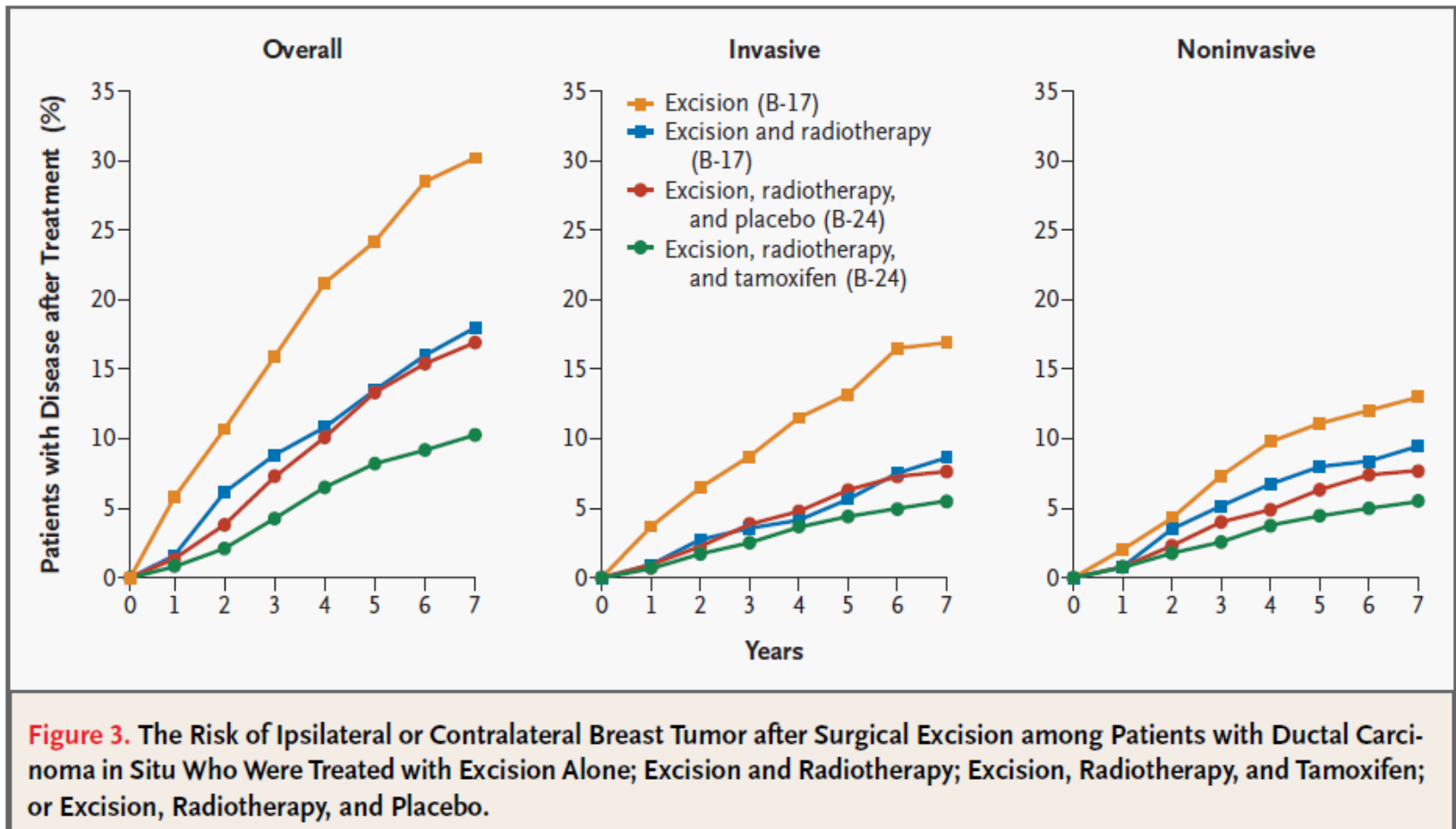
- DCIS is a non invasive precursor of invasive cancer
- DCIS does not always invade in a person's lifetime
- DCIS becomes invasive in 14 - 60% in 10 years (BMJ 2009)
- DCIS 10 - 15% medico legal autopsies in young / middle aged women (1987)

Table 1. Natural history of untreated DCIS

Reference	<i>n</i> of patients	Patients developing IBC (%)	Follow-up (years)	Relative risk
Rosen et al. (1980) [15]	15	53	1–24	NC
Page et al. (1982) [69]	28	32	3–31	9.1
Eusebi et al. (1994) [70]	80	14	1–14	NC
Collins et al. (2005) [16]	13	46	4–18	13.5

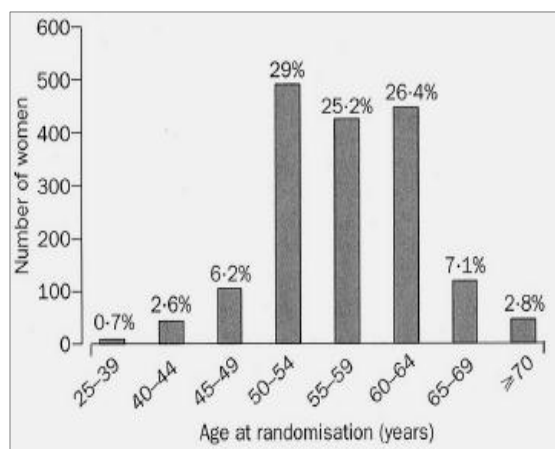
Abbreviations: DCIS, ductal carcinoma in situ; IBC, invasive breast cancer; NC, not calculated.

DCIS - outcomes after treatment



Radiotherapy and tamoxifen in women with completely excised ductal carcinoma in situ of the breast in the UK, Australia, and New Zealand: randomised controlled trial

	No adjuvant treatment (n=544)	Tamoxifen alone (n=567)	Radiotherapy alone (n=267)	Radiotherapy and tamoxifen (n=316)	Total (n=1694)
Breast events					
Ductal carcinoma in situ	76 (14%)	57 (10%)	10 (4%)	7 (2%)	150 (9%)
Invasive carcinoma	39 (7%)	43 (8%)	12 (4%)	14 (4%)	108 (6%)
Unknown	4 (<1%)	1 (<1%)	0	0	5 (<1%)
Total	119 (22%)	101 (18%)	22 (8%)	21 (6%)	263 (16%)
Woman-years of follow-up	2494	2613	1246	1456	7809
Event rate per 100 woman-years	4.77	3.86	1.76	1.44	3.37
All cause deaths (deaths attributable to breast cancer)	10 (4)	13 (10)	7 (2)	15 (7)	45 (23)

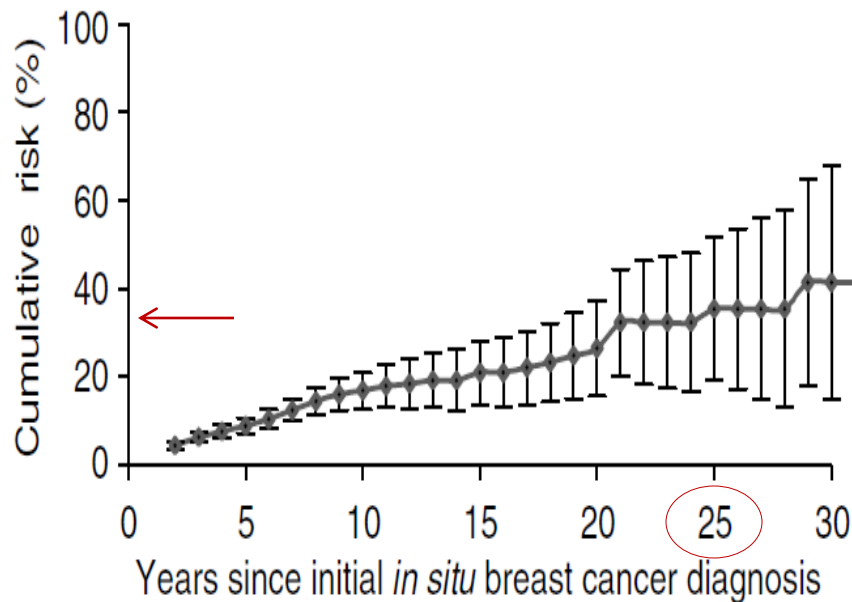


- 1700 DCIS
- majority were screen detected DCIS
- 90% age > 50
- 4 years follow up (1 - 10 years)

CIS breast - cancer risk after any breast cancer in situ BCIS

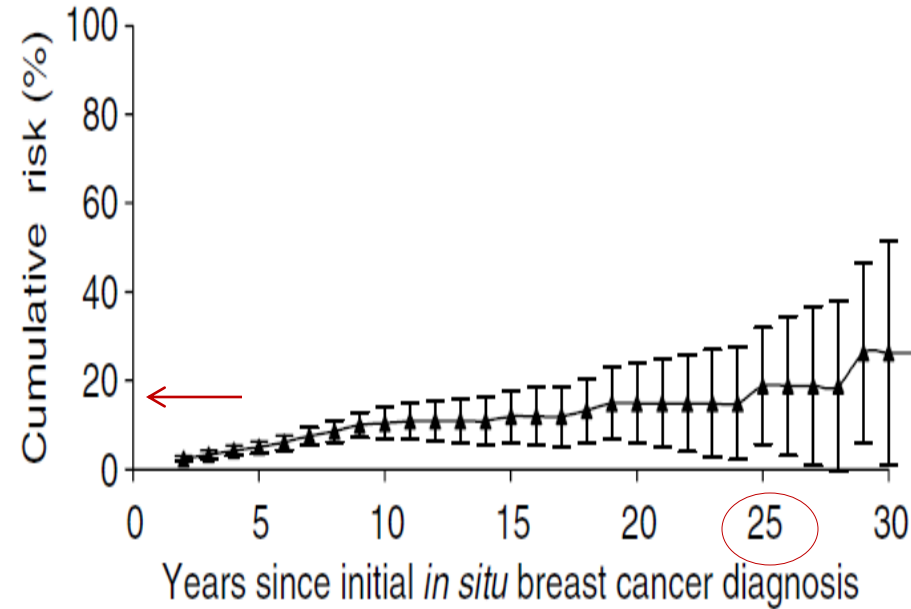
cancer all sites after BCIS

A



breast cancer after BCIS

B



CIS breast - cancer risk after any breast cancer in situ BCIS

Period of follow-up	PYR ^a	Second breast cancer				Other second cancers			
		Obs ^b	Exp ^c	SIR	AER	Obs ^b	Exp ^c	SIR	AER
1–4 years	3596	33	9.7	3.4 ^d	65	31	18.9	1.6 ^d	34
5–9 years	1815	22	5.0	4.4 ^d	94	12	10.1	1.2	11
≥ 10 years	1127	6	3.3	1.8	24	9	7.4	1.2	14

^aPYR: person-years. ^bObs: observed numbers of second primary cancers. ^cExp: expected numbers of second primary cancers. ^d95% confidence interval excludes 1. ^eBreast cancer screening in southern Netherlands began to have impact in 1993 (Fracheboud *et al*, 2004).

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L. Joseph Melton III, M.D., and Daniel W. Visscher, M.D.

BACKGROUND

Benign breast disease is an important risk factor for breast cancer.

Relative Risk (95% CI)[†]

1.56 (1.45–1.68)

CONCLUSIONS

Risk factors for breast cancer after the diagnosis of benign breast disease include the histologic classification of a benign breast lesion and a family history of breast cancer.

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- 9000 women
- benign breast disease on biopsy
- excess risk for breast cancer
- median time to cancer diagnosis 10 years
- risk for cancer persisted for at least 25 years
- family history was an independent risk factor
- proliferation on biopsy was an independent risk factor
- non proliferative findings on biopsy with no family history had no excess risk

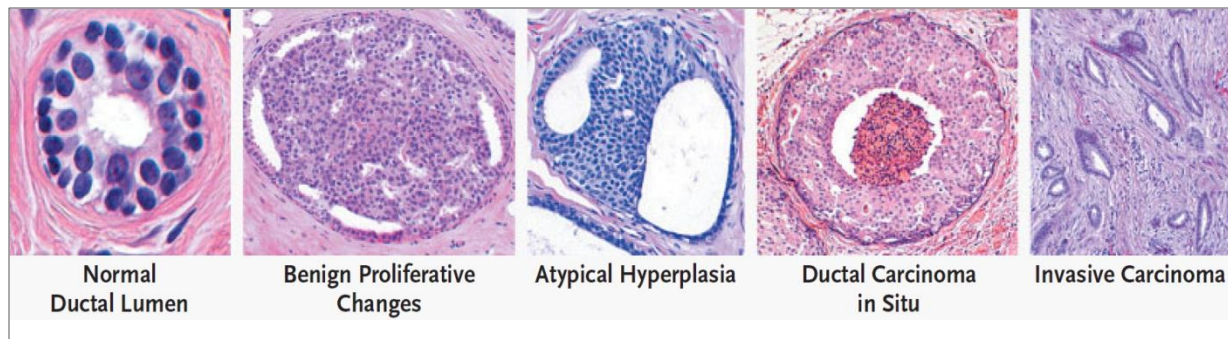
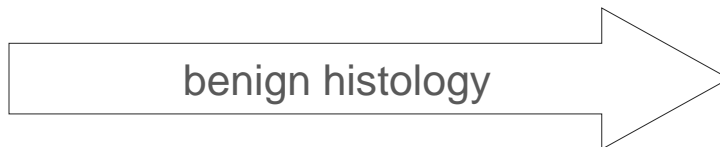
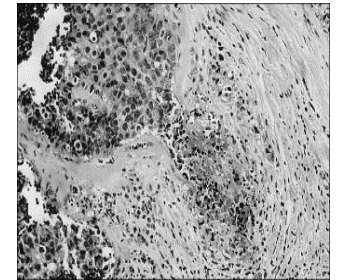
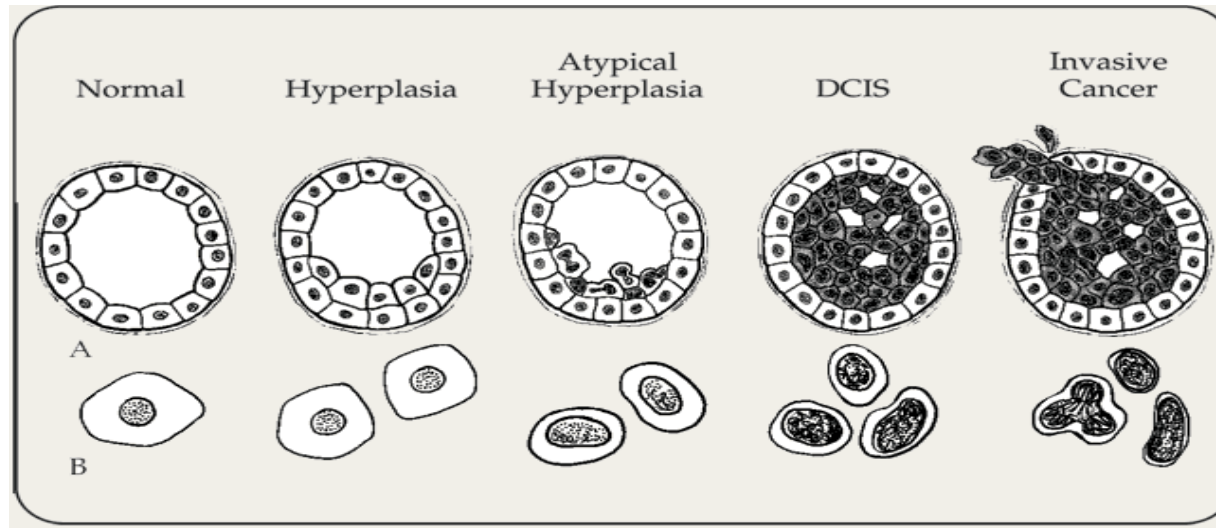
breast cancer risk factors - benign breast disease

Table 2. Risk Factors for Breast Cancer after the Diagnosis of Benign Breast Disease.*

Characteristic	No. of Women	Person-Years	No. of Observed Events	No. of Expected Events	Relative Risk (95% CI) [†]
Overall	9087	144,881	707	453.0	1.56
Age at diagnosis of benign breast disease					
<30 yr	726	13,593	21	11.5	1.83
30–39 yr	1115	20,169	71	38.3	1.85
40–49 yr	2474	45,780	212	136.3	1.56
50–59 yr	2145	34,100	196	125.9	1.56
60–69 yr	1639	21,364	142	94.5	1.50
≥70 yr	988	9,874	65	46.6	1.40
Menopausal status [‡]					
Premenopausal (age <45 yr)	2948	54,419	169	106.1	1.59
Perimenopausal (age 45–55 yr)	2583	45,872	245	153.4	1.60
Postmenopausal (age >55 yr)	3556	44,590	293	193.6	1.51

benign disease is a risk for cancer which can develop in either breast

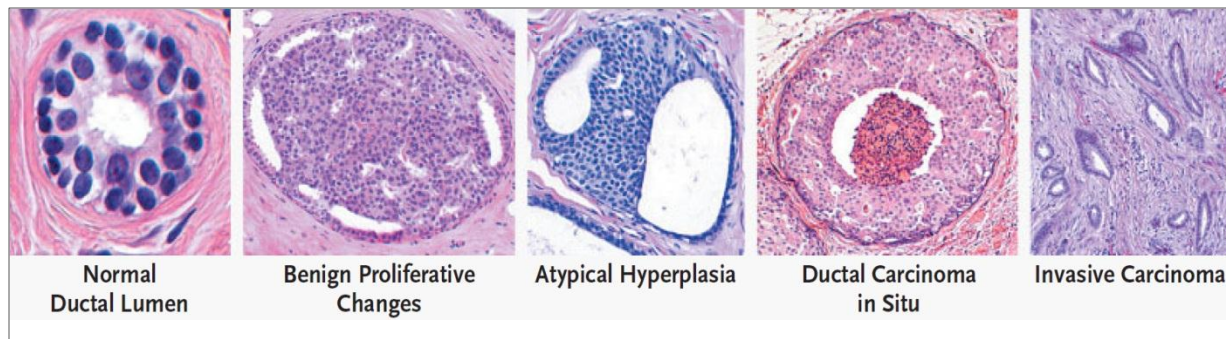
breast cancer risk factors - cancer precursor lesions



breast cancer risk factors - benign breast disease

- non proliferative
- proliferative
 - no atypia - normal appearing duct cells
 - atypia - atypical hyperplasia - duct cells with atypical features

BBD Category	Cases	Controls	RR (95% CI) ^a
Nonproliferative	67 (27.9)	393 (37.9)	1.0 [Referent]
Proliferative without atypia	116 (48.3)	538 (51.9)	1.29 [0.93-1.79]
Atypical hyperplasia	57 (23.8)	105 (10.1)	3.47 [2.26-5.34]



low cancer risk lesions

TABLE 1. Low-Risk Breast Lesions^a

Pathologic finding on core needle biopsy	Risk association (RR)	Consider surgical consultation about excisional biopsy
Fibroadenoma	2.17 ¹⁷	No ^b
Complex fibroadenoma	3.10 ¹⁷	No ^b
Hamartoma	None	No ^b
Fat necrosis	None	No ^b
Sclerosing adenosis	2.1 ¹⁸	No ^b
Columnar cell change	None	No ^b
Columnar cell hyperplasia	None	No ^b
Radial scar (≤ 10 mm)	1.99 ¹⁹	No ^b
Complex sclerosing lesion (>10 mm)	1.99 ¹⁹	Yes

high cancer risk lesions

TABLE 2. High-Risk Breast Lesions^a

Pathologic finding on core needle biopsy	Risk association (RR)	Consider surgical consultation about excisional biopsy
Flat epithelial atypia	To be defined ^{b20}	Yes
Single papilloma, without atypia	2.04 ²¹	Surgical consultation for lesions >10 mm ^c
Multiple papillomas without atypia	3.01 ²¹	Surgical consultation for lesions >10 mm ^c
Single papilloma with atypia	5.11 ²¹	Yes
Multiple papillomas with atypia	7.01 ²¹	Yes
Atypical lobular hyperplasia	4.2 ²²	Yes
Lobular carcinoma in situ	8-10 ²²	Yes
Atypical ductal hyperplasia	4.3 ²²	Yes

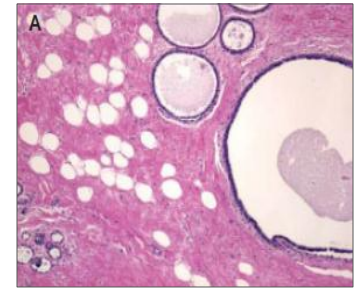
benign breast disease - cancer risk

Table 2. Benign Breast Disorders and Breast Cancer Risk

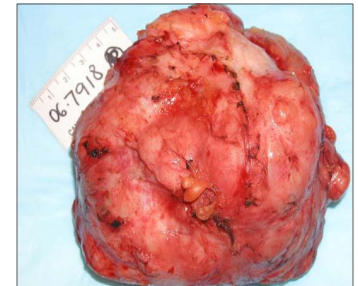
Type of Lesion	Relative Risk of Future Breast Cancer
Nonproliferative	1
Simple cysts	
Mild hyperplasia (usual)	
Papillary apocrine change	
Proliferative without atypia	1.3–1.9
Fibroadenoma	
Moderate/florid hyperplasia of the usual type	
Intraductal papilloma	
Sclerosing adenosis/radial scar	
Proliferative with atypia	4.1–5.3
Atypical ductal hyperplasia	
Atypical lobular hyperplasia	
Lobular carcinoma in situ	7–18

Data from Dupont WD, Page DL. Risk factors for breast cancer

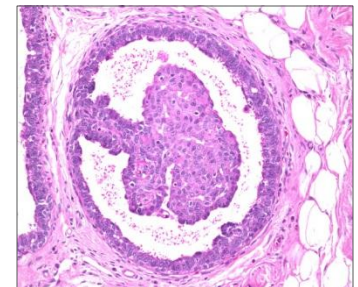
non proliferative



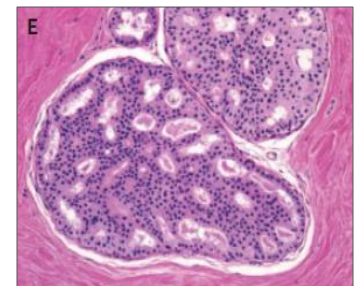
fibroadenoma



benign papilloma



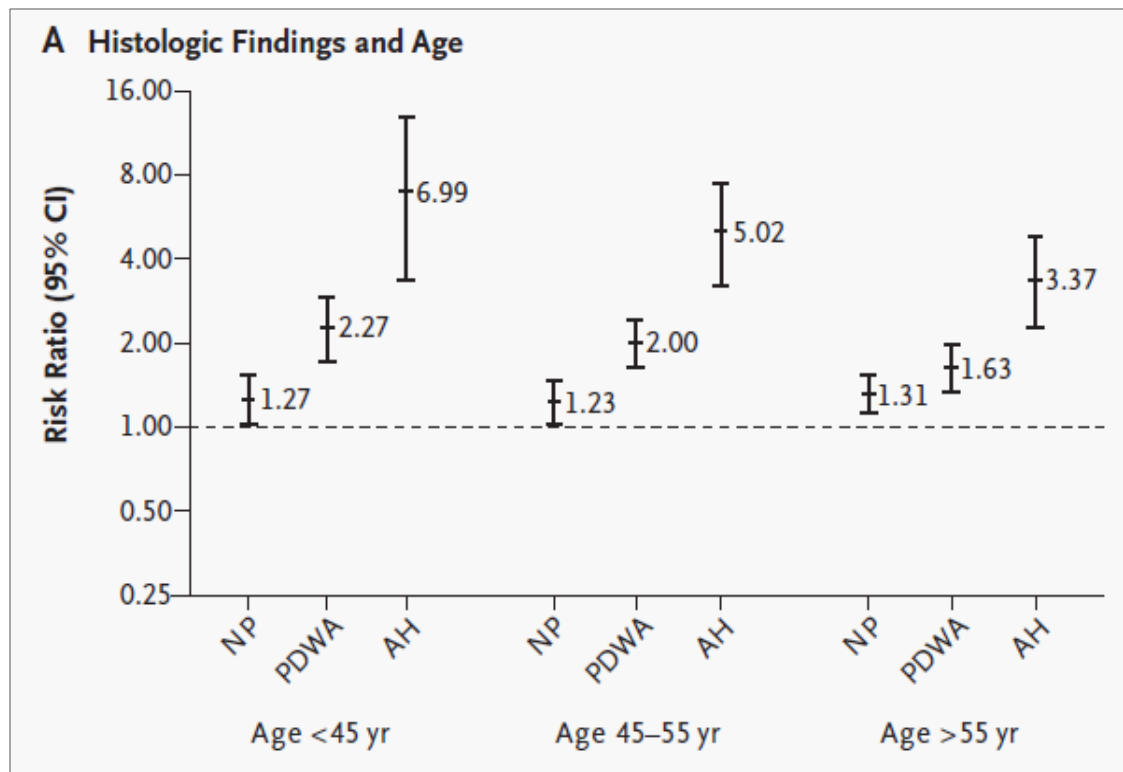
atypical hyperplasia



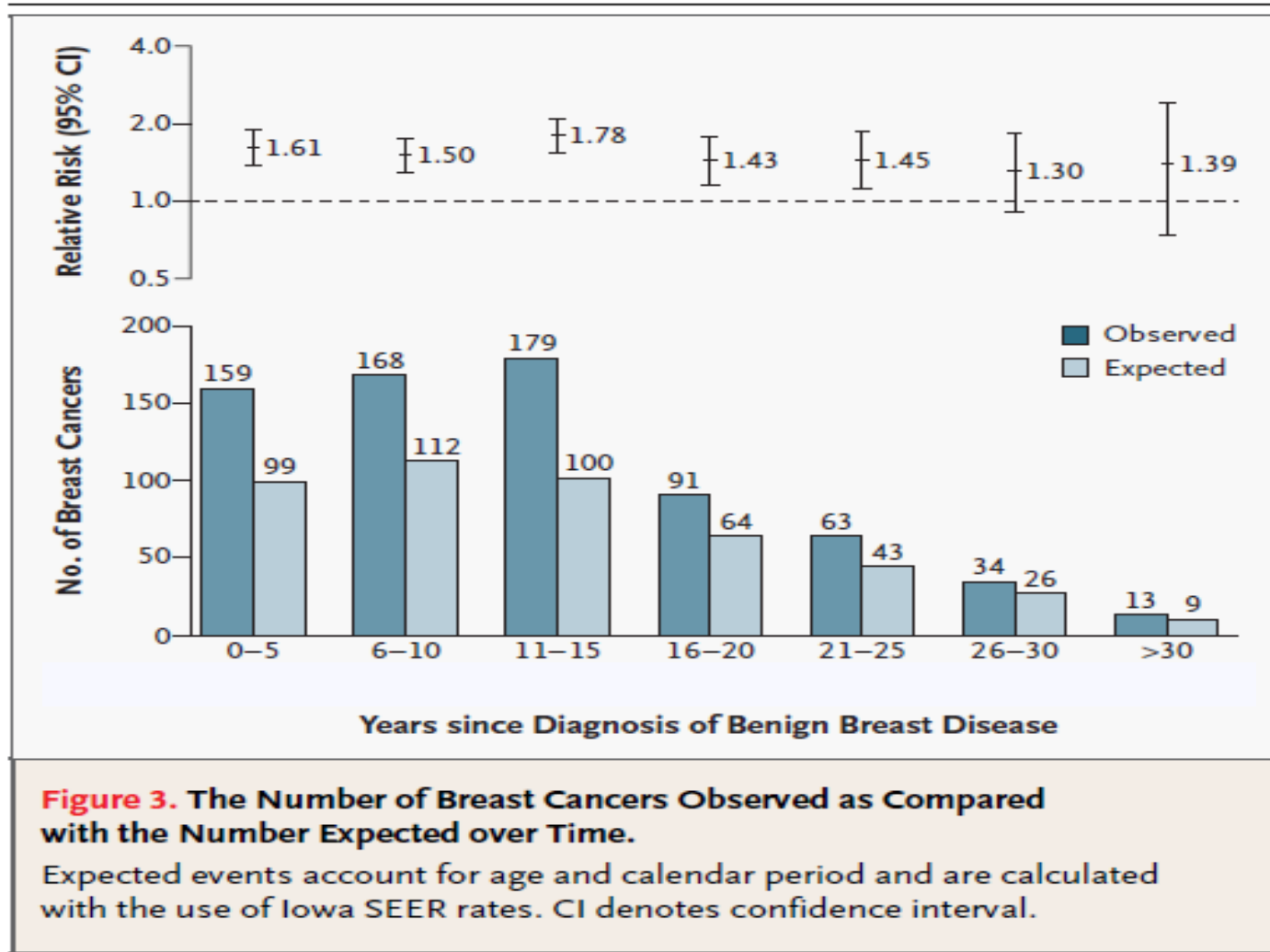
benign breast disease & cancer risk

histology and age

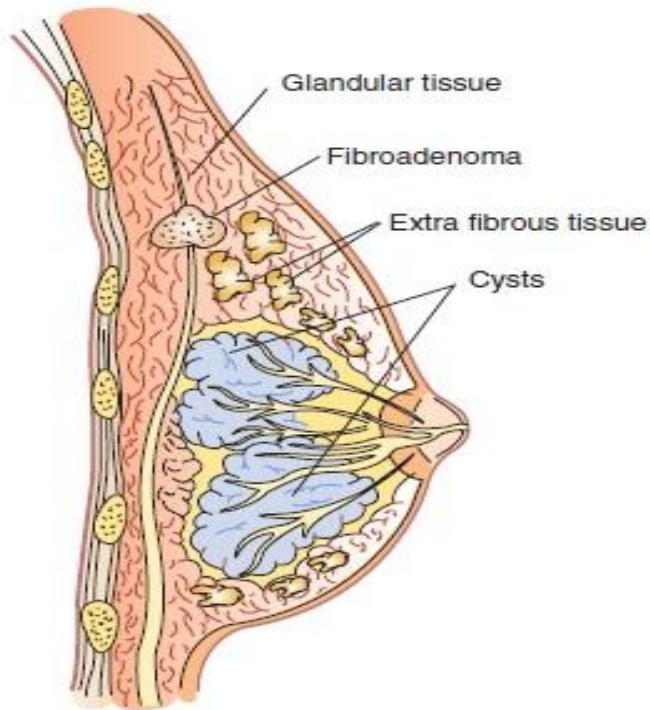
- NP non proliferative
- PDWA proliferative with hyperplasia
- AH proliferative with atypical hyperplasia



cancer risk after benign disease by time



benign breast disease and cancer risk



lifetime cancer risk RR 1.0

non proliferative disease

- simple cysts
- simple fibrocystic disease

lifetime cancer risk RR 1.3 - 5.0

proliferative disease with no atypical cells

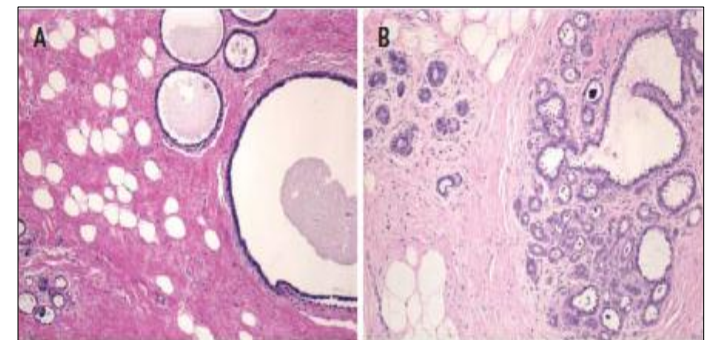
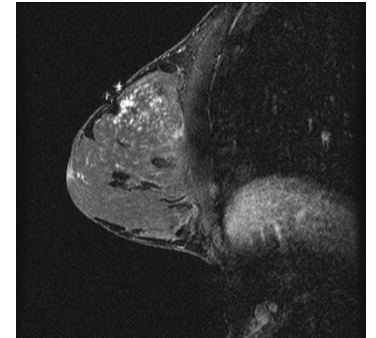
- benign tumours with no atypical cells RR 1.3 -1.9
 - simple tumours - fibroadenoma
 - simple tumours - duct papilloma

proliferative disease with atypical cells RR 4.0 - 5.0

- benign tumours with atypical cells
- any benign tissue with atypical cells

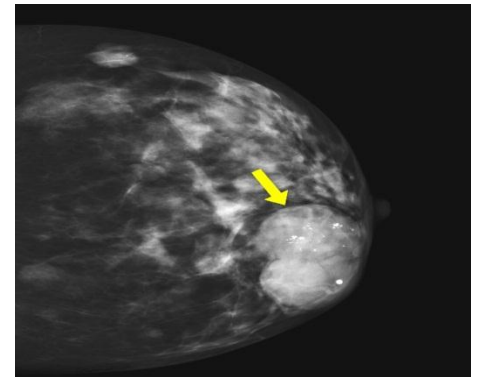
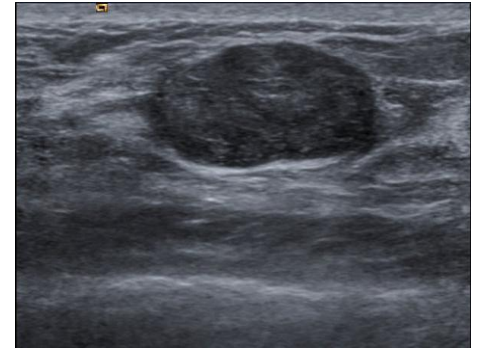
fibrocystic disease - a non disease

- fibrocystic breasts or fibrocystic change
- bilateral lumpy breasts (40 - 50% females)
- lumps fluctuate with menses with pain & tenderness
- age 20 → 50
- progressively worsens until menopause
- no cancer risk - unless atypical cells on any biopsy
- pathology
 - fluid filled cysts
 - fibrous tissue
 - hyperplasia of cells in milk ducts
 - hyperplasia of cells in milk lobules



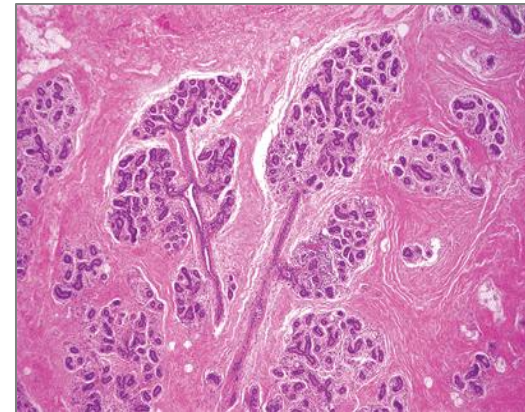
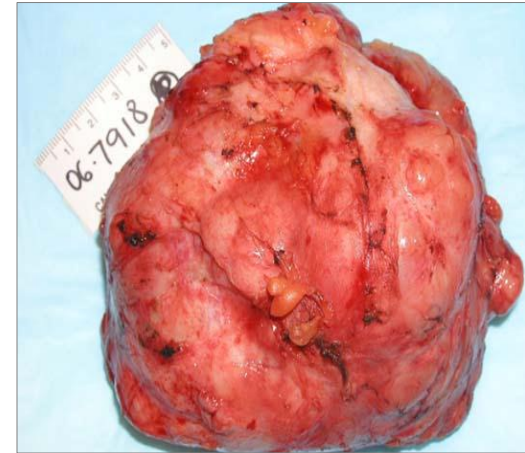
fibroadenoma

Fibroadenomas are common breast tumors that occur at any age, although the peak incidence is during the second and third decades of life. Management varies depending on the patient's age at the time of diagnosis. In women older than 35 years, resection of fibroadenomas is advised²³ because the associated finding is in situ carcinoma in 2% of patients and the risk of invasive breast cancer is increased.¹⁷ A large proportion of fibroadenomas in women younger than 20 years spontaneously resolve.²⁴



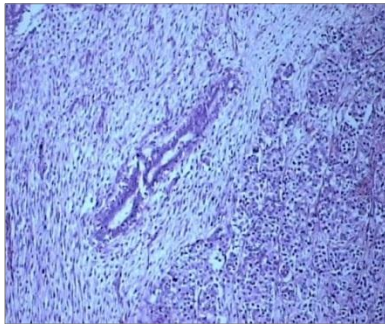
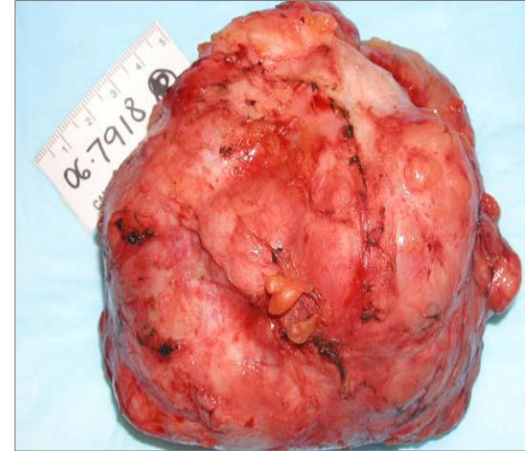
fibroadenoma

- common benign tumours
- 10% autopsies
- discrete lumps 1 - 2 cms in young women
- begin at menarche as lobules grow
- aberrant hyperplastic lesions
- early adolescence with peak age 15 - 25
- usually stabilise and may regress
- atrophy at menopause
- rarely cancerous
 - most cancers lobular cancers
 - cancer risk age <35 small
 - full excision recommended age >35 >25
- associated with increased lifetime risk breast cancer

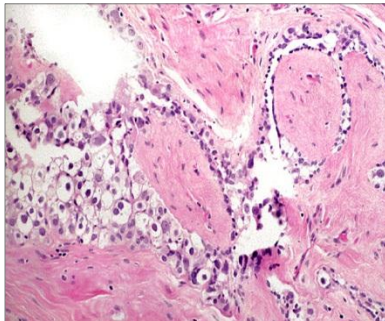


fibroadenoma age >35

- more dysplasia
- more cancer
- more associated LCIS and DCIS
- CIS within or adjacent 8%

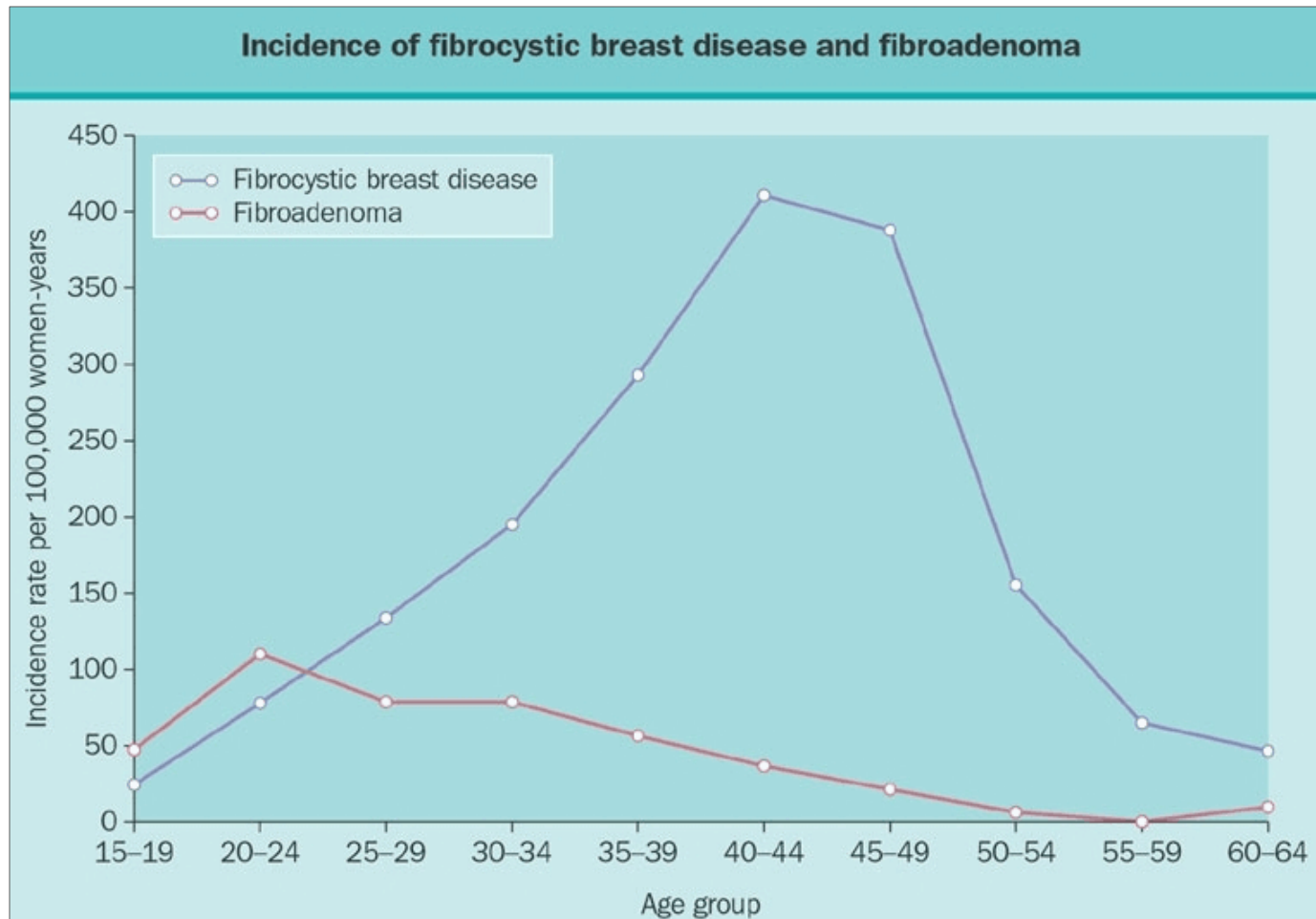


infiltrating lobular cancer in fibroadenoma



DCIS in fibroadenoma

fibroadenoma and fibrocystic disease by age





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diseases of the breast - insurance issues

- benign breast disease
- breast cancer risk factors
- breast cancer screening
- early breast cancer - breast cancer in situ

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December 2013