



Ms Katherine Gale

Oncoplastic Breast Surgeon

Waitemata District Health Board

Auckland

Sunday, June 11, 2017

(Room 8)

8:30 - 9:25 WS #187: Identifying the Risks of Breast Cancer

9:35 - 10:30 WS #199: Identifying the Risks of Breast Cancer (Repeated)

Identifying the risks of breast cancer

**Katherine Gale FRACS
Oncoplastic Breast Surgeon**



Waitemata
District Health Board

Best Care for Everyone



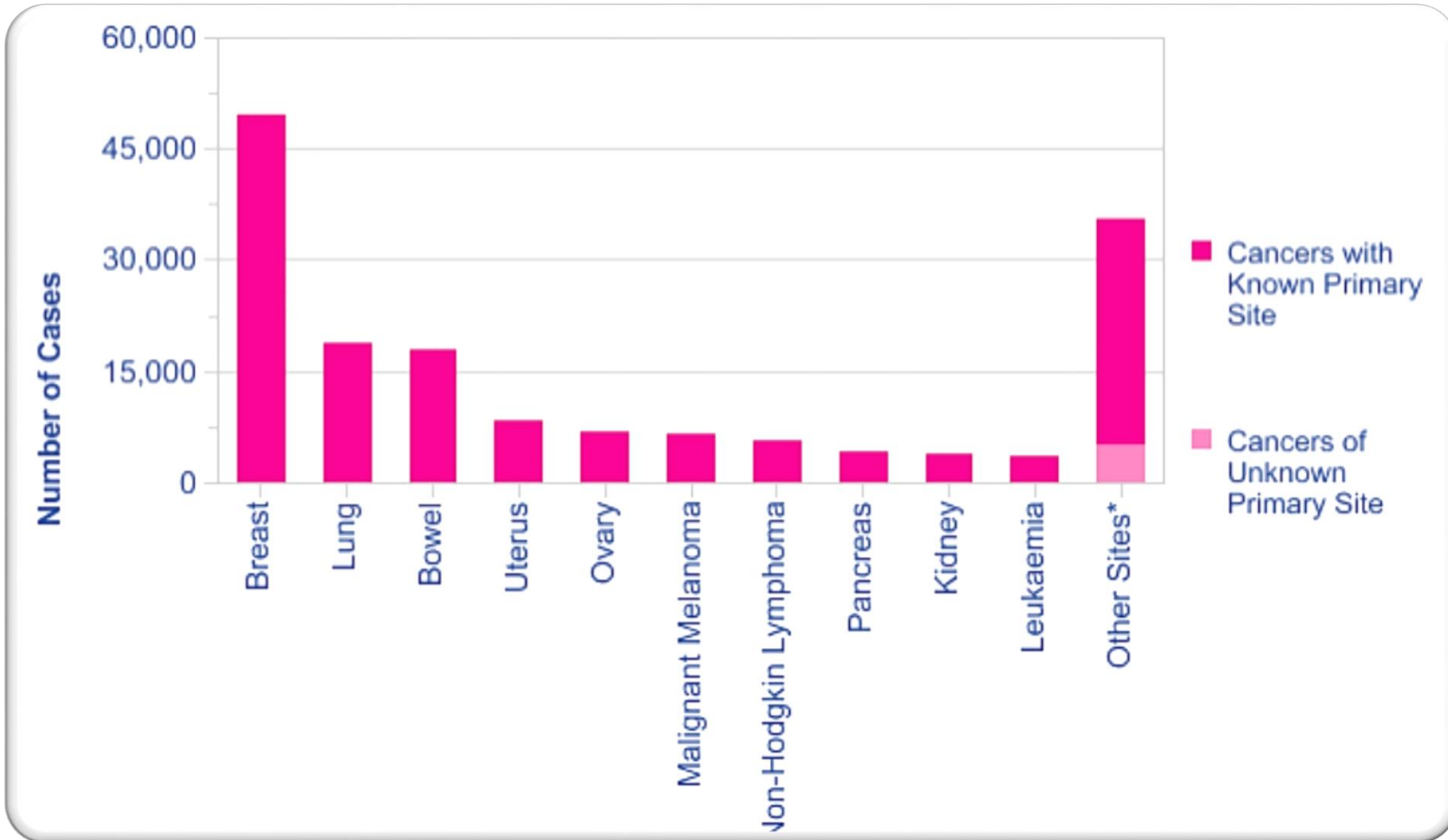
Auckland Oncoplastic Breast Institute

Agenda

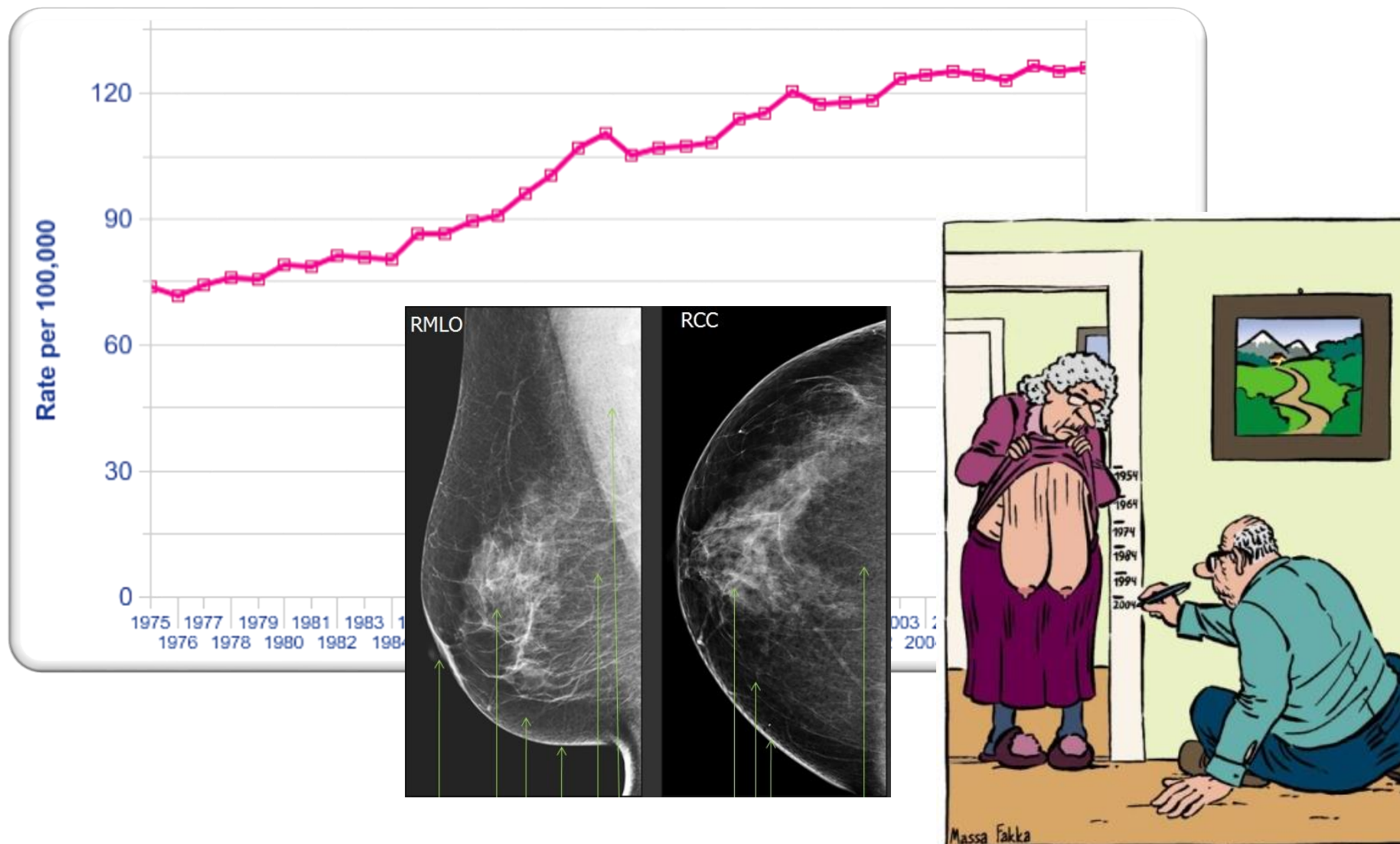
- Epidemiology
- Signs & symptoms
- Risk factors
 - Lifestyle
 - Genetics
 - Medical Conditions
- Diagnosis & Rx
- Prevention
 - Lifestyle
 - Chemoprophylaxis
 - Risk reducing surgery
 - BRCA in perspective



Breast Cancer



Incidence increasing...



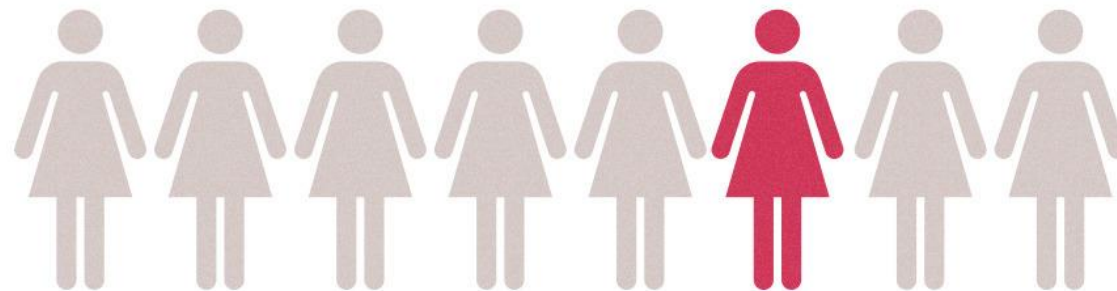
1 *in* 8

WOMEN

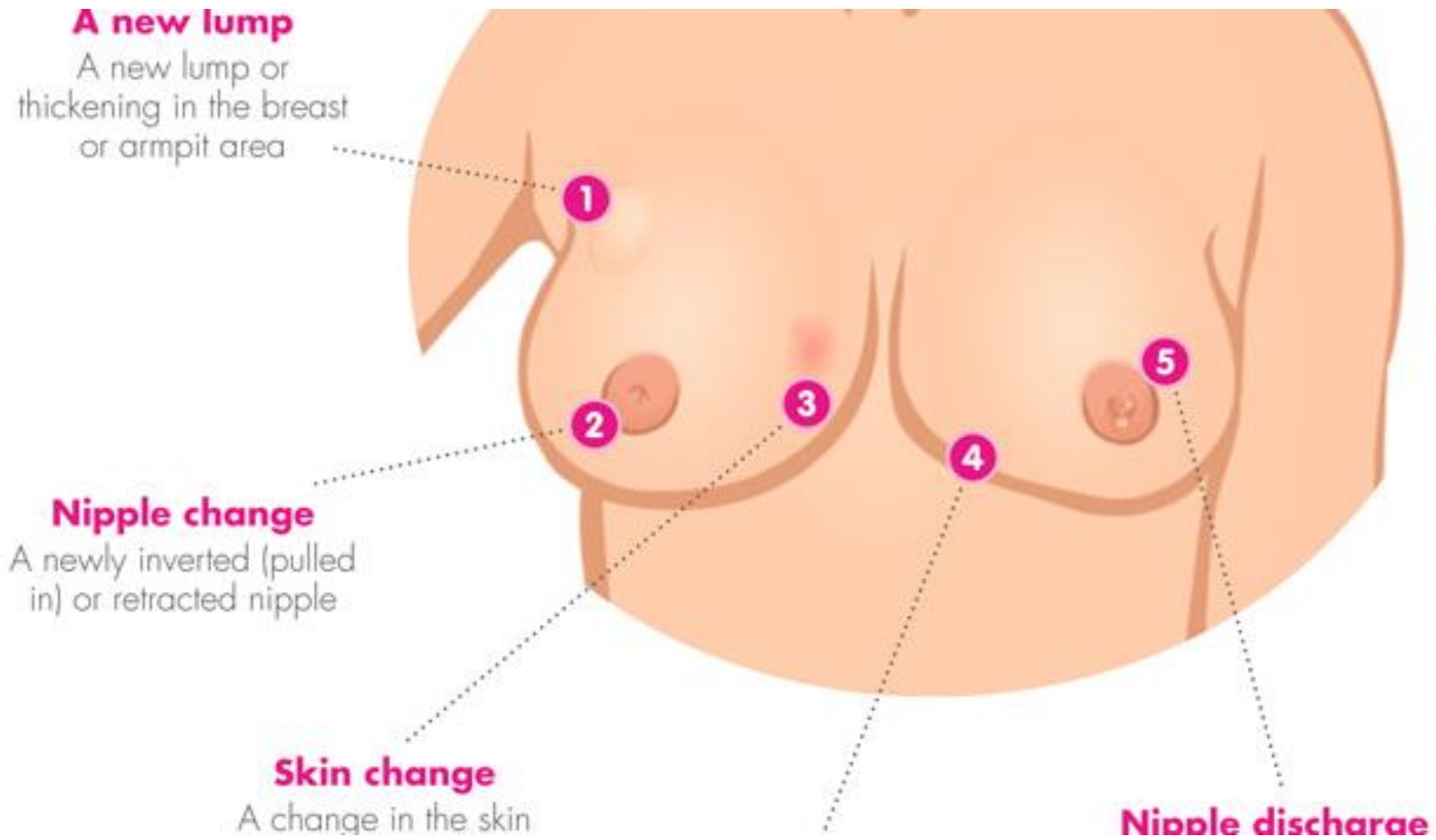
WILL BE DIAGNOSED WITH

Breast Cancer

IN THEIR LIFETIME

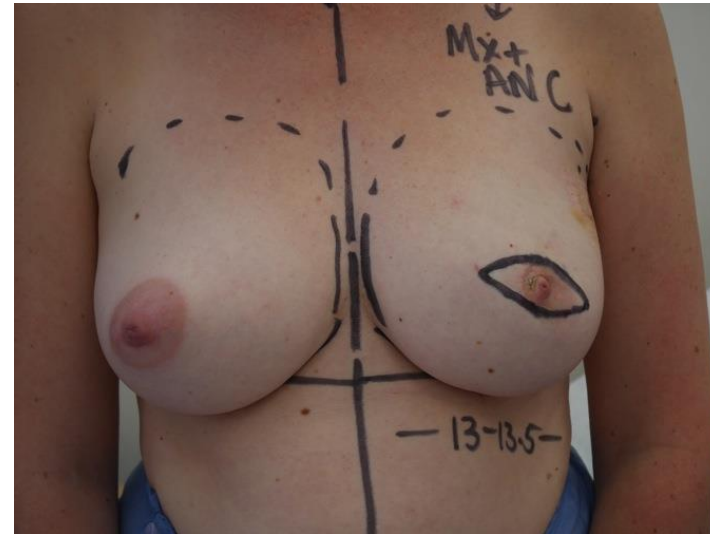


Symptoms.....

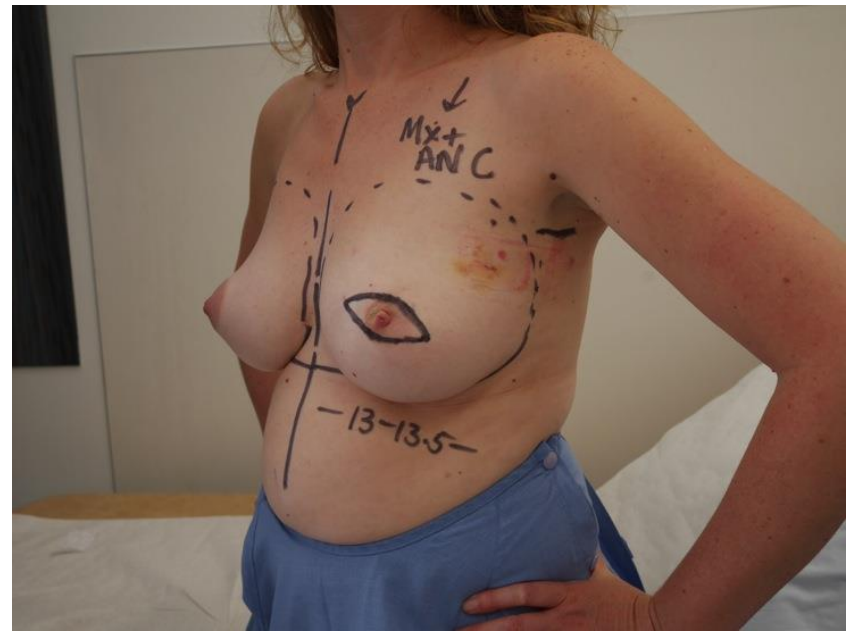
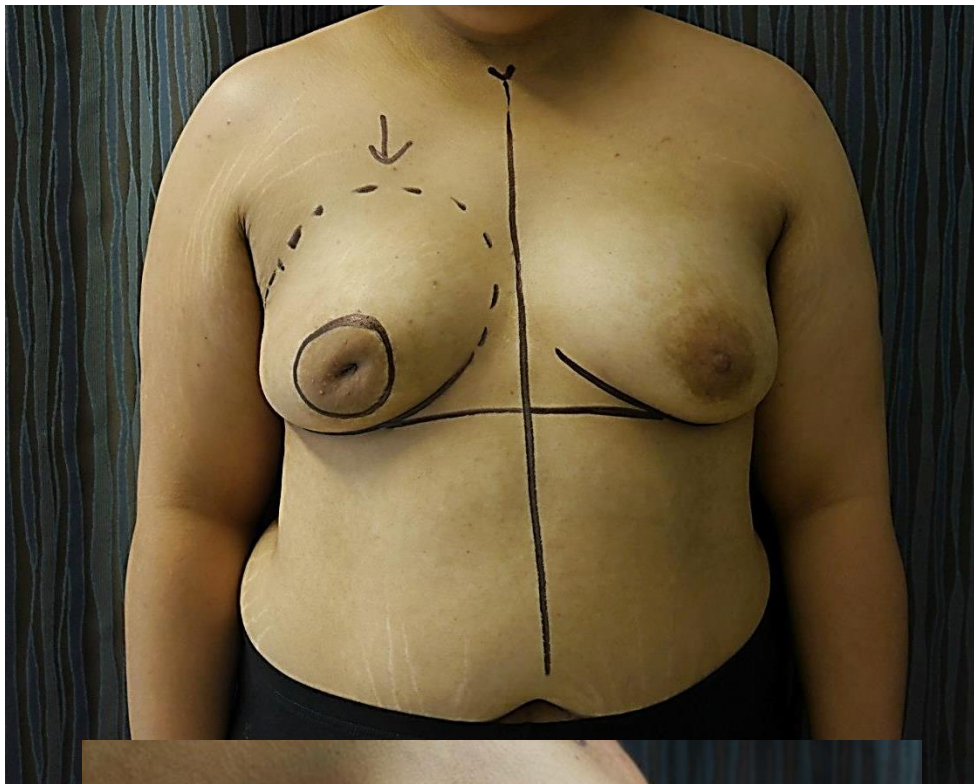


Presentation

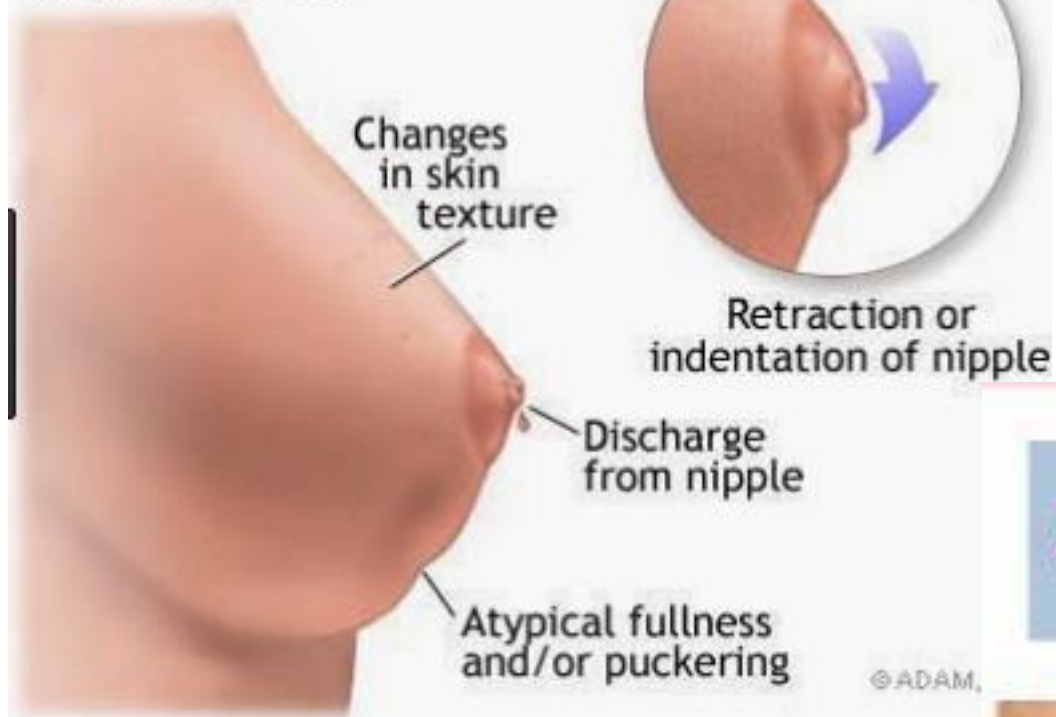
- Lump
- Change in shape
- Dimpling
- Nipple discharge
- Red scaly patch of skin



- Metastatic Sx; weight loss, fatigue, bone pain, SOB, lymphadenopathy, jaundice

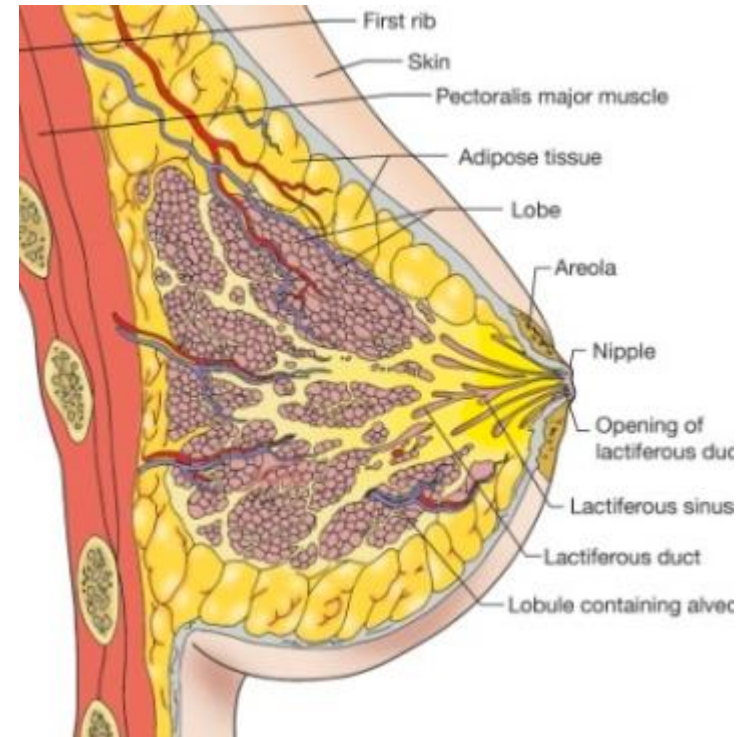


Breast self-exam:
Visual inspection



Breast cancer

- Breast epithelial cells
- Cause multifactorial;
 - Genetic
 - Hormonal/Reproductive
 - Environmental
- Breast cancer progression from accumulated cellular changes -> malignant phenotype
- In situ or non invasive disease in 15-30%,
- Invasive malignancy in 70-85%



Breast Cancer Types (20)

- DCIS – Ductal carcinoma in situ (40% progress)
- Invasive Ductal Carcinoma
- Invasive Lobular carcinoma
- Tubular carcinoma
- Mucinous carcinoma
- Invasive papillary carcinoma
- Basal/Medullary carcinoma
- Uncertain premalignant significance; Atypical ductal hyperplasia (ADH), Lobular carcinoma in situ (LCIS)

Breast Cancer Risk Factors

FIXED;

- Female (100x more common than men)
- Age
- Hormonal
 - Estrogen exposure; early menarche, late menopause, late children/nulliparity
 - Carcinomas secrete Growth Factors in response to Estrogen
- Dense breasts/Fibrocystic change/benign epithelial change/cysts (2-4x)

MODIFIABLE;

- Obesity (high cholesterol, ? diabetes)
- Lack of exercise (10%)
- Alcohol
- Smoking (35-50%)
- ? Dietary (high fat intake, low fibre, iodine deficiency)
- HRT (?OCP – probably not)
- Mantle radiation

Factors influencing the risk of breast cancer

	High risk	Low risk
Relative risk 1.1–2.0		
Age at first full-term pregnancy (years)	≥30	<20
Age at menarche (years)	<12	>14
Age at menopause (years)	≥55	<45
Obesity (postmenopausal)	Obese	Thin
Parity	Nulliparous	Multiparous
Breastfeeding (premenopausal)	None	Several years
Hormonal contraceptives (age <45 years)	Yes	No
Hormone replacement therapy	Yes	No
Socio-economic status	High	Low
Place of residence	Urban	Rural
Ethnicity		
Risk of premenopausal breast cancer	White	Asian
Risk of postmenopausal breast cancer	Black	Asian
Relative risk 2.1–4.0		
Mammographic appearance	Dense nodular	Fatty
One first-degree relative with breast cancer	Yes	No
Biopsy-confirmed atypical hyperplasia	Yes	No
High-dose radiation to chest	Yes	No
Ovariectomy before age 35	No	Yes
Relative risk >4.0		
Age (years)	>50	<30
Region of birth	North America, Northern Europe	Asia, Africa
Two first-degree relatives with breast cancer diagnosed at an early age	Yes	No
History of cancer in one breast	Yes	No

Genetics

- Genetic (5-10%)
- Family Hx: 2-3x increased risk with 1st degree relative
 - Increased further if premenopausal/bilateral
- BRCA1
 - 17q21
 - Tumor suppressor oncogene, AD inheritance
- BRCA2
 - 13q12.3

Family History Risk

- Mother dx <50yrs: 1.7x risk
- Mother dx at or after 50yrs: 1.4x risk
- Those with 0, 1 or 2 affected relatives, risk of BC before 80yrs is 7.8%, 13.3% & 21.1% (mortality 2.3%, 4.2% and 7.6%)

Genetics & BC risk

- BRCA1 (50-80% BC, 35-46% ovarian by 70yrs)
- BRCA2 (40-57% BC, 13-23% ovarian by 70yrs)
- P53 (Li-Fraumeni syndrome) – 4% women with BC <30yrs have mutation in this gene
- PTEN (Cowden)
- STK11 (Peutz-Jeghers syndrome)
- CDH1 (gastric & lobular breast cancer)
- CHEK2, ATM, BRIP1, PALB2

Key



Male



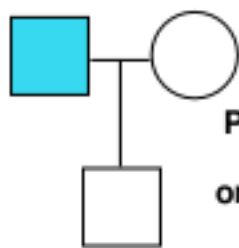
Female



Affected Individual : breast cancer



Affected Individual : ovarian cancer

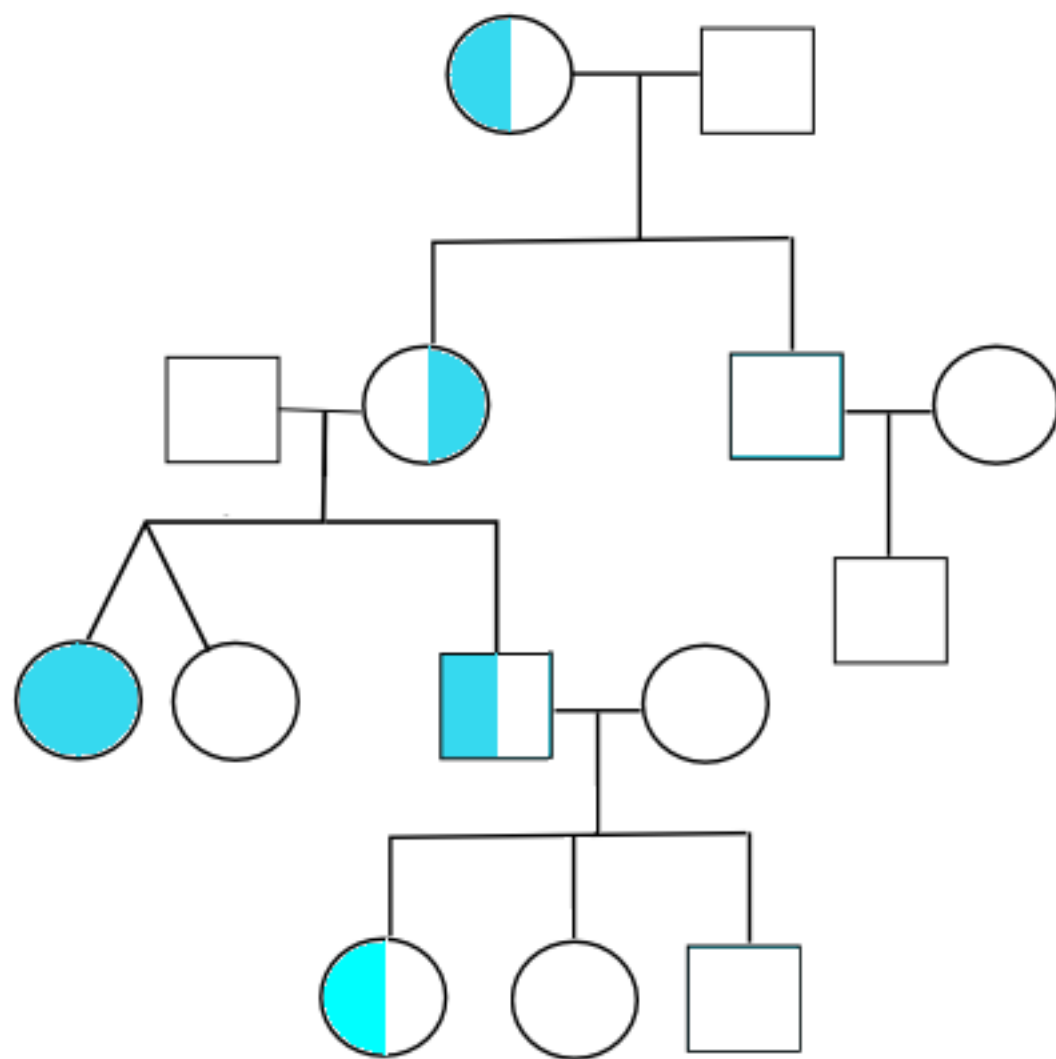


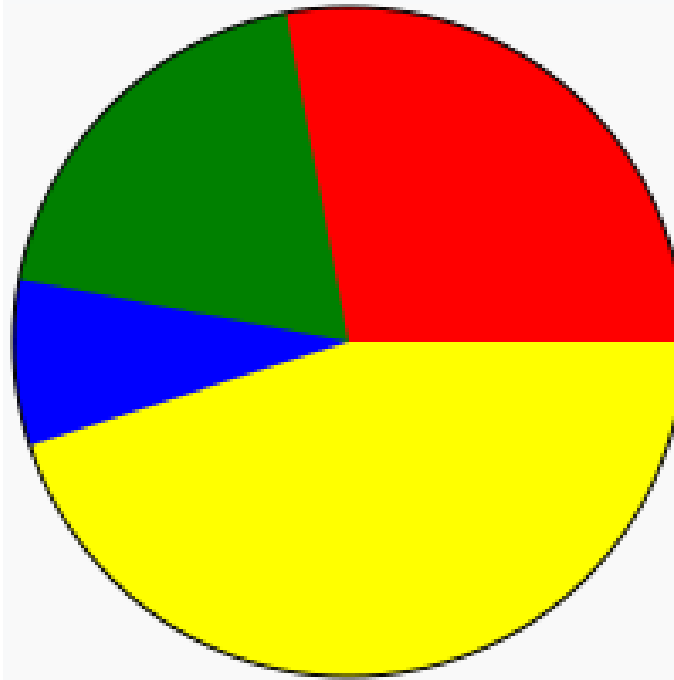
Parents
and
one child



twins

Hereditary breast and ovarian cancer in a pedigree chart





Approximate proportion of hereditary breast cancer cases caused by each gene

- *BRCA1* mutations (28%)
- *BRCA2* mutations (19%)
- All other known genes (8%)
- Unknown genes or multiple genes (45%)

Genetic Testing

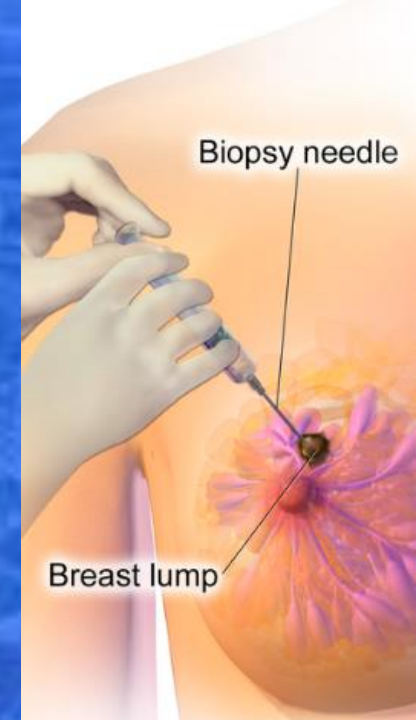
- Known mutation (BRCA1/2) in family
- Women affected <30yrs
- TNBC <50yrs
- 2 relatives <45yrs (first or second degree)
- 3 relatives <50yrs (first or second degree)
- 4 relatives at any ages
- Ovarian cancer with either an additional relative diagnosed OR male BC
- Male BC
- Pancreatic cancer with BC or ovarian cancer in same patient or same side of family
- Ashkenazi Jew or Polish ancestry with 1 family member affected by breast or ovarian cancer at any age

Male breast cancer

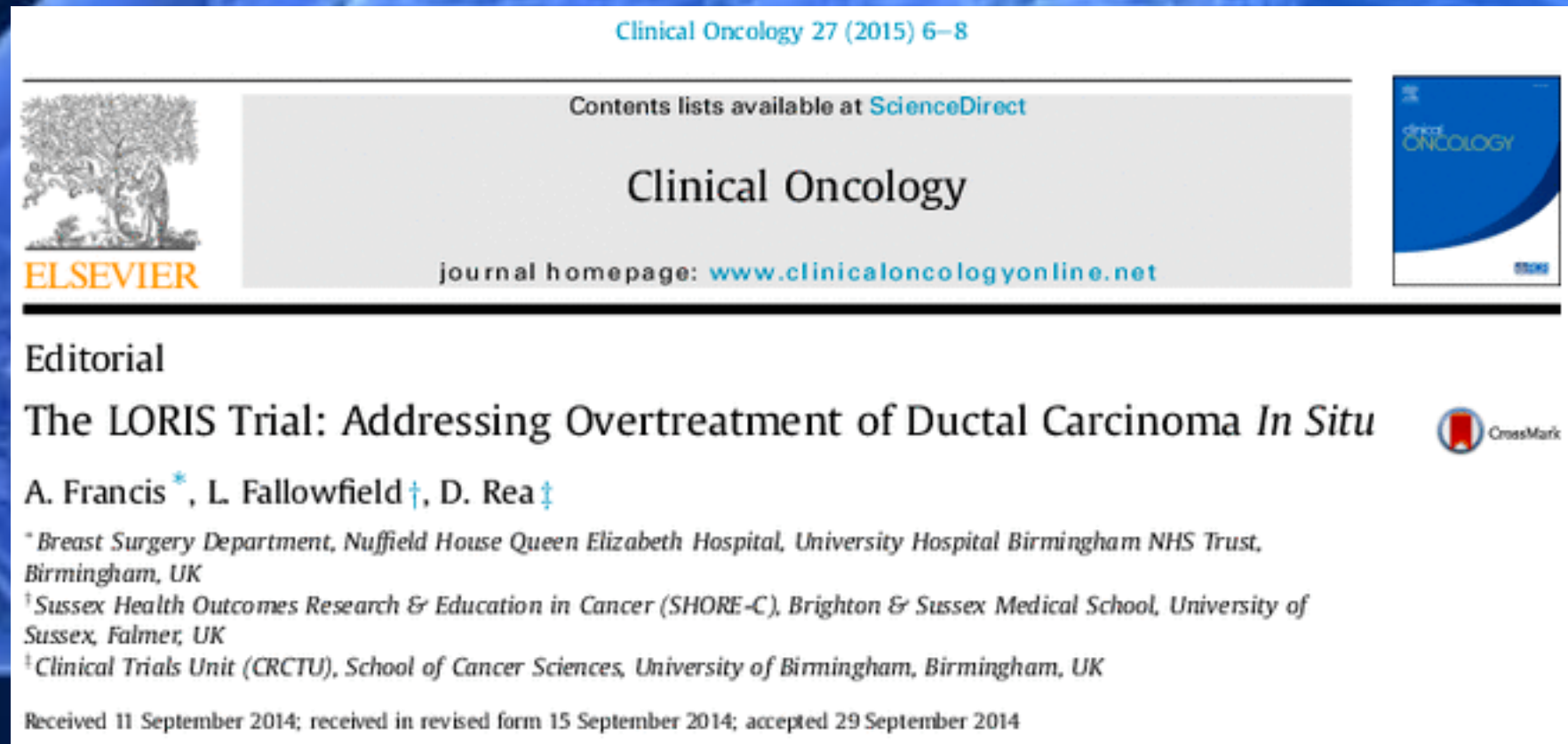
- High relative risk of BC in BRCA mutation men, but because overall incidence is so low, absolute risk is that of women without a BRCA mutation
- 1-2% BRCA1 men develop BC before 70yrs
- 6% BRCA2 men develop BC before 70yrs
- Very few men with/without a predisposing genetic mutation develop BC <50yrs

Triple Diagnosis =

- Examination
- Radiology
- Biopsy

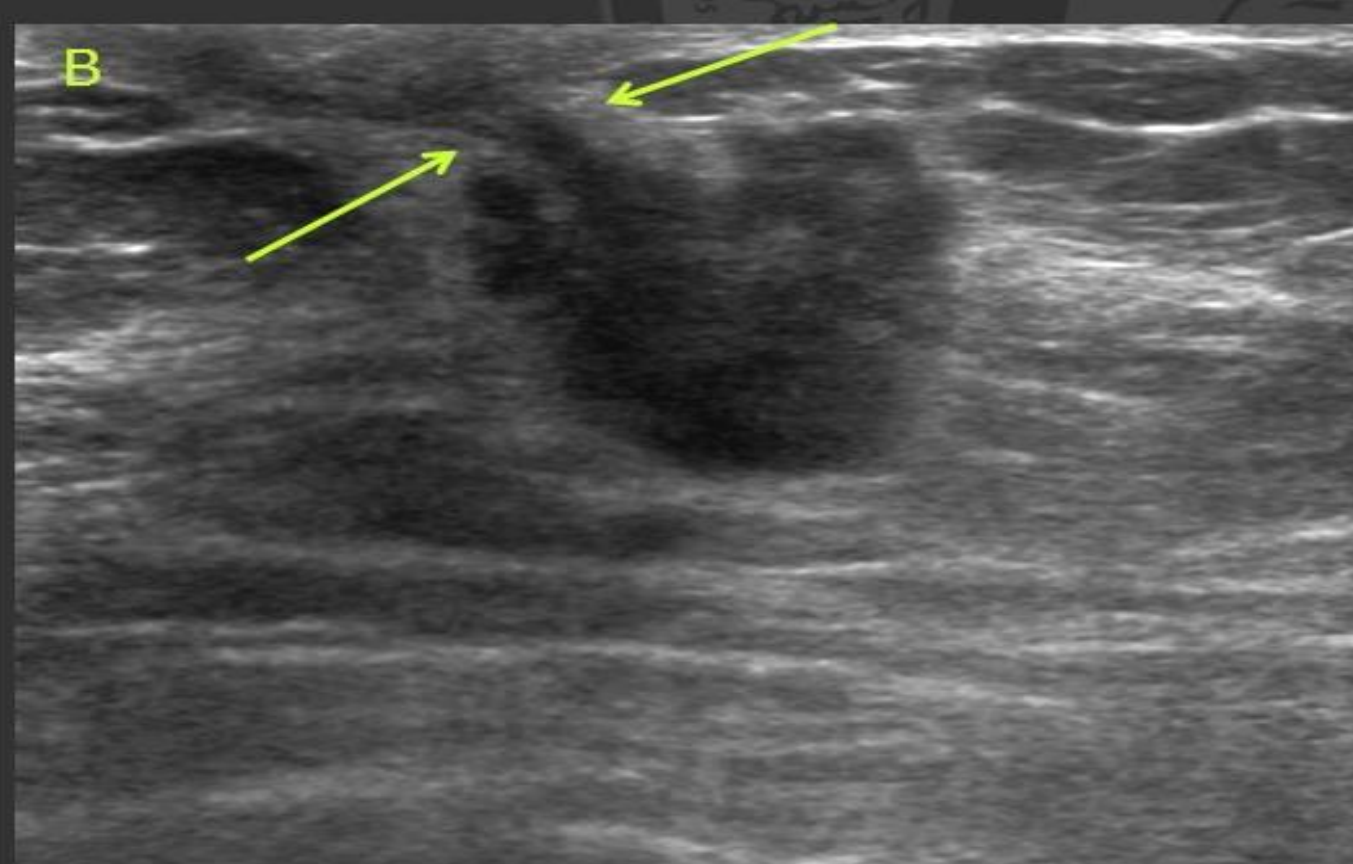
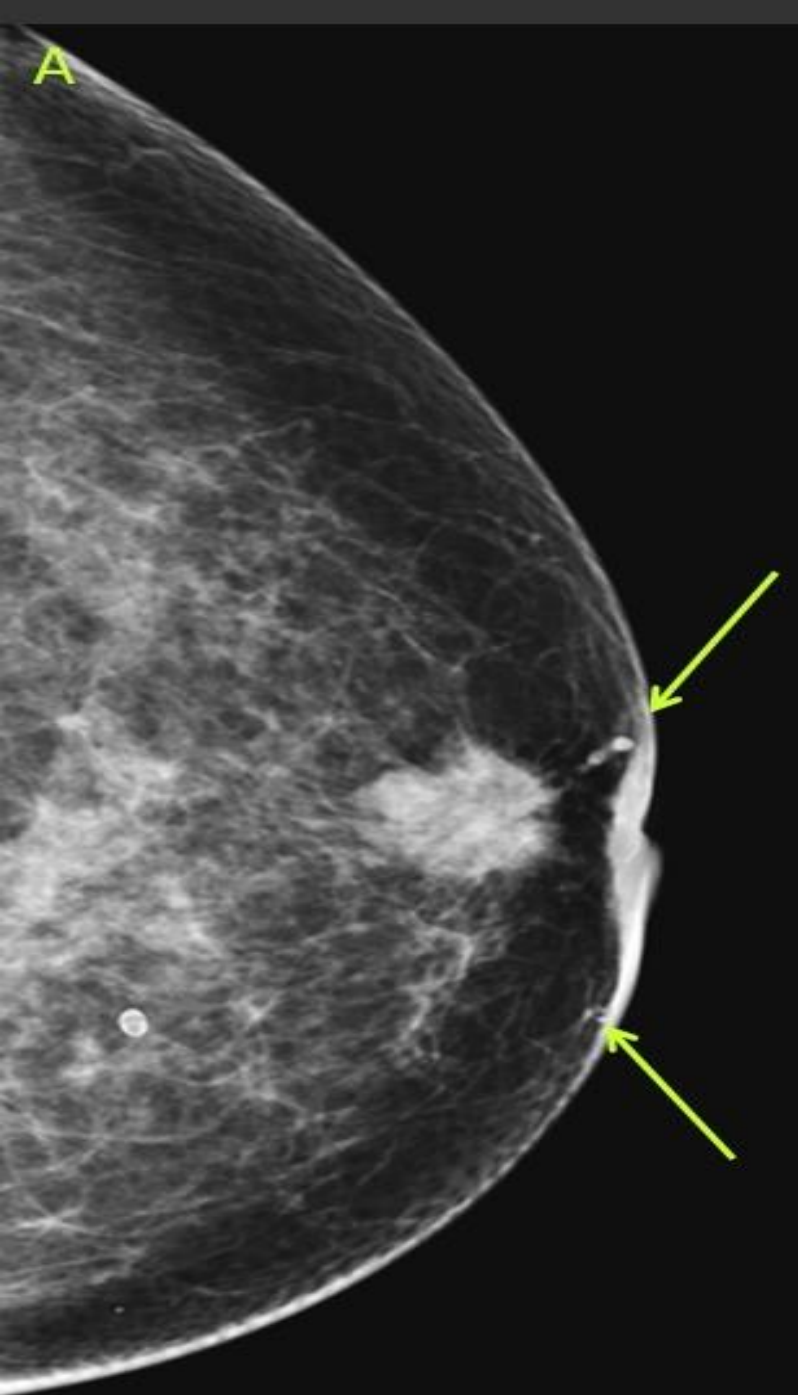


Breast screening



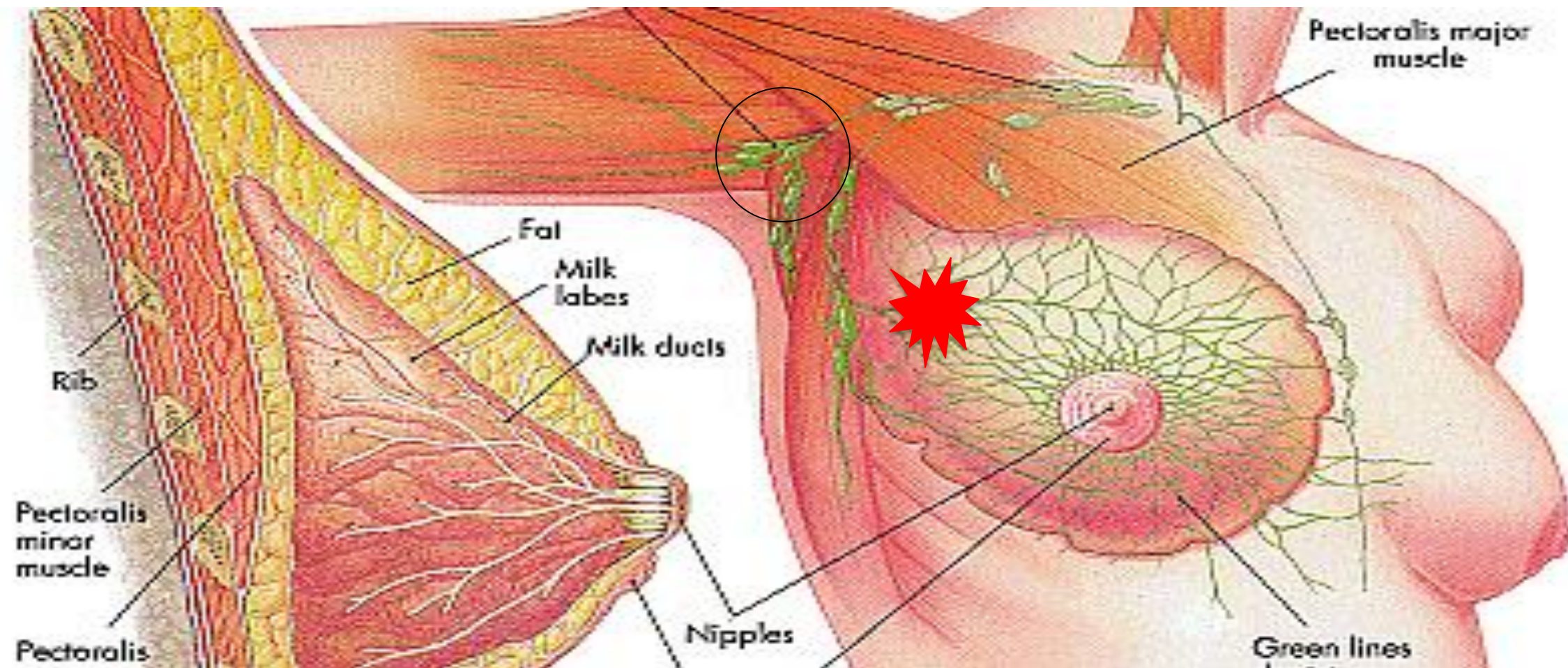
detected

- ? *Overtreatment*



Invasive ductal carcinoma, direct nipple invasion

Surgery....



Surgery

- **The breast**

- Breast conserving surgery (lumpectomy) + Radiotherapy
- Mastectomy
- +/- Reconstruction

- **The Armpit (Axilla)**

- Sentinel Lymph node biopsy
- Axillary Lymph Node Dissection



**Systemic
Treatments**

Chemotherapy

Hormonal Therapy

Immunotherapy

**Radiation
Therapy**

Surgery

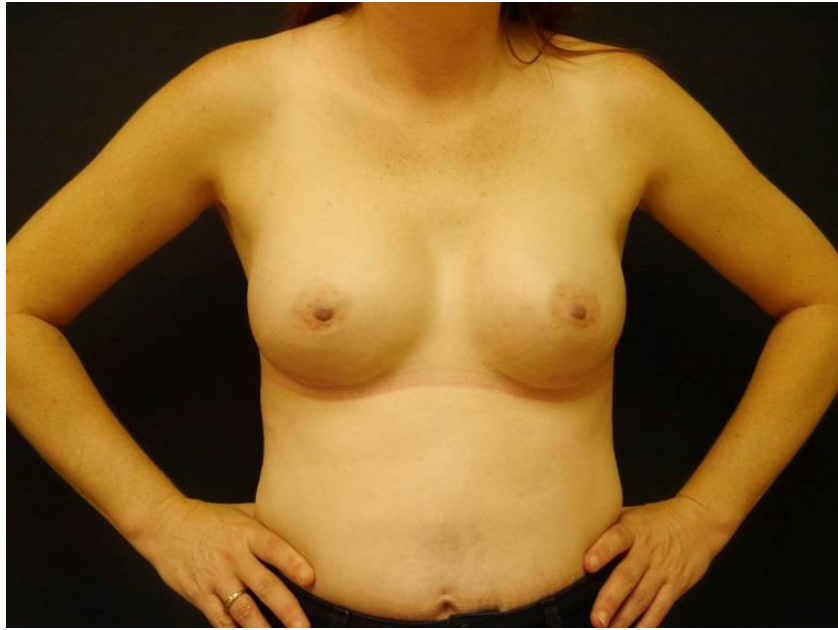
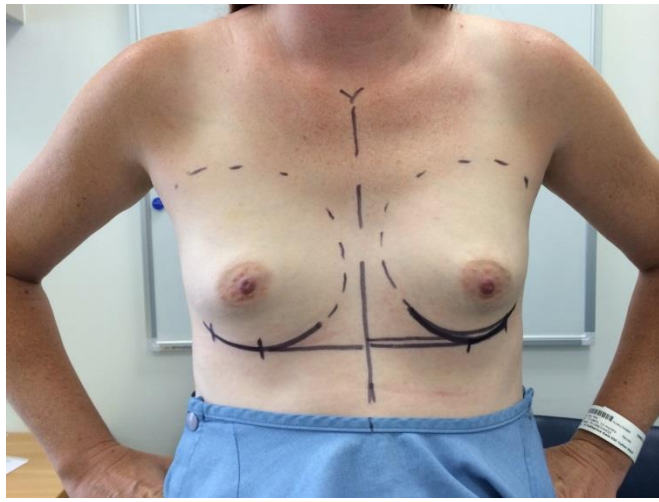


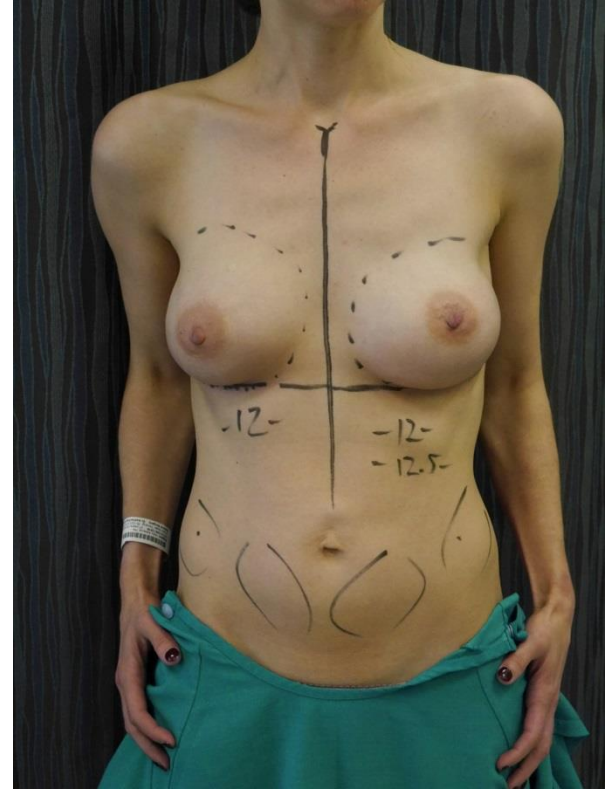
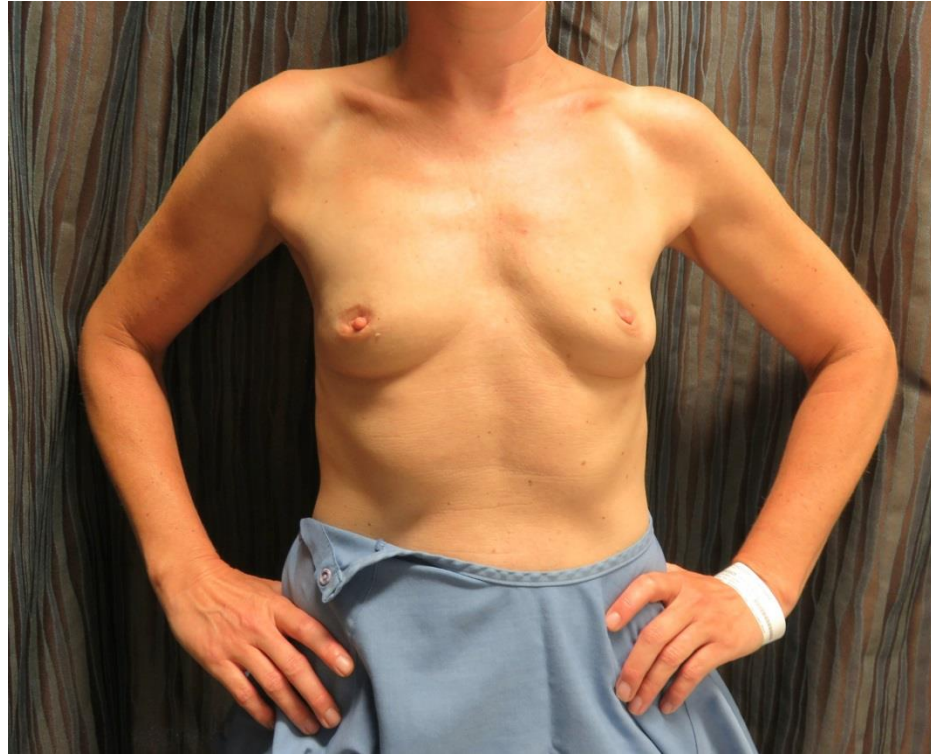
Prevention

- Lifestyle (may reduce risk 20-40%)
 - Maintain healthy weight
 - Exercise (by 14%)
 - Limit alcohol intake
 - Breastfeeding
 - Dietary; intake high citrus fruits may get a 10% risk reduction, marine omega-3 polyunsaturated fatty acids

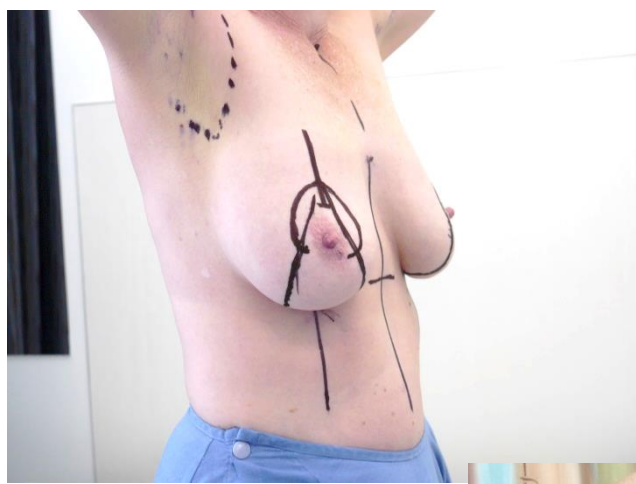
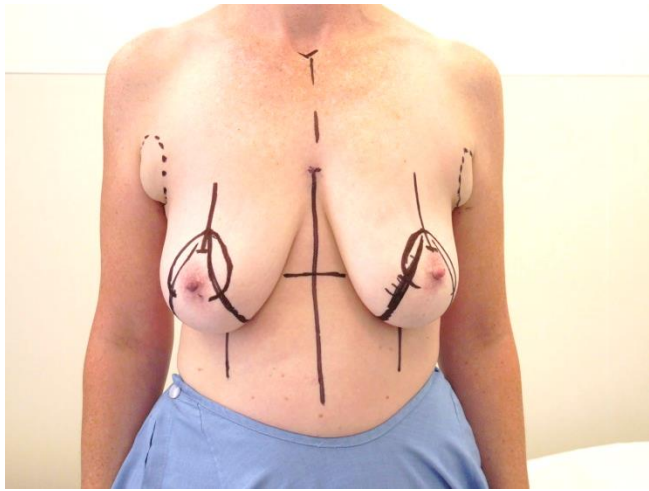
Risk Reduction in Genetic Mutation carriers

- Lifestyle
- Chemoprevention
- Oophorectomy
- Risk reducing surgery









Breast cancer treatment, prevention and surveillance pathways for BRCA-mutation carriers at NBI

Gale KL, Caracappa D, James R, Scott NAL, Macmillan RD

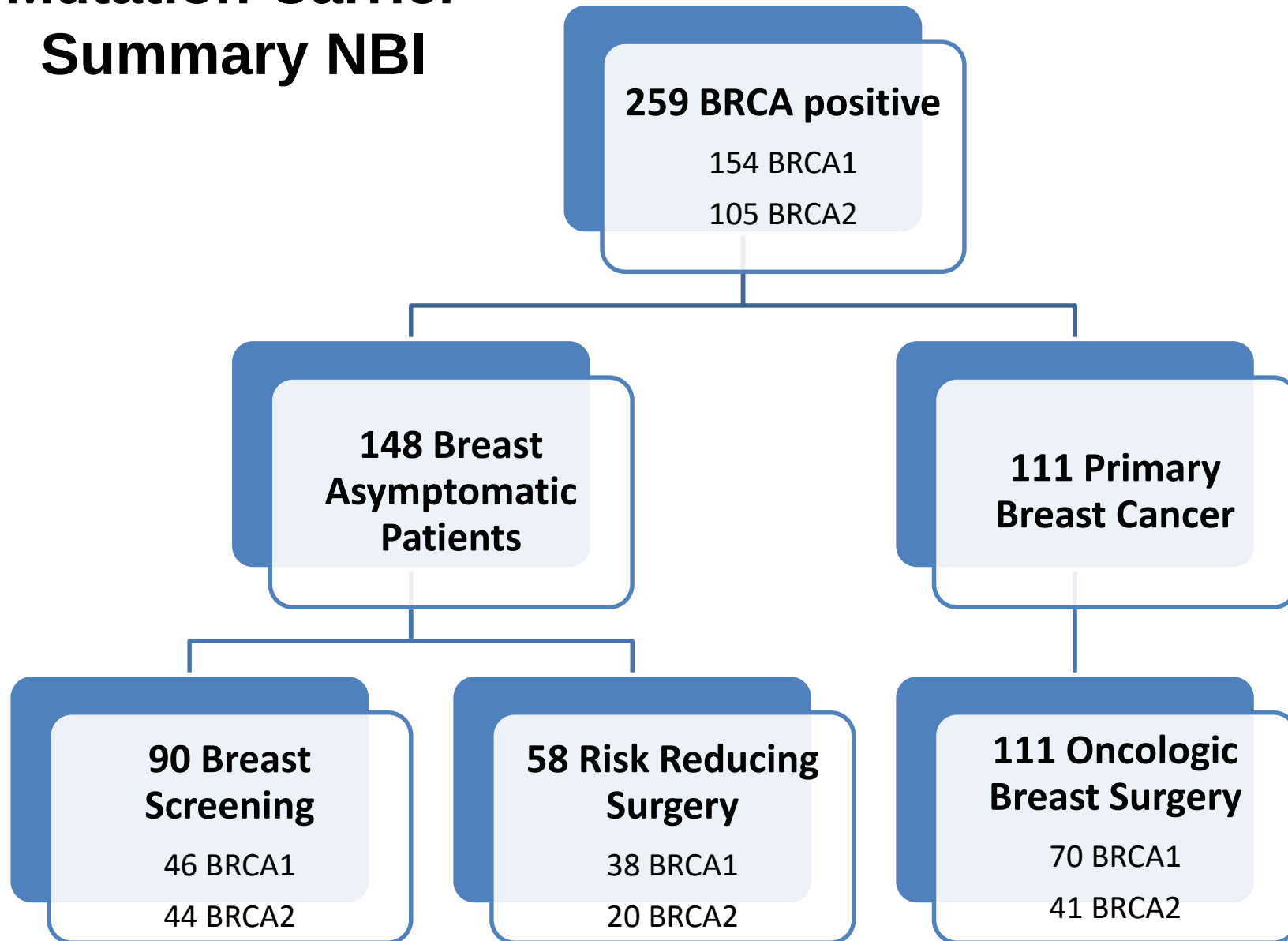


Overview

- BRCA mutation carriers;
 - **breast cancer**
 - **prophylactic surgery**
 - **Screened**

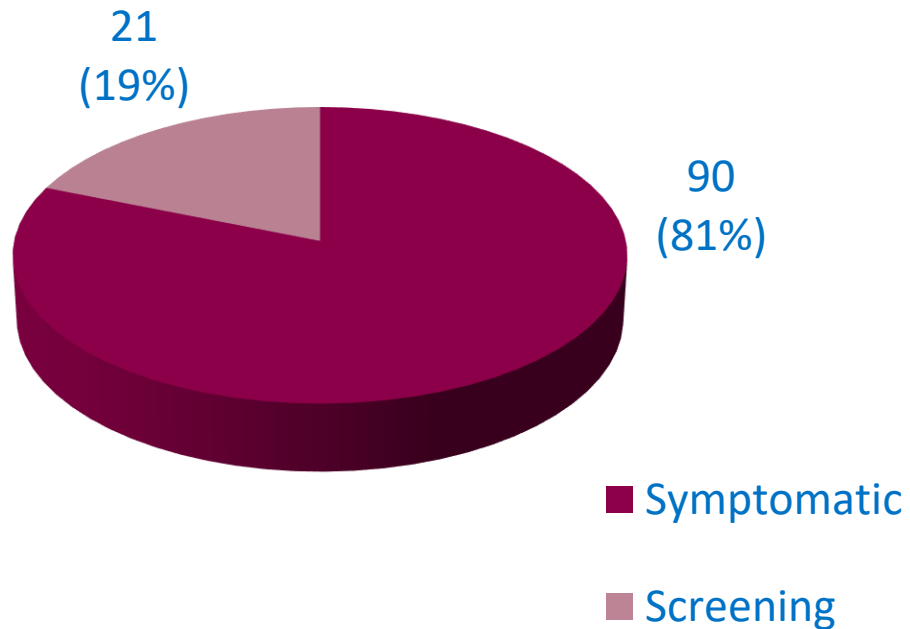


Mutation Carrier Summary NBI

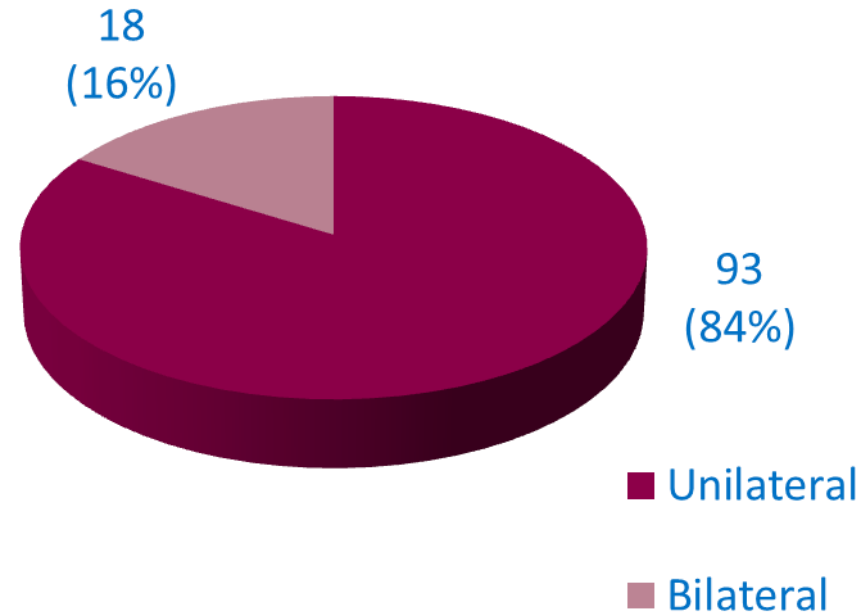


111 BRCA Cancer patients

Method of Cancer Presentation



Laterality of Cancer



BRCA	Mean age	Mean size (mm)	Grade	Node Status	VI	Mean NPI
Total (n=111)	40.7	22.9	2.94 Grade 1; 2 Grade 2; 11 Grade 3; 96 Unknown; 2 (88% Gd3)	1.45 Stage 1; 72 Stage 2; 28 Stage 3; 8 Unknown; 3 (33% node +)	Present 32 (29%) Absent 69 (62%) Unknown 10 (9%)	4.75
Screen detected (n=21)	46.7 ↕	18.5 ↕	2.76 Grade 1; 1 Grade 2; 3 Grade 3; 17 (81% Gd3)	1.10 Stage 1; 19 Stage 2; 2 (10% node +)	Present 6 (29%) Absent 13 (62%) Unknown 2 (9%)	4.41
Symptomatic (n=90)	39.3	23.8	2.88 Grade 1; 1 Grade 2; 8 Grade 3; 79 Unknown; 2 (90% Gd3)	1.48 Stage 1; 48 Stage 2; 31 Stage 3; 8 Unknown; 3 (45% node +)	Present 36 (40%) Absent 56 (62%) Unknown 8 (18%)	4.85

BRCA 1	Mean age (range)	Mean size (mm)	Grade	Node Status	VI	Mean NPI
All (n=70)	39.5 (22-61)	16.8	2.94 Grade 1; 1 Grade 2; 2 Grade 3; 66 Unknown; 1	1.35 Stage 1; 48 Stage 2; 16 Stage 3; 4 Unknown; 2	Present 20 (32%) Absent 43 Unknown 7	4.77
Screen detected* (n=12)	43.4 (28-58)	16.9	3.00 Grade 3; 12	1.08 Stage 1; 11 Stage 2; 1	Present 3 (30%) Absent 7 Unknown 2	4.41
Symptomatic* (n=58)	38.7 (22-61)	24.0	2.93 Grade 1; 1 Grade 2; 2 Grade 3; 54 Unknown; 1	1.41 Stage 1; 37 Stage 2; 15 Stage 3; 4	Present 27 (43%) Absent 36 Unknown 5	4.85

BRCA 2	Mean age (range)	Mean size (mm)	Grade	Node Status	VI	Mean NPI
All (n=41)	42.8 (28-70)	22.6	2.73 Grade 1; 1 Grade 2; 9 Grade 3; 30 Unknown; 1	1.50 Stage 1; 24 Stage 2; 12 Stage 3; 4 Unknown; 1	Present 12 (32%) Absent 26 Unknown 3	4.71
Screen detected* (n= 9)	51.1 (33-65)	20.6	2.44 Grade 1; 1 Grade 2; 3 Grade 3; 5	1.11 Stage 1; 8 Stage 2; 1	Present 3 (33%) Absent 6	3.97
Symptomatic* (n= 32)	40.7 (28-70)	23.3	2.81 Grade 1; 0 Grade 2; 6 Grade 3; 25 Unknown; 1	1.61 Stage 1; 11 Stage 2; 16 Stage 3; 4 Unknown; 1	Present 9 (31%) Absent 20 Unknown 3	4.95

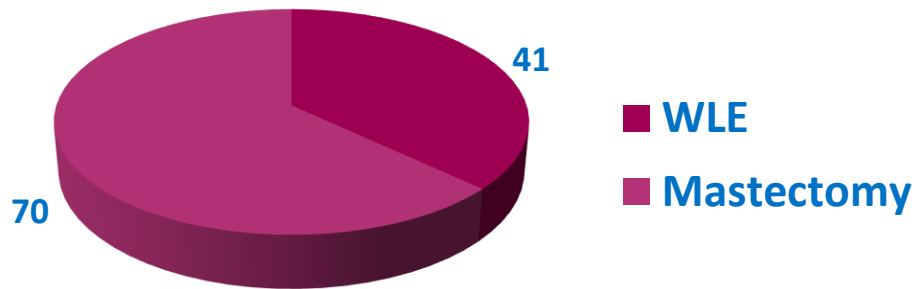
	ER Status	PR Status	Her2 Status
All (n=111)	Positive 40 (37%) Negative 67 UK/NT 4	Positive 10 Negative 40 UK/NT 61	Positive 4 (8%) Negative 46 UK/NT 61
BRCA1 (n= 70)	Positive 12 (18%) Negative 55 UK/NT 3	Positive 2 Negative 27 UK/NT 41	Positive 2 (7%) Negative 28 UK/NT 40
BRCA2 (n= 41)	Positive 28 (70%) Negative 12 UK/NT 1	Positive 8 Negative 13 UK/NT 20	Positive 2 (10%) Negative 18 UK/NT 21

**ER positive in 26% of 94 BRCA1 cancers &
78% of 72 BRCA2 cancers**

Goodwin PJ et al. Breast Cancer Prognosis in BRCA1 and BRCA2 Mutation Carriers: An International Prospective Breast Cancer Family Registry Population-Based Cohort Study. *Am Soc Clin Oncol* 30 (2012): 19-26

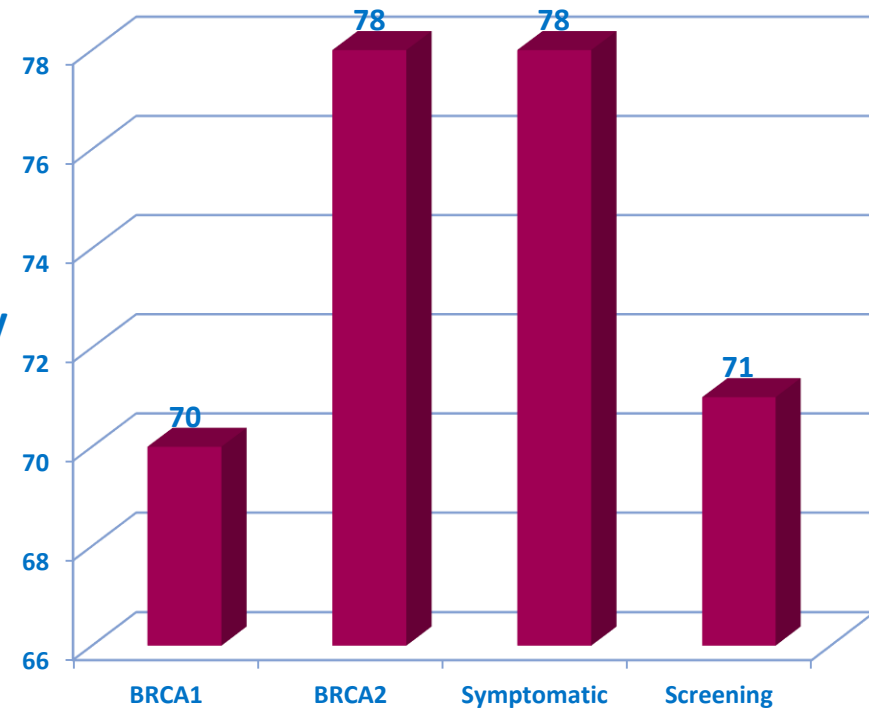
Treatment

Breast Cancer Operation



63% mastectomy
(initial Mx 47%/WLE 53%)

% Post Mastectomy RxT



73% Post-Mx radiotherapy

Reconstruction After Mx for Cancer

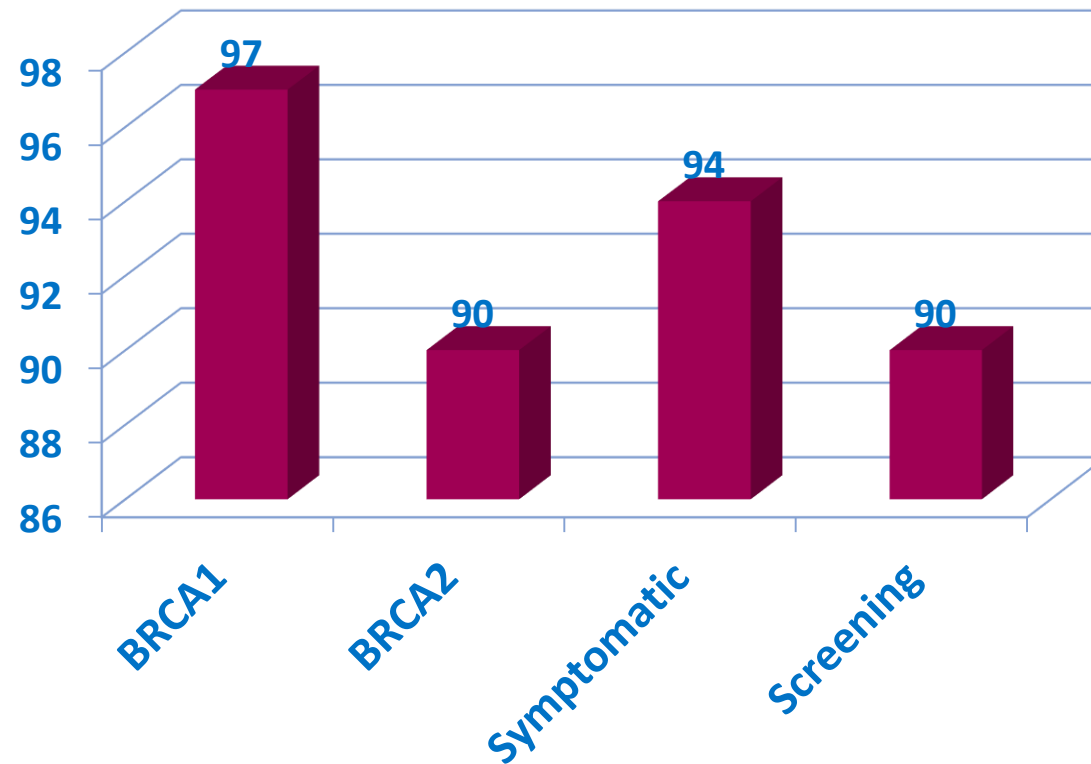
Reconstruction	Number	Percentage
None	24	34
Implant	24	34
LD	6	9
DIEP	6	9
Serial Lipofilling	1	1
Allo/Autograft combination	9	13
TOTAL	70	100

Risk Reducing Surgery after Cancer Treatment

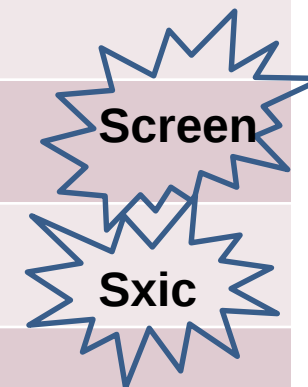
Final Cancer Operation	Risk Reducing Measure	Number	Percentage
WLE	WLE Only	23	21
WLE	Bilateral WLE Only	3	3
WLE	Bilat WLE then Bilateral RRM	15	13
Mastectomy	Bilat Mx for Ca	13	12
Mastectomy	None	17	15
Mastectomy	Contralat RRM	40	36
	TOTAL	111	100

Chemotherapy

- Chemotherapy indicated in 95% all cases



NPI	Prognostic Group	Observed Breast Cancer 10yr % Survival	Observed (all causes) 10yr % Survival
2.08-2.4	Excellent	96	88
2.42 to ≤3.4	Good	93	86
3.42 to ≤ 4.4	Moderate I	81	78
4.42 to ≤ 5.4	Moderate II	74	69
5.42 to ≤ 6.4	Poor	50	53
6.5-6.8	Very Poor	38	32



$$\% \text{ 10yr Survival (even)} = -1.62\text{NPI}^2 + 1.25\text{NPI} + 102.77$$

$$\text{R}^2 = 0.97$$

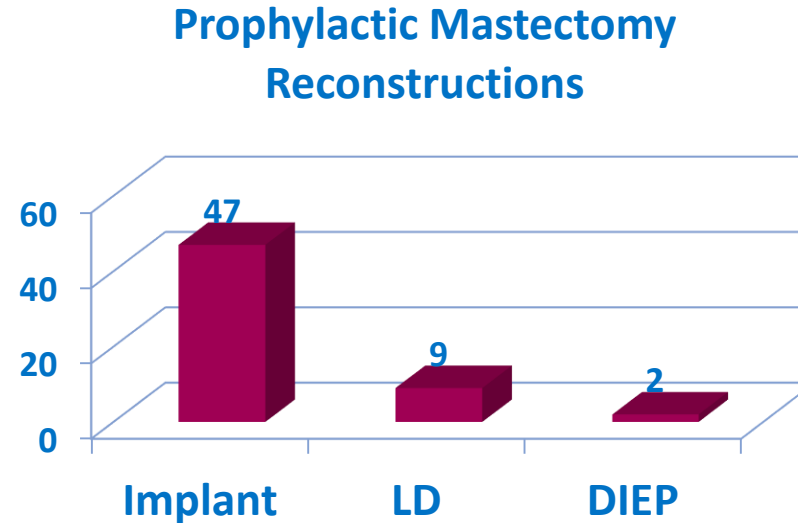
Blamey RW, Ellis IO, Macmillan RD et al. Survival of invasive breast cancer according to the Nottingham Prognostic Index in cases diagnosed 1990-1999. *Eur J Cancer* 43 (2007):1548-55

BRCA	Mode of Presentation	Mean age (yrs)	Size	Average Grade/ Node Status	Mean NPI	NPI Predictn 10yr survival	10yr Survival*
BRCA1	Screening	43	17	3/+	4.41	77%	89%
	Symptomatic	39	24	3/+	4.85	71%	86%
BRCA2	Screening	51	21	2/-	3.97	82%	90%
	Symptomatic	41	23	3/+	4.95	69%	91%

* www.lifemath.net/cancer/breastcancer/outcome; With Chemotherapy in ER- patients, or Chemotherapy & Endocrine Rx in ER+ patients

58 Prophylactic Surgery

- Mean age 39 yrs
- No breast cancers in 125 096 woman-years follow up (mean 6.6 years)
- 81% Implant based reconstruction

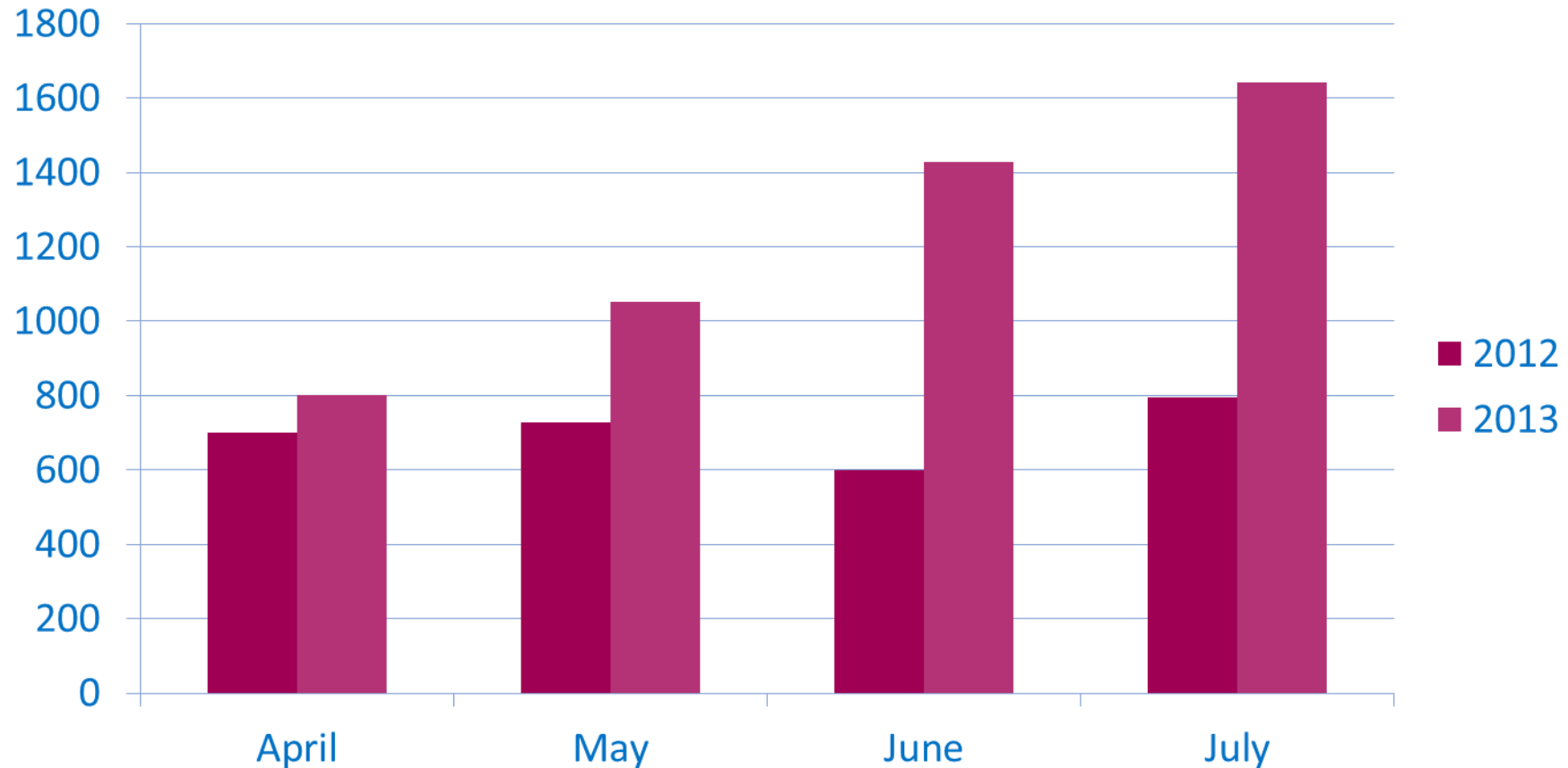


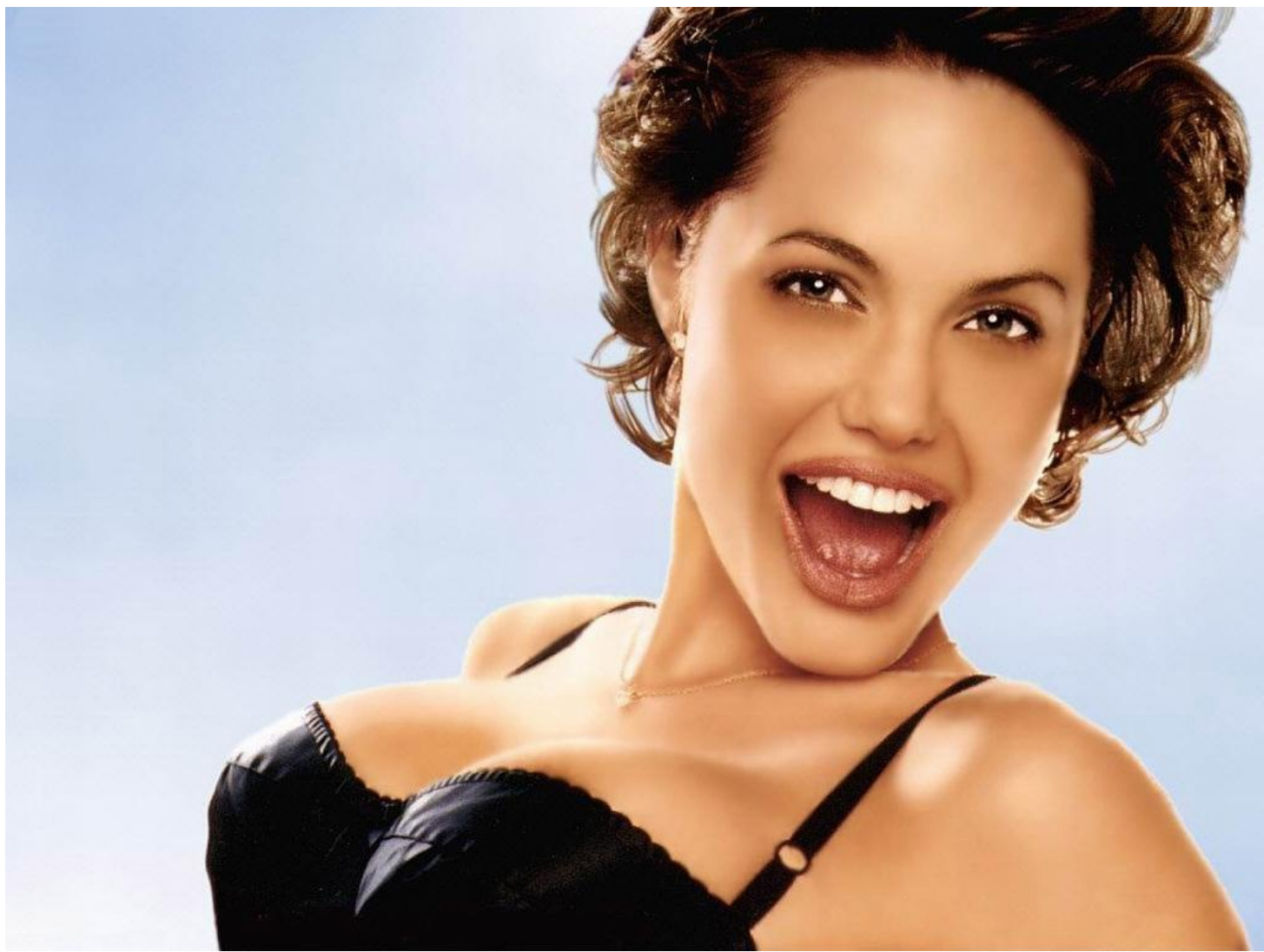
Conclusions

- 259 BRCA mutation carriers through NBI family history service
- Treatment of BRCA-related breast cancer is very likely to involve chemotherapy and radiotherapy, both for symptomatic and screen-detected cases
- Risk estimates of developing life-threatening breast cancer may be useful
- BRCA 1 risk approx 1.5X BRCA 2 risk if Sx ic
- No proven method to reduce this risk other than surgery

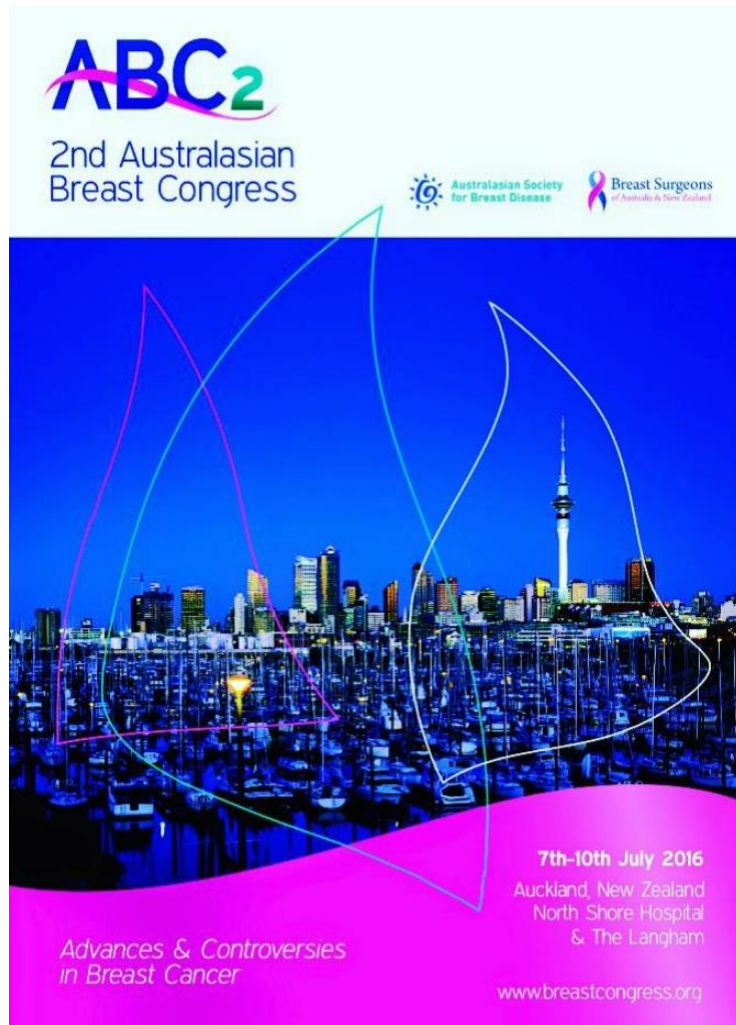
FH referrals 2012/13

Wales, Manchester, Crewe, Bath, RMH, Edinburgh, Leicester, Guys, Derby, Belfast, Nottingham, Coventry, Bristol, Soton, Barts, Grantham, Sandwell





In summary....take home messages



- Breast cancer is common & risk can be modified
 - *Be aware of symptoms and signs*
- BRCA related breast cancer rare
 - *Ways to reduce risk*
- Quality of life without compromising treatment
 - *There is usually a lot of life after breast cancer*

Thanks!



