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Breast cancer: demographics, presentation, diagnosis & patient pathway

Charlotte Coles, Hilary Stobart, Jean Abraham, John Benson, Richard Baird Luke Hughes-Davies & Matthew Wallis

On behalf of Cambridge Breast Unit

Objectives

To be able to answer the following questions about breast cancer:

- How common is it and how does it present?
- What are the causes?
- What are the major types of treatment?
- What role does the patient have in management?
- Questions before and after talk

Research creates evidence-based best practice

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Cancer Research UK Major Centre, OECI Comprehensive Cancer Centre, EACS Comprehensive Cancer Center of Excellence

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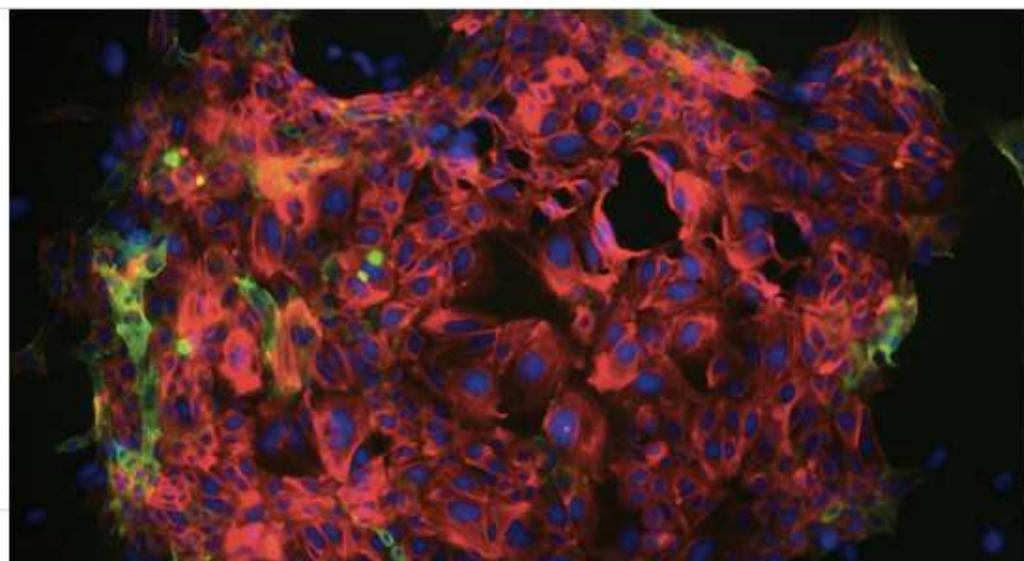
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Breast Cancer

Every year around 50,000 new cases of breast cancer are diagnosed in the UK. Five out of six women with breast cancer in England and Wales survive for at least five years; however, around 1,000 UK women still die of breast cancer every month. Our research is aiming to increase the survival rate through...

Large-scale population studies to determine which genes are responsible for causing breast cancer,
Genetic barcoding to identify different cancer types and to help develop specific treatments,
Clinical trials to test new treatments on patients.



Patient perspective



Hilary Stobart

Demographics, presentation, diagnosis & patient pathway

Key facts

Cases

55,122



New cases of invasive
breast cancer, 2015,
UK

Deaths

11,433



Deaths from breast
cancer, 2014, UK

Survival

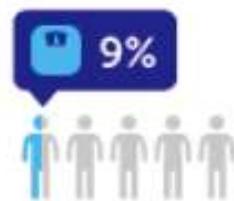
78%



Survive breast cancer
for 10 or more years
(females only),
2010-11, England and
Wales

Risk factors & prevention

Excess bodyweight



Breast cancer cases
linked to excess
bodyweight, UK

Alcohol



Breast cancer cases
linked to alcohol
consumption, UK

Physical inactivity



Breast cancer cases
linked to too little
physical activity, UK

Presentation: signs & symptoms

When to see your doctor

You should see your doctor if you have:

- a change in the size, shape or feel of a breast
- a new lump or thickening in a breast or armpit
- skin changes such as puckering, dimpling, a rash or redness of the skin
- fluid leaking from a nipple and you aren't pregnant or breastfeeding
- changes in the position of a nipple
- breast pain

Your symptoms are unlikely to be cancer but it is important to get them checked by a doctor.

Screening

**200 women who don't attend
breast screening**
(every 3 years from age 50 to 70)



12 diagnosed with
breast cancer



8 treated and
survive



4 treated but
die



**200 women who do attend
breast screening**
(every 3 years from age 50 to 70)



15 diagnosed with
breast cancer



12 treated and
survive



3 over-treated

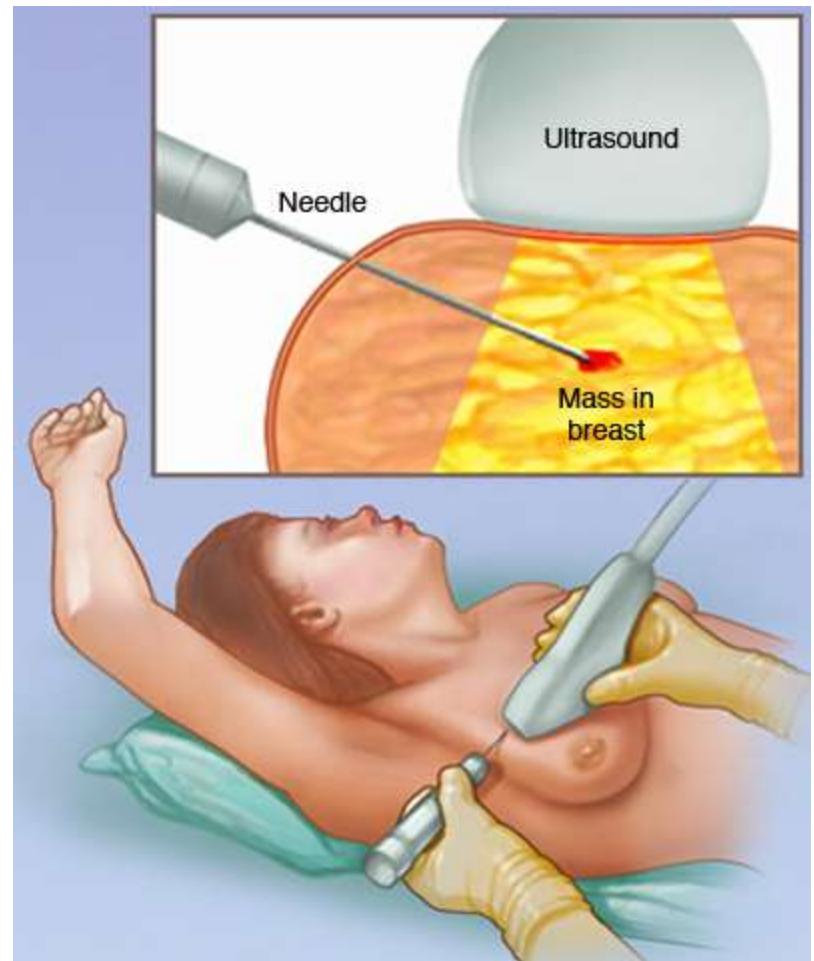


3 treated but
die

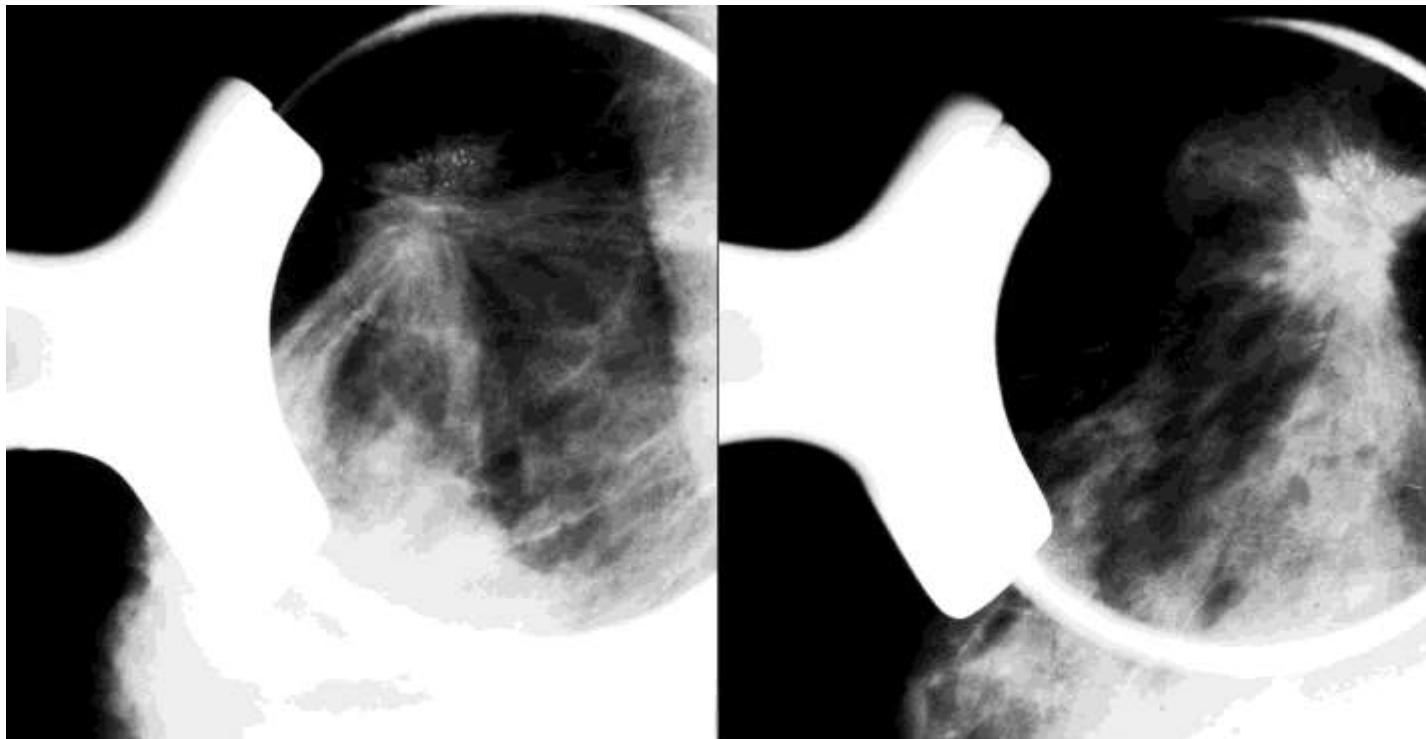


Diagnosis

- Triple assessment:
 - Mammogram
 - Ultrasound
 - Biopsy
- (Staging)

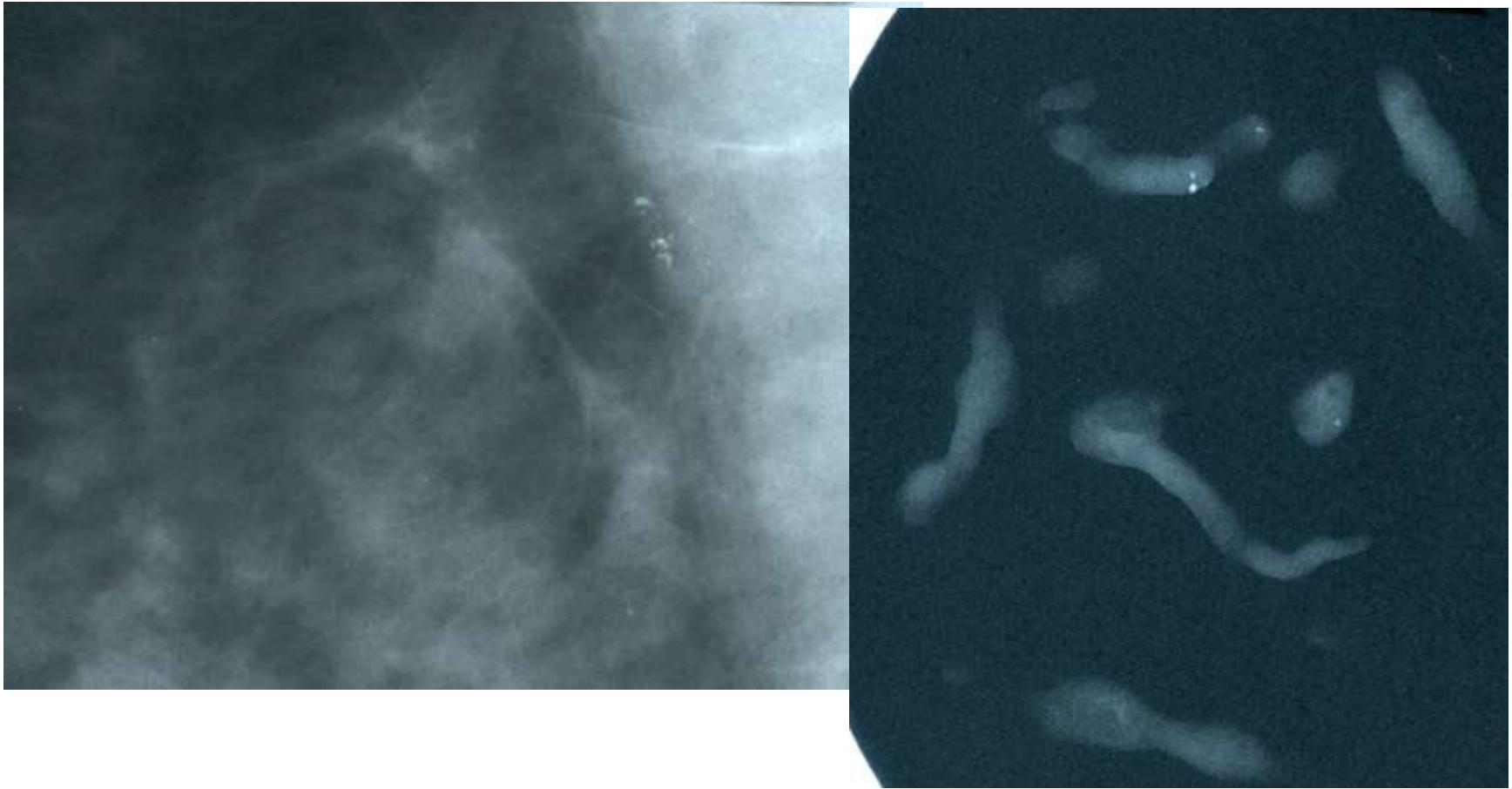


Mass Spiculate



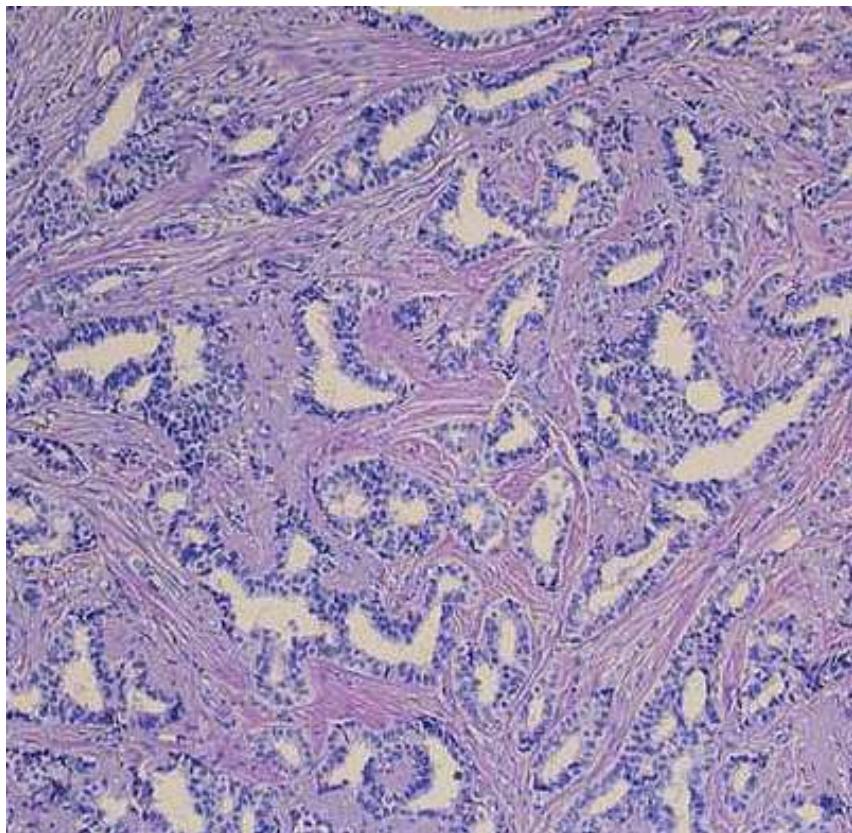
Dr Matthew Wallis, Cambridge

Microcalcification



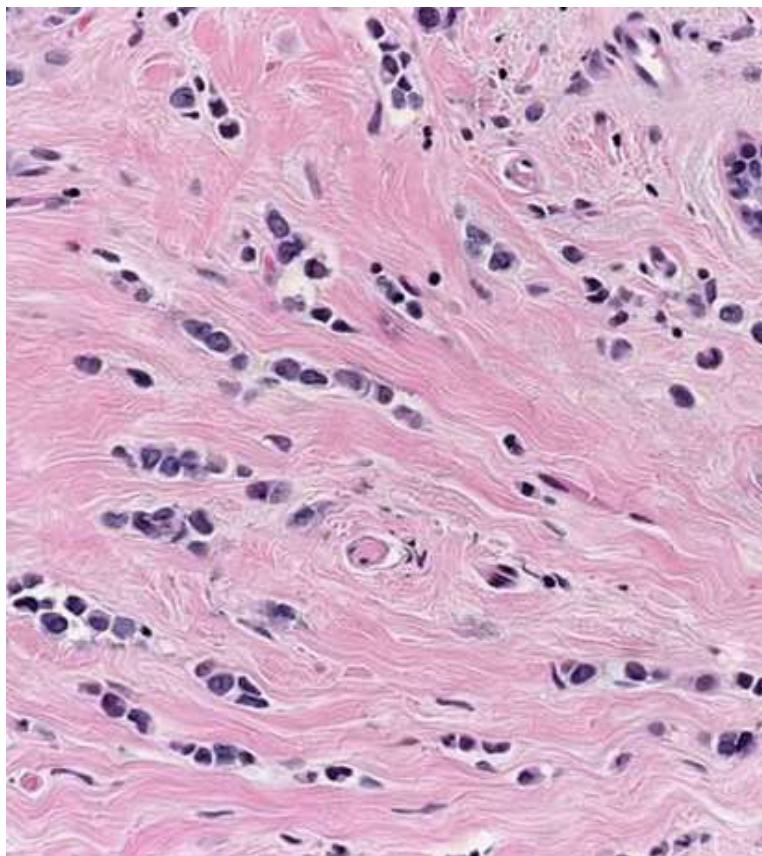
Dr Matthew Wallis, Cambridge

Histology – Invasive ductal carcinoma



- 75% of breast cancers
- No specific histologic characteristics other than invasion through the basement membrane of a breast duct

Histology – Invasive lobular carcinoma



- 15% of cases of invasive breast cancer
- “Single file” arrangement of small tumor cells
- Staining for E-cadherin
- Link between cadherin (CDH1) gene and invasive lobular breast cancers - 50% contain E-cadherin mutations (affects “stickiness” of cells)

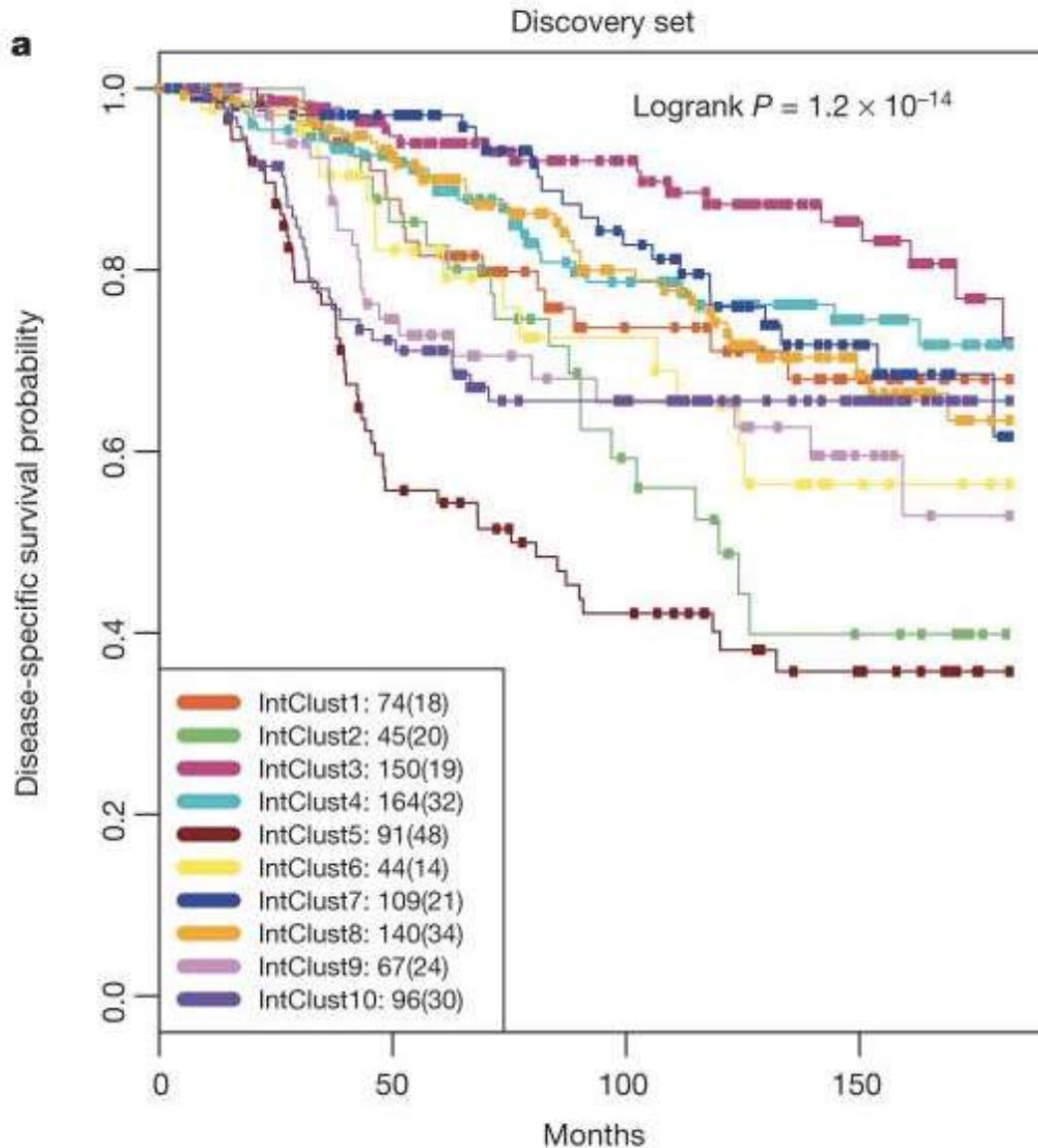
Breast cancer receptors

- 70% - hormone receptor +ve
 - ER (oestrogen) and/or PR (progesterone) +ve
- 15% -HER2 +ve
 - human epidermal growth factor 2
- 15-20% - “triple negative”
 - ER, PR & HER2 -ve

Molecular subtypes of breast cancer

- Molecular subtypes:
 - Luminal A, Luminal B, HER2-enriched, triple negative/basal-like, normal-like
- More complex:
 - >10 molecular subtypes
 - Heterogeneity within subtypes and within individual tumours

Breast cancer is not just one disease...



- One size treatment no longer fits all
- Need to tailor to patient:
 - Risk of recurrence
 - (Molecular subtype)



Personalised
Breast Cancer
Program



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Personalised Breast Cancer Program

Professor Carlos Caldas & Dr Jean
Abraham

Courtesy of Dr Jean Abraham



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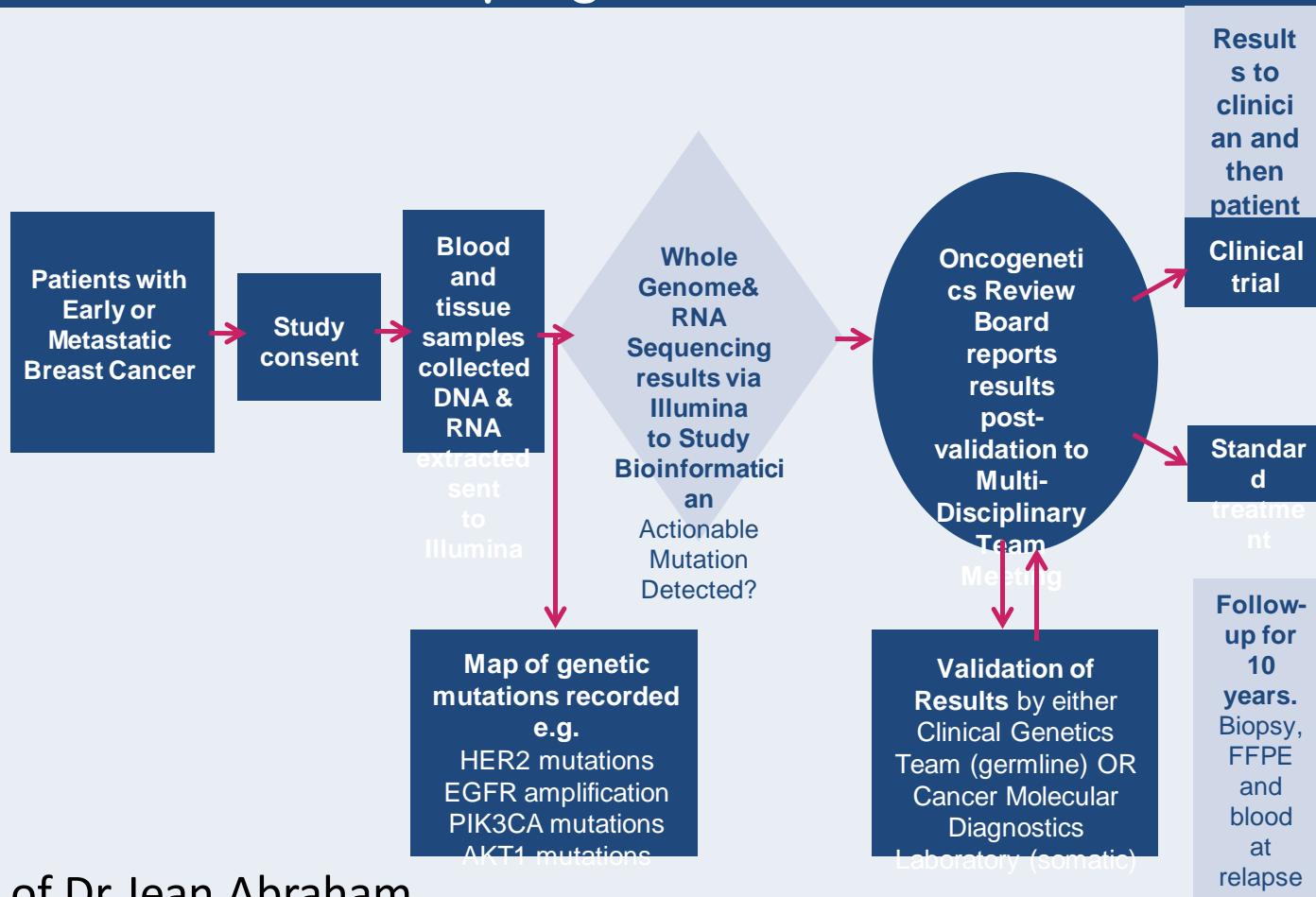
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FEASIBILITY STUDY ASSESSMENTS run alongside standard or clinical trial management with no impact on clinical pathway except additional blood and tumour sampling



Multi-disciplinary team meeting





‘Often wrong but never uncertain’

Courtesy of the late Prof Adele Francis, consultant surgeon,
Birmingham, UK

Cambridge breast cancer MDT



Aims of treatment

- Curative:
 - Best chance of cure with least side effects, including long term (months & years later) physical & psychological toxicity
- Palliative:
 - To help live as long as possible with best quality of life

Components of curative treatment

- Radical: “curative” – usually surgery
- (Neo-)Adjuvant: “in addition”
 - Radiotherapy
 - Chemotherapy & biological therapy
 - Endocrine therapy



Breast surgery – mastectomy v breast conservation

- Majority of patients undergo primary surgery followed by adjuvant therapies (some downstaged with neoadjuvant chemotherapy):
 - breast conserving surgery (BCS) = 60%
 - mastectomy = 40%
- BCS established as preferred standard of care for early stage breast cancer (endorsed by National Institute of Health 1991)
- Mature data from prospective randomised clinical trials have demonstrated equivalent survival outcomes for BCS compared with mastectomy

Breast Conserving Surgery

- BCS involves removal of tumor & surrounding normal breast tissue: negative surgical margins + acceptable cosmetic result
- Surgeon aims to resect 1 – 2cm of macroscopically normal tissue around a tumor that may be palpable or wire-localized (radial margins must be microscopically negative)
- Surgical decision for BCS:
 - AGE
 - TUMOUR/BREAST SIZE RATIO
 - EXTENSIVE DCIS
 - LOBULAR PHENOTYPE



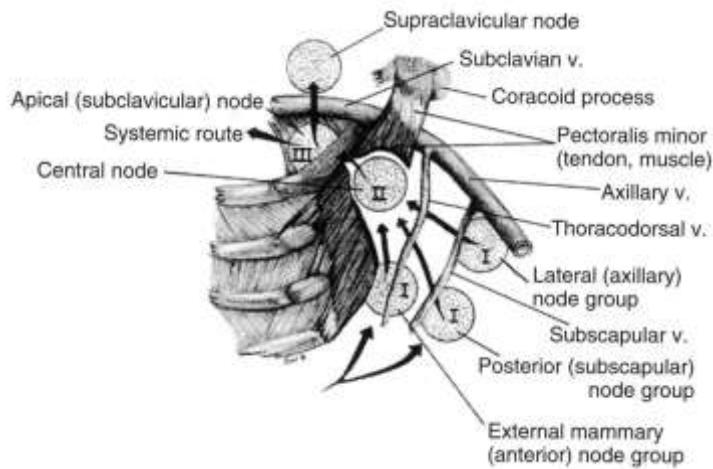
Oncoplastic Surgery

- Consensus statement from Society of Surgical Oncologists/American Society of Radiation Oncology: acceptance of a minimal margin - 'no tumor at ink' for invasive cancer (NB - minimum margin of 1mm is recommended in UK)
- Balance between risk of local recurrence & cosmetic results for BCS – new techniques of oncoplastic surgery are advancing limits of resection
- Development: skin & nipple-sparing mastectomy with immediate breast reconstruction to improve cosmesis



Axillary Surgery

- Some form of axillary surgery is **integral** component in the loco-regional management of early breast cancer
- Standard axillary dissection refers to clearance of nodes at levels I and II only



- Sentinel lymph node biopsy – *targeted* sampling of nodes (usually at level I, occasionally at level II)

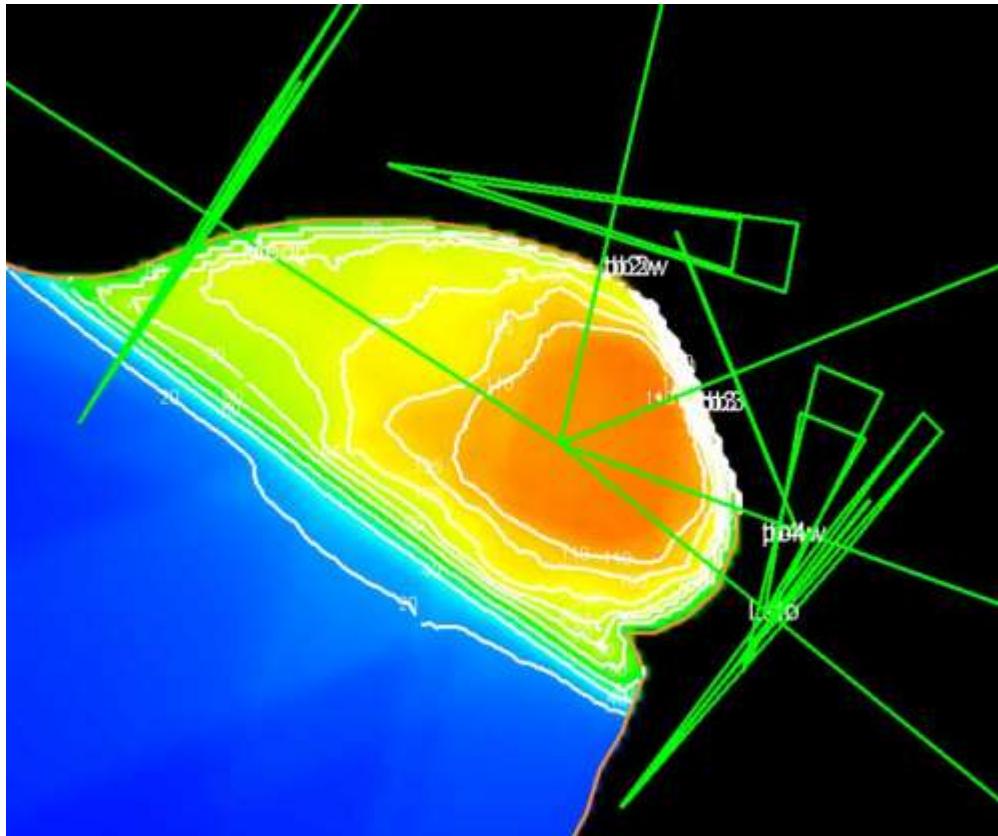
Sentinel lymph node biopsy

- Sentinel lymph node (SLN) biopsy now widely practiced and accepted as standard of care for early breast cancer patients
- More than half of SLN biopsy positive cases (**60%**) have involvement of single node only



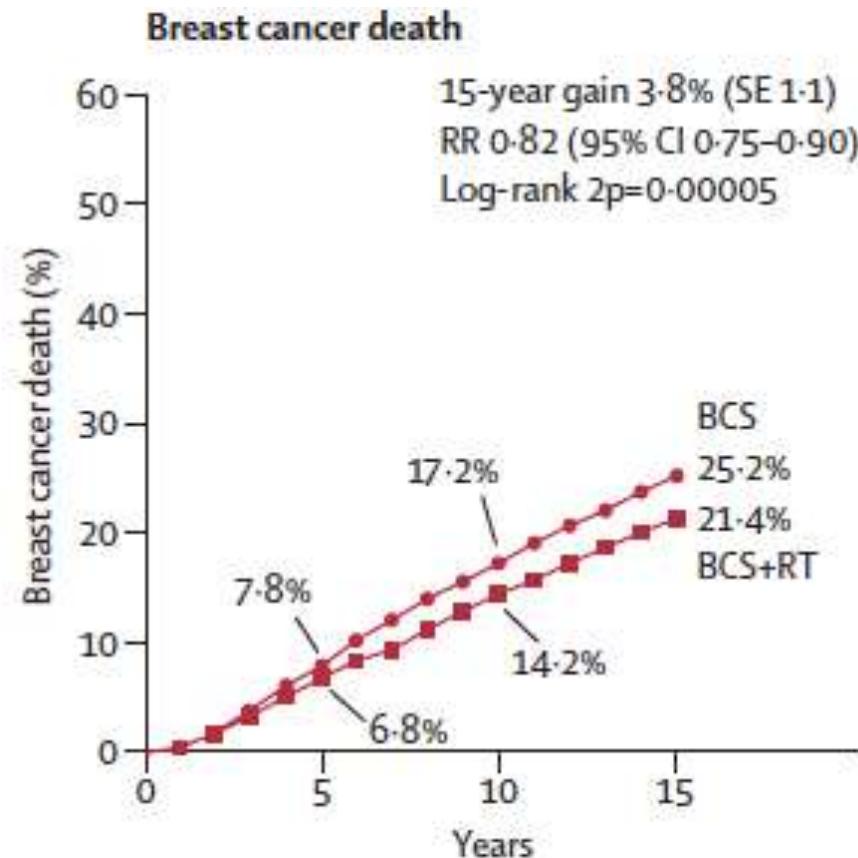
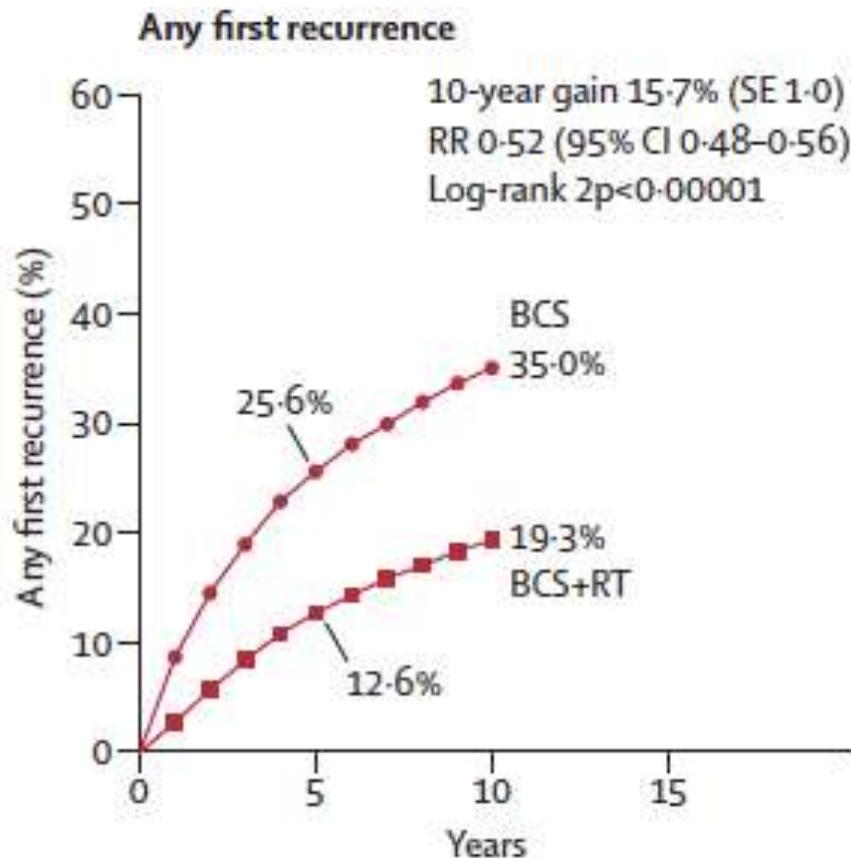
- Procedure of SLN biopsy effectively therapeutic for some patients

Breast radiotherapy (RT)



- Usually after BCS
 - After mastectomy
for higher risk
cancers

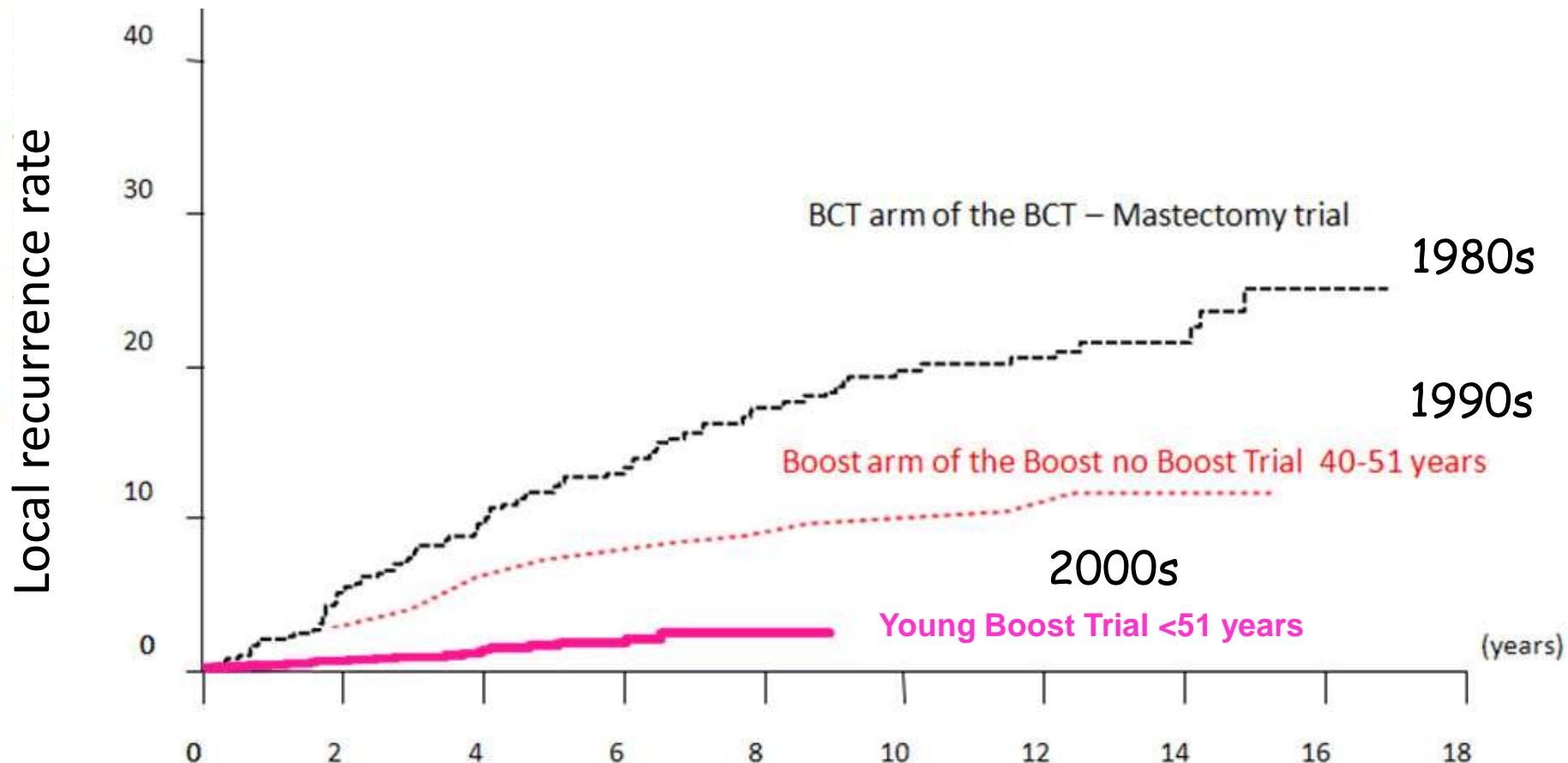
Benefit of breast radiotherapy (RT)



- RT reduces risk of any recurrence by 0.5
- 4:1 ratio for breast cancer death

Falling local relapse = lower *absolute* benefit

- De-escalate treatment for the majority & escalate for those with worse prognosis

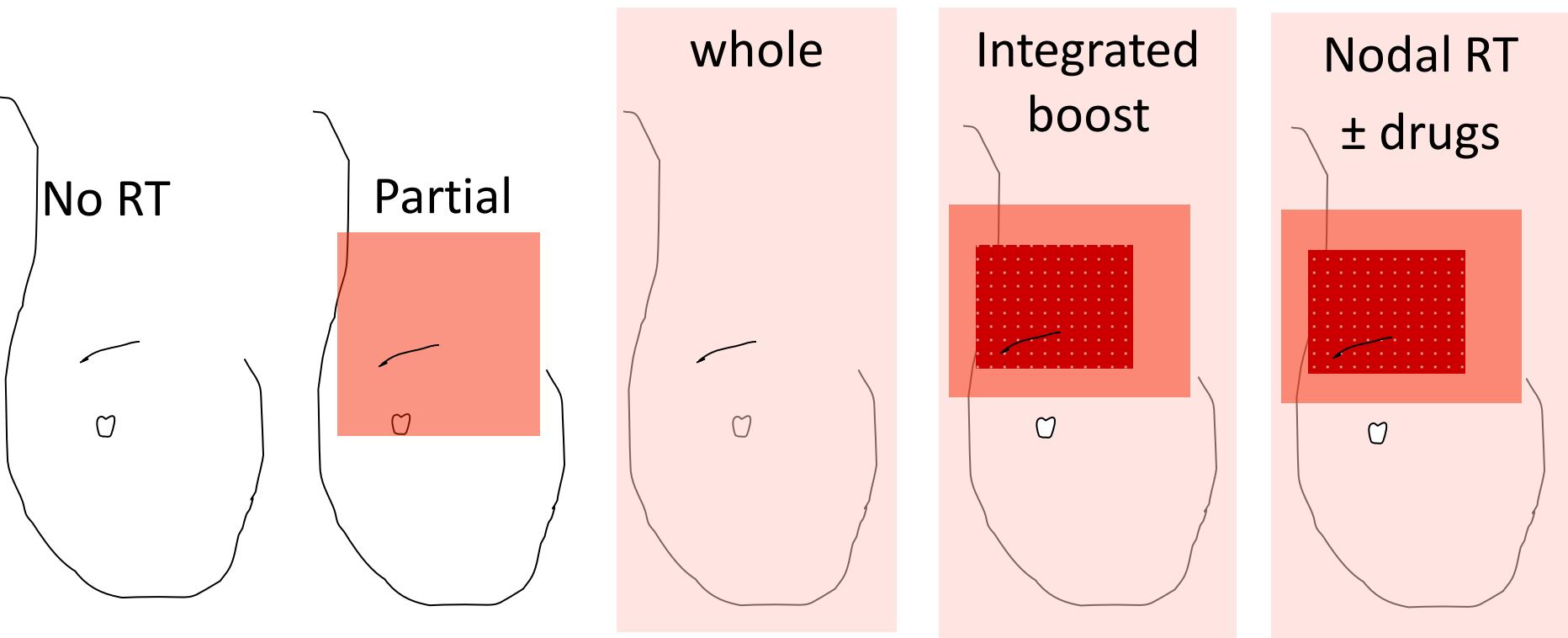


Risks of breast RT

- Breast RT usually well tolerated, but not without side effects....
- Breast shrinkage & fibrosis: chronic pain & stiffness, poor cosmesis & psychological distress
- Rare:
 - Risk of major coronary events
 - Second radiation induced malignancy (especially if smoker)

Future Stratification?

Very low risk to very high risk of local relapse

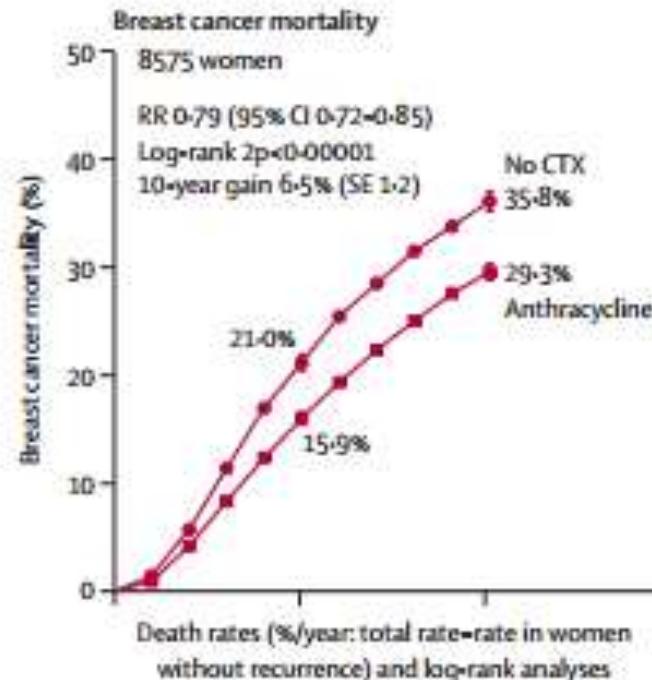
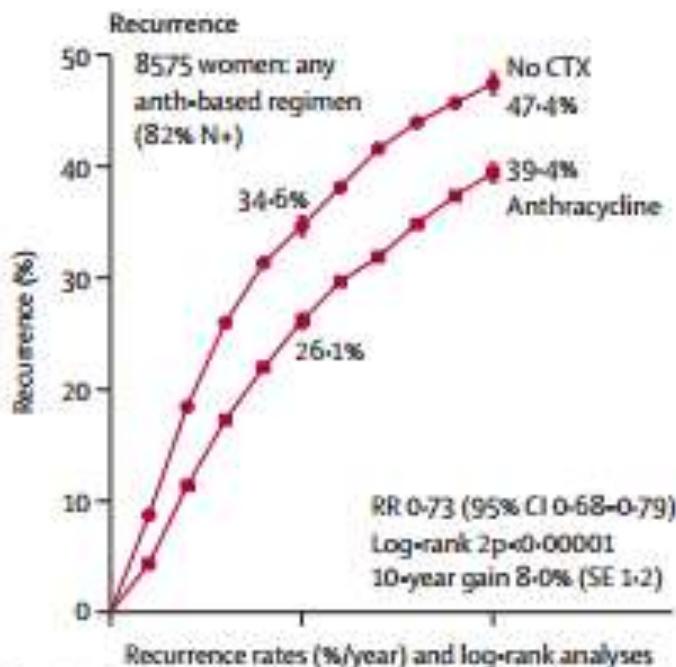


Chemotherapy

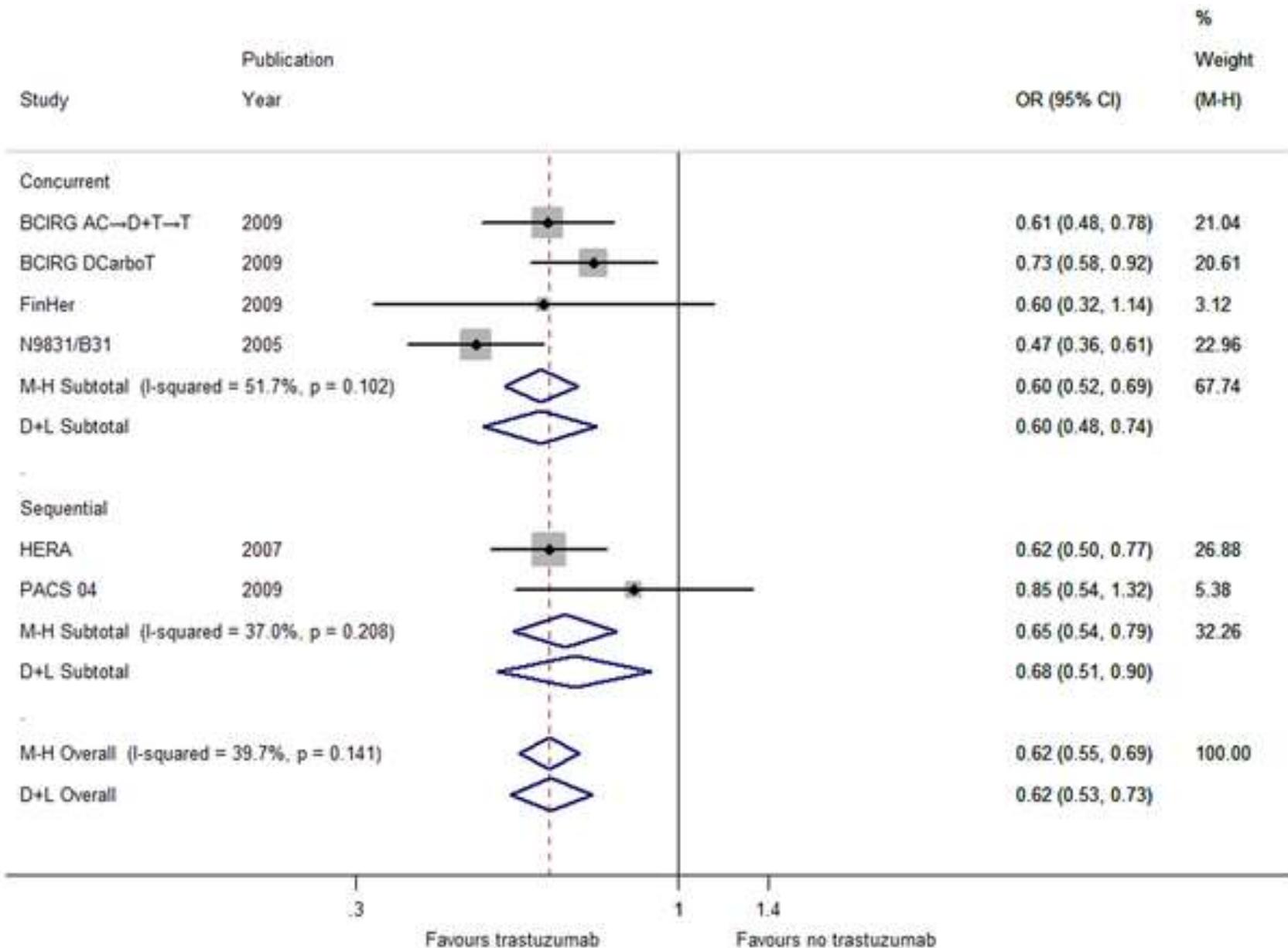


Comparisons between different polychemotherapy regimens for early breast cancer: meta-analyses of long-term outcome among 100 000 women in 123 randomised trials

Early Breast Cancer Trialists' Collaborative Group (EBCTCG)



Biological therapy: Trastuzumab

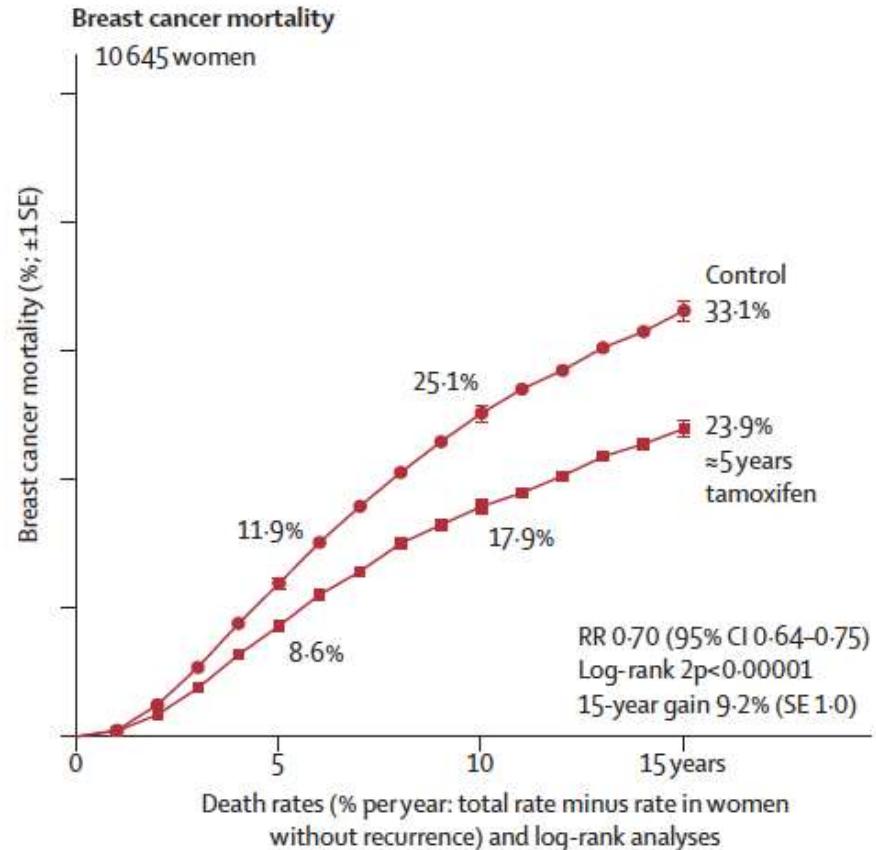
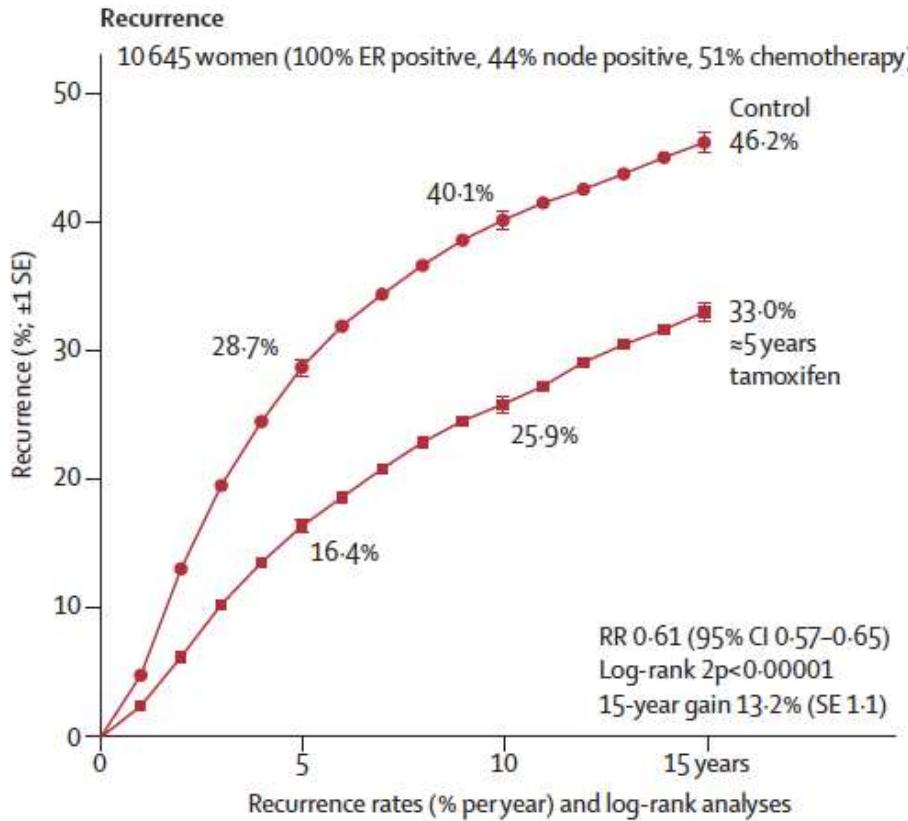


Endocrine therapy

Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials



Early Breast Cancer Trialists' Collaborative Group (EBCTCG)*



Endocrine Therapies for Breast Cancer

Anti-oestrogens

Inhibit the production of oestrogens

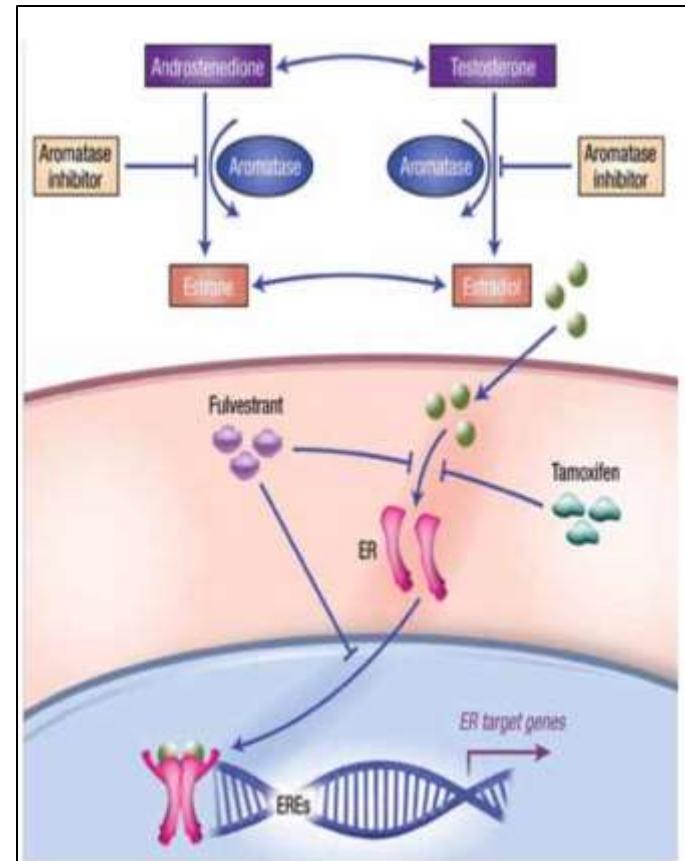
- Aromatase inhibitors
 - eg. letrozole, anastrozole, exemestane

Disrupt oestrogen binding to oestrogen receptor

- Selective estrogen receptor modulators (SERMs)
 - eg. tamoxifen

Degradate oestrogen receptor

- Selective estrogen receptor degraders (SERDs)
 - eg. fulvestrant (but intramuscular injection)
 - novel oral SERDs now in development



Streiner. Comm.Oncol. 2011

Dr Richard Baird, Cambridge

Potential side effects of chemotherapy & endocrine therapy

- Chemotherapy/biological therapy tend to have short term side effects that are temporary
 - Rarely - some drugs can cause permanent cardiotoxicity
 - Very rarely – death from neutropenic sepsis
- Endocrine therapy often considered “gentler”
 - However, can cause debilitating symptoms that affect quality of life; many patients stop taking before 5 years
 - Can cause bone fractures (AIs) & rarely endometrial cancer & thromboembolism (tamoxifen)

Understanding risk & benefit

Hazard ratios for adjuvant therapy consistent across populations of patients with breast cancer (& additive), but absolute benefit depends on individual patient's overall risk of death (this is variable)

RELATIVE RISK

New drug reduced cancer incidence by 50%

ABSOLUTE RISK

New drug reduced cancer incidence from 2 per 1000 to 1 per 1000

Absolute risk is more useful at communicating the true impact of an intervention, yet it's often not reported in the research and the news

Predicting benefit of adjuvant therapy

predict



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PREDICT V2.0

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PREDICT Tool Version 2.0: Breast Cancer Overall Survival; Input

Age at diagnosis:	35	<input type="button" value="▼"/>	<input type="button" value="▲"/>	<input checked="" type="radio"/> Screen-detected	<input checked="" type="radio"/> Symptomatic	<input type="radio"/> Unknown
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Tumour Grade:	<input type="radio"/> 1	<input type="radio"/> 2	<input checked="" type="radio"/> 3			
Number of positive nodes:	4	<input type="button" value="▼"/>	<input type="button" value="▲"/>	<input type="checkbox"/> Micromet		
ER status:	<input checked="" type="radio"/> Positive	<input type="radio"/> Negative				
HER2 status:	<input checked="" type="radio"/> Positive	<input type="radio"/> Negative	<input type="radio"/> Unknown			
KI67 status:	<input type="radio"/> Positive	<input type="radio"/> Negative	<input checked="" type="radio"/> Unknown			
Gen chemo regimen:	<input type="radio"/> No chemo	<input type="radio"/> Second	<input checked="" type="radio"/> Third			

Ten year survival

24 out of 100 women are alive at 10 years with no adjuvant therapy after surgery

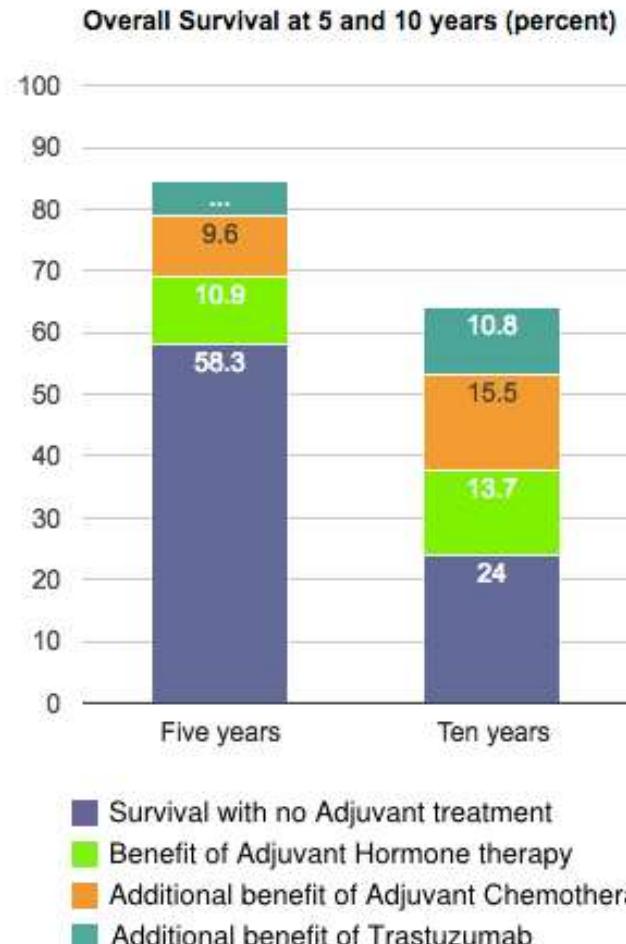
An extra 14 out of 100 women treated are alive because of hormone therapy

An extra 29 out of 100 women treated are alive because of hormone therapy & chemotherapy

An extra 40 out of 100 women treated are alive because of hormone therapy, chemotherapy & Trastuzumab

To view the numbers in bars hover pointer over each bar-segment

(Or tap segment if using a mobile device)



Predicting benefit of adjuvant therapy 2

predict



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PREDICT Tool Version 2.0: Breast Cancer Overall Survival; Input

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HER2 status:	<input type="radio"/> Positive	<input checked="" type="radio"/> Negative	<input type="radio"/> Unknown
KI67 status:	<input type="radio"/> Positive	<input type="radio"/> Negative	<input checked="" type="radio"/> Unknown
Gen chemo regimen:	<input type="radio"/> No chemo	<input type="radio"/> Second	<input checked="" type="radio"/> Third

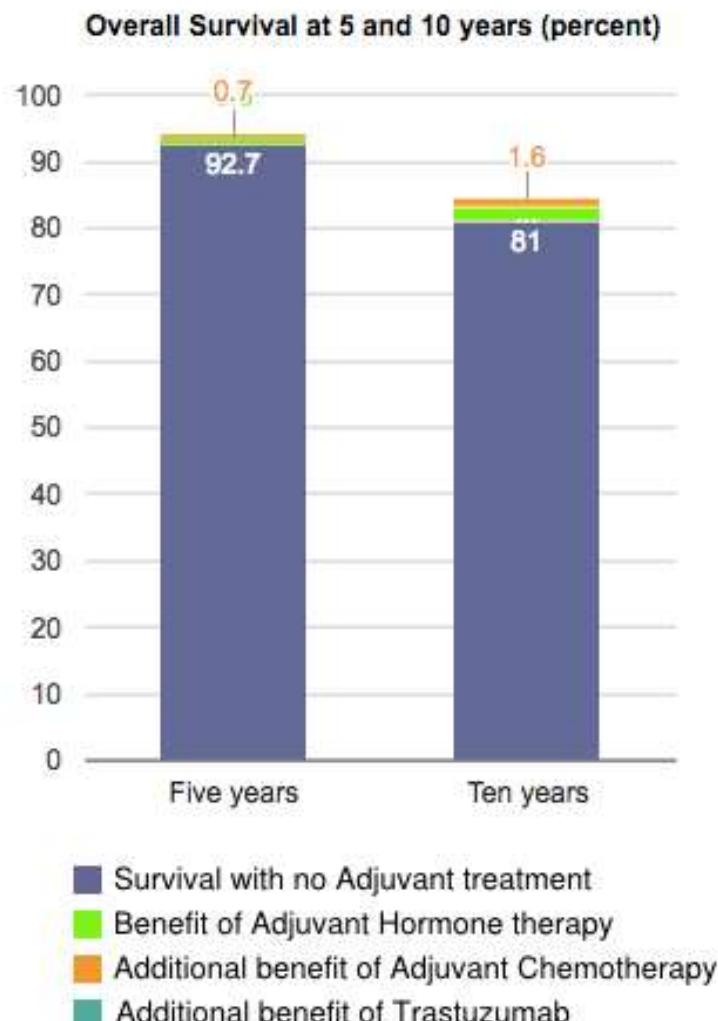
Ten year survival

81 out of 100 women are alive at 10 years with no adjuvant therapy after surgery

An extra 2 out of 100 women treated are alive because of hormone therapy

An extra 4 out of 100 women treated are alive because of hormone therapy & chemotherapy

To view the numbers in bars hover pointer over each bar-segment
(Or tap segment if using a mobile device)



Metastatic Breast Cancer – Key Points to Remember

- Metastatic breast cancer (mBC) is nearly always incurable, treatment is palliative
- Continual improvements in treatment of mBC with chemotherapy & endocrine therapy in recent years - led to improvements in quality & quantity of life
- Response to chemotherapy can be associated with improved symptoms & survival
- Not everyone responds
- Patients failing to respond to 2 lines of chemotherapy should be considered for clinical trials or best supportive care
- Caring for patients with metastatic breast cancer is both a science and an art ...

Metastatic Breast Cancer – Treatment Modalities

- Systemic therapies
 - Cytotoxic chemotherapy
 - Anthracyclines
 - Taxanes
 - Capecitabine
 - Endocrine therapies
 - Tamoxifen
 - Aromatase inhibitors
 - Supportive therapies (eg.bisphosphonates)
 - Molecular targeted therapies
- For ER+ patients – try endocrine therapy first unless high burden of fast-growing visceral disease
- Radiotherapy
 - Brain metastases
 - Spinal cord compression
 - Painful bone metastases
- Surgery
 - Not common
 - For selected patients
 - Eg. solitary brain metastasis
- Palliative care

Summary

- Breast cancer is not just one disease, but a whole spectrum
- Therefore, one approach does not fit all – need to personalise management to the individual
- Majority of breast cancers can be cured, so need to de-escalate treatment, but also need to identify those at higher risk to escalate treatment

Patients must be in the centre of all decision making!



Courtesy of “ICR Ladies”

Final words from patient perspective...



Hilary Stobart