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Cancer survival: what is the role of body composition pre- and post-diagnosis?

Dr Ellen Copson

Associate Professor in Medical Oncology, University of Southampton

I have no conflicts of interest

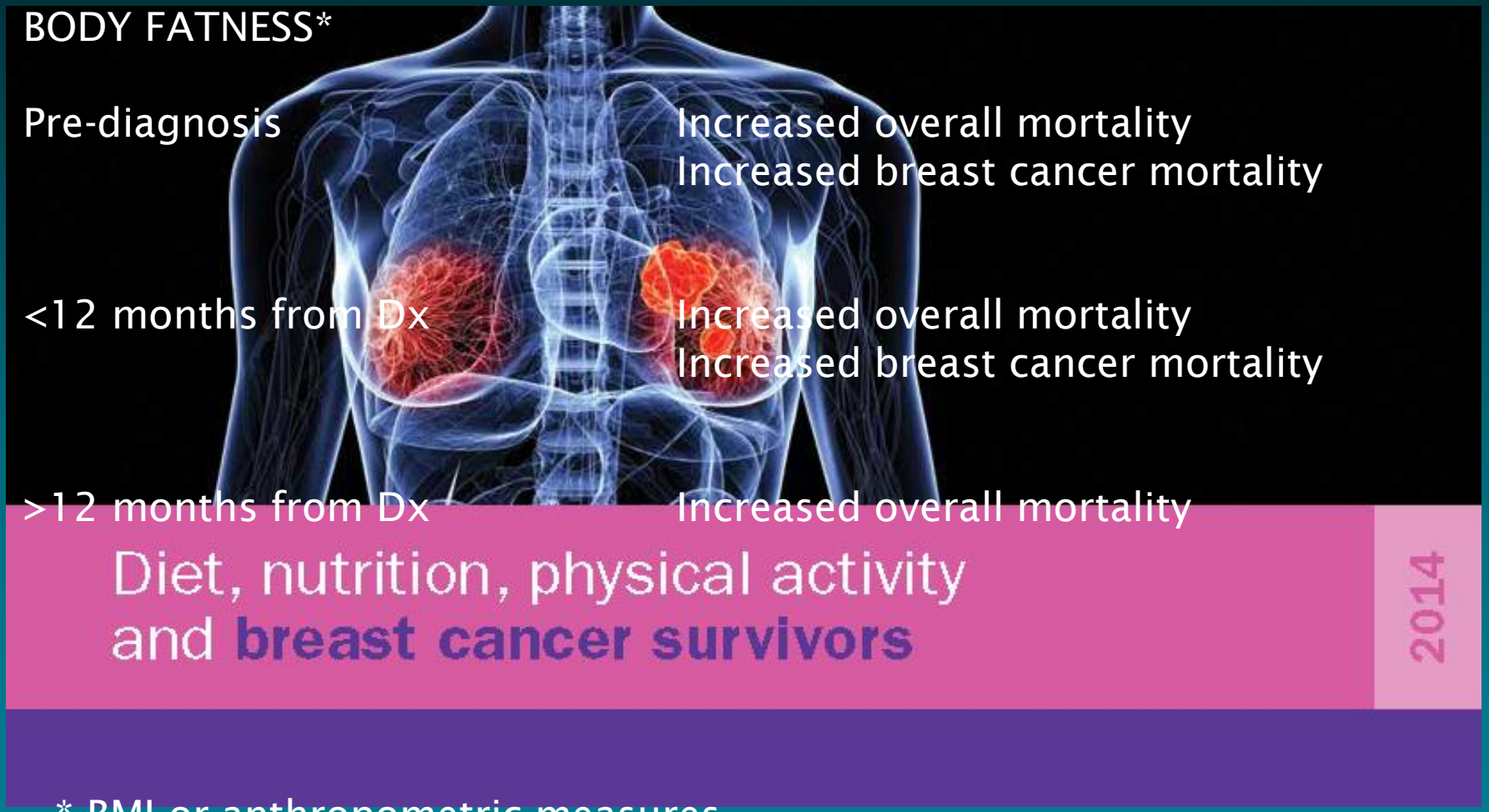
WCRF Second Expert Report, 2007

” Research on food, nutrition, physical activity, and cancer survival is at an early stage.

The available evidence on cancer survivors has a number of limitations: it is of variable quality; it is difficult to interpret; and it has not yet produced any impressive results

Definite general judgements are made more problematic because of differences in the health of cancer survivors at various stages; between cancers of various sites; and between the effects of the many types of conventional and other therapies used.”

2014: WCRF Continuous Update Project



* BMI or anthropometric measures

Obesity and survival of early breast cancer patients

Chan et al. 2014:

Meta-analysis of 82 studies, 213075 breast cancer survivors

Pre-diagnosis:

BMI >30 : RR total mortality = 1.41

BMI 25-30 : RR = 1.07

For each additional 5kg/m2

pre,	<12 months	>12 months from diagnosis	
17%	11%	8%	increase in total mortality
18%	14%	29%	increase in breast cancer mortality

Post-menopausal vs Premenopausal breast cancer

Pre-diagnosis:

Pre-menopausal BMI > 30: RR total mortality = 1.75

Post-menopausal BMI >30: RR total mortality = 1.34

Chan et al, 2015

Even though obesity is not a risk factor for developing pre-menopausal breast cancer

WCRF CUP 2013:
Breast Cancer Survivors

	Timing of exposure assessment	BEFORE DIAGNOSIS		LESS THAN 12 MONTHS AFTER DIAGNOSIS		12 MONTHS OR MORE AFTER DIAGNOSIS	
		DECREASES RISK	INCREASES RISK	DECREASES RISK	INCREASES RISK	DECREASES RISK	INCREASES RISK
		Exposure Outcome	Exposure Outcome	Exposure Outcome	Exposure Outcome	Exposure Outcome	Exposure Outcome
STRONG EVIDENCE	Convincing						
	Probable						
LIMITED EVIDENCE	Limited-suggestive	Physical activity — All mortality, BC mortality Foods containing fibre — All mortality	Body fatness — All mortality, BC mortality[2], 2nd BC Total fat — All mortality Saturated fatty acids — All mortality		Body fatness — All mortality, BC mortality[2], 2nd BC	Physical activity — All mortality Foods containing fibre — All mortality Foods containing soy — All mortality	Body fatness — All mortality
	Limited-no conclusion[1]	Fruits, vegetables, foods containing folate, foods containing soy, carbohydrate, glycaemic index, glycaemic load, protein, dietary supplements, alcoholic drinks, dietary patterns, underweight, body fatness (premenopause), adult attained height, energy intake		Foods containing fibre, carbohydrate, protein, total fat, saturated fatty acids, alcoholic drinks, physical activity, underweight, body fatness (premenopause), adult attained height, energy intake		Fruits, vegetables, foods containing fibre, foods containing folate, foods containing soy, carbohydrate, glycaemic index, glycaemic load, protein, total fat, saturated fatty acids, alcoholic drinks, dietary patterns, physical activity, body fatness, underweight, height, energy intake	
STRONG EVIDENCE	Substantial effect on risk unlikely						

RCTs: patient selection

Cohort: confounders poorly reported

Prospective study of Outcomes in Sporadic versus Hereditary breast cancer (POSH)

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- Prospective multicentre cohort study of young breast cancer patients
- Primary aim:
    - Determine whether underlying BRCA1/2 mutation influences prognosis and clinical course of breast cancer
- Secondary aims:
    - To determine whether inherited genetic variants influence tumour biology
    - Determine influence of other host factors on pathology and outcome of breast cancer in pre-menopausal patients
        - » BMI
        - » Ethnicity

POSH cohort in brief

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- 3025 cases < 41 years at diagnosis or known gene carriers aged 41-50
- Diagnosed between 1st January 2000 – 31st December 2007
- Eligibility: Invasive breast cancer
- 127 UK recruiting centres

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POSH: Patients and methods

- Treated as per local protocols
- Blood sample stored for genetic analysis
- Family history by questionnaire
- **Height and weight measured by research nurse**
- Pathology, treatment and clinical course obtained from records
- Central pathology review and tissue microarray analysis ongoing
- Annual follow-up
- Flagging of deaths

POSH: Southampton based multicentre cohort study

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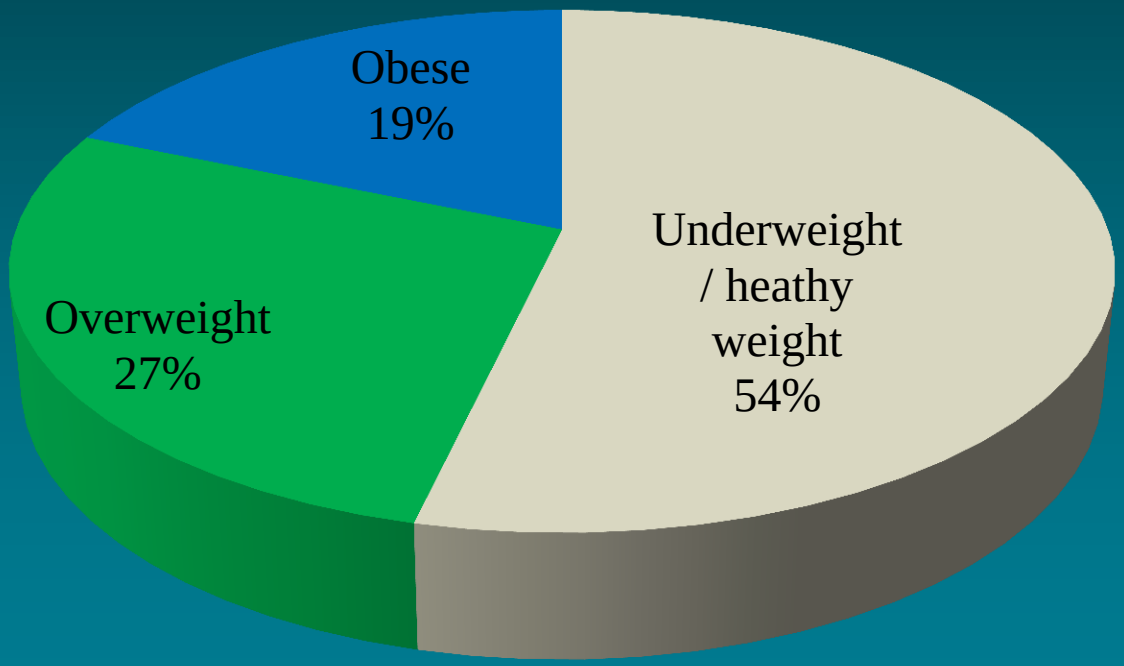
2956 Patients age <41 years at first diagnosis of breast cancer

2843 BMI data

1526 BMI < 25

784 25 ≥ BMI <30

533 BMI ≥ 30



Copson et al. *Ann Oncol*. 2015;26(1):101-12

Overall survival

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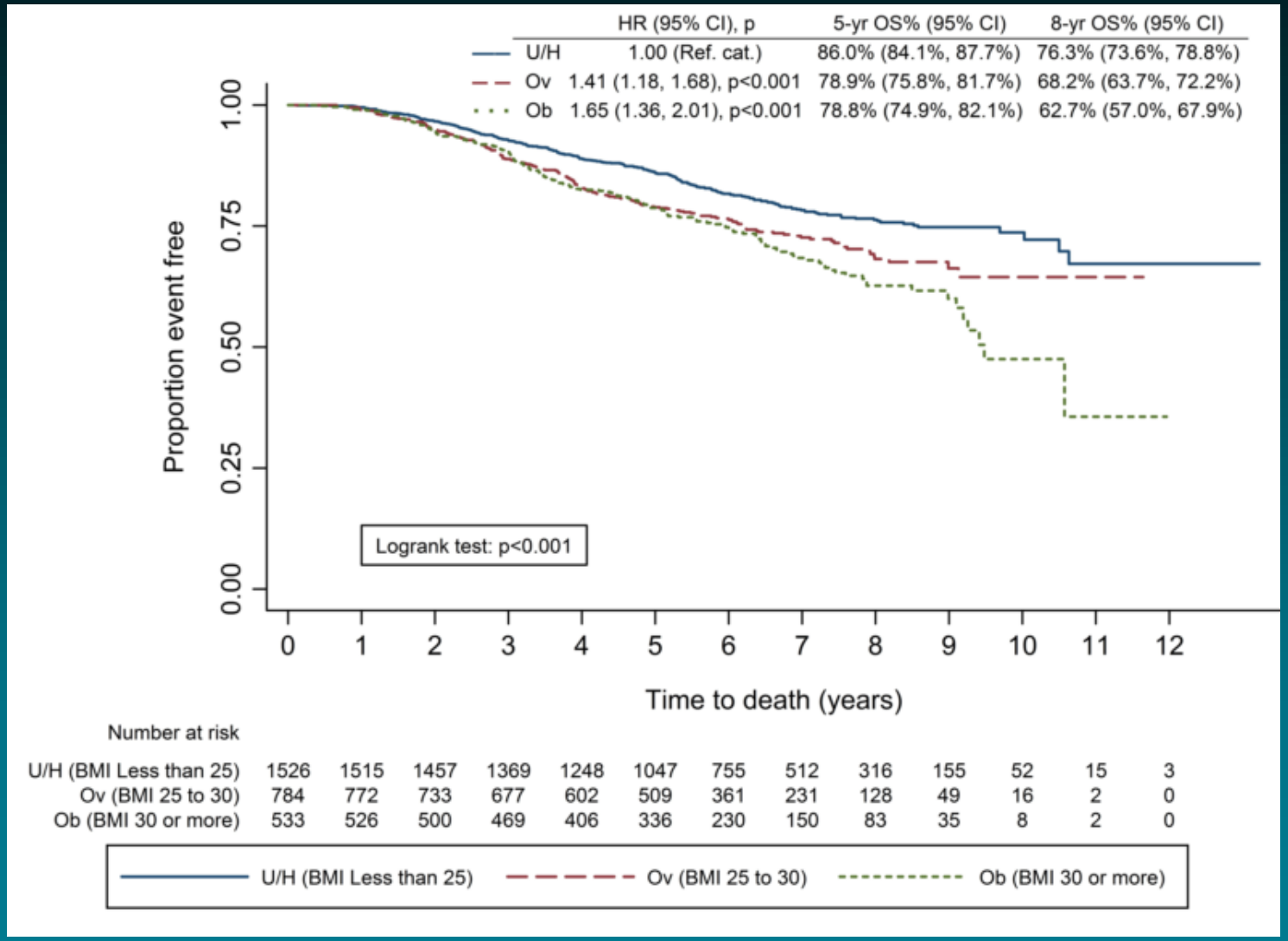

Copson et al. Ann Oncol. 2015;26(1):101-12

Distant disease free survival

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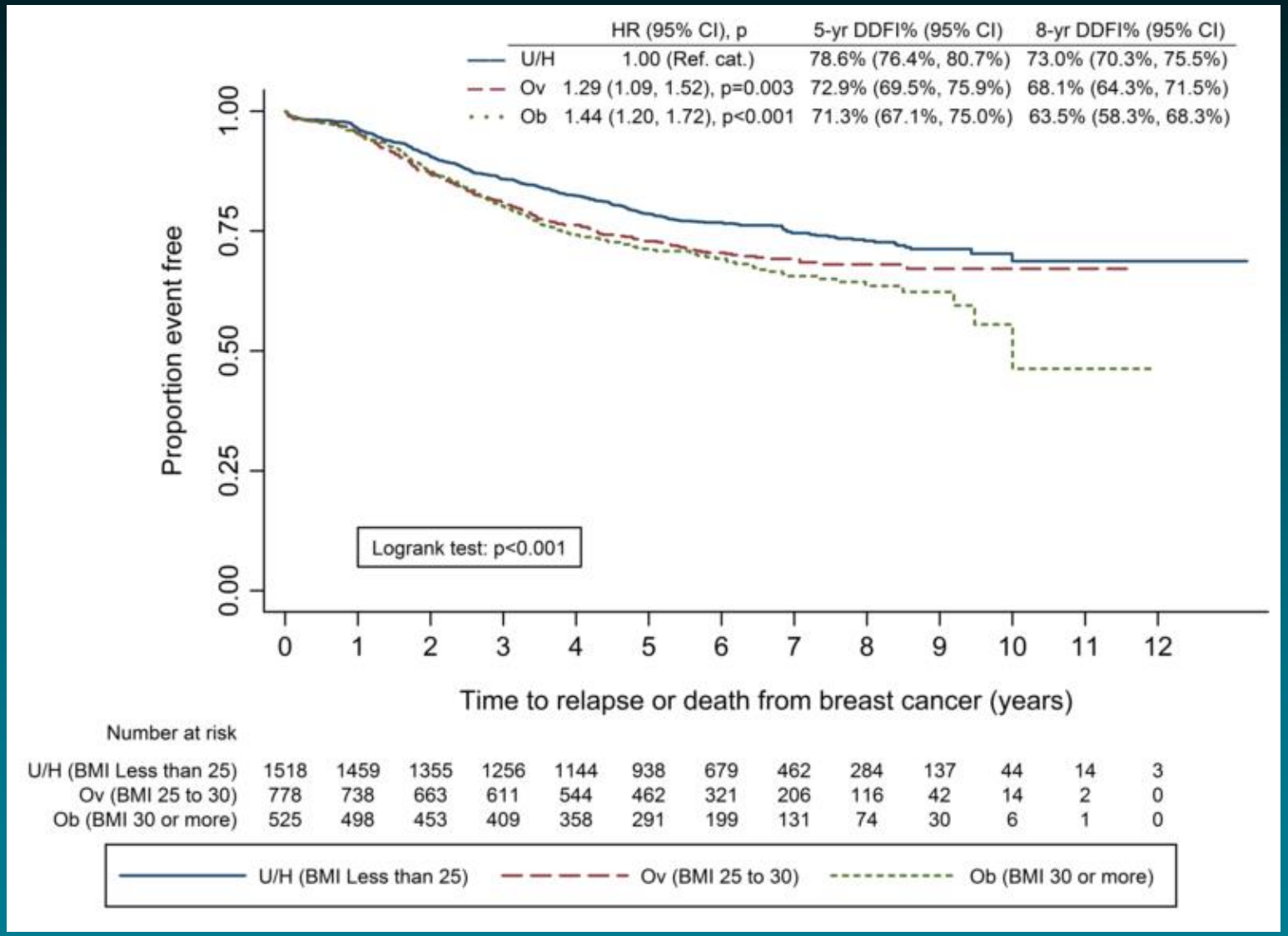

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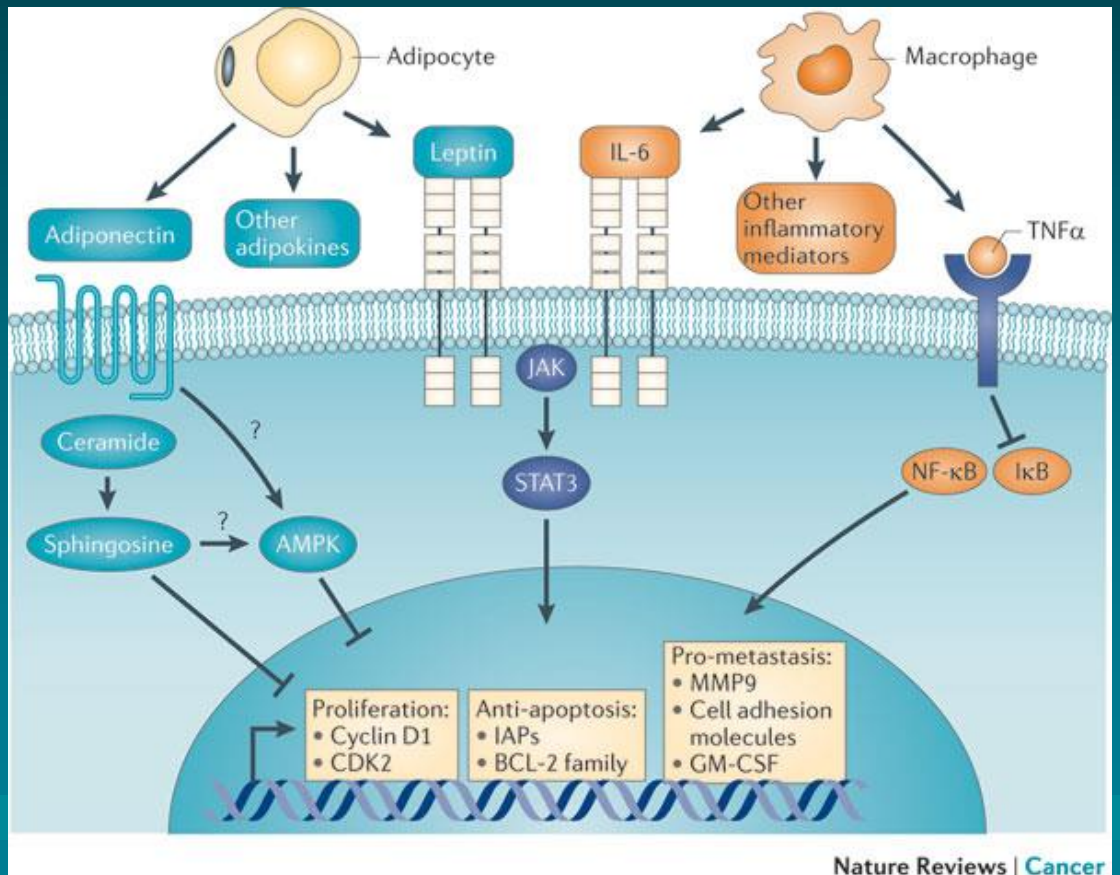
Pathological features

	Underweight or Healthy weight n=1526	Overweight n=784 (27.6%)	Obese n=533 (18.8%)	
Mean tumour size/ mm	20 (0-170)	24 (0-199)	26 (0.5-130)	U/H vs. Ov: p<0.0001 U/H vs. Ob: p<0.0001
Multifocal	12 (30.6%)	220 (30.4%)	130 (27.2%)	NS
Grade 3	879 (59.0%)	485 (63.6%)	331 (63.9%)	U/H vs. Ob: p =0.04
Node positive	736 (49.0%)	419 (54.2%)	284 (54.6%)	U/H vs. Ov: p=0.019 U/H vs. Ob: p=0.027
ER negative	483 (31.7%)	273 (34.9%)	213 (40.1%)	U/H vs Ob: p<0.001
HER 2 positive	381 (28.2%)	180 (26.4%)	129 (27.3%)	NS
ER/ PR/ HER 2 negative	305 (20.8%)	176 (23.4%)	136 (26.8%)	U/H vs. Ob: p=0.005

Copson et al. *Ann Oncol*. 2015;26(1):101-12

Tumour biology and microenvironment

- Insulin like growth factor/ adipocytokines
- Pro-inflammatory tumour environment



Khandekar 2013
Nature Rev
Cancer

Multivariate analysis: adjusted for tumour size, grade, nodal status and HER 2 status

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Oestrogen receptor (ER) positive patients:

- Obesity: HR for recurrence 1.37 (p=0.015)
- Obesity: HR for overall survival 1.46 (p=0.007)

Oestrogen receptor (ER) negative patients:

- Obesity not a significant independent influence on DDFS or OS

Copson et al. Ann Oncol. 2015;26(1):101-12

Why is obesity an adverse prognostic factor?

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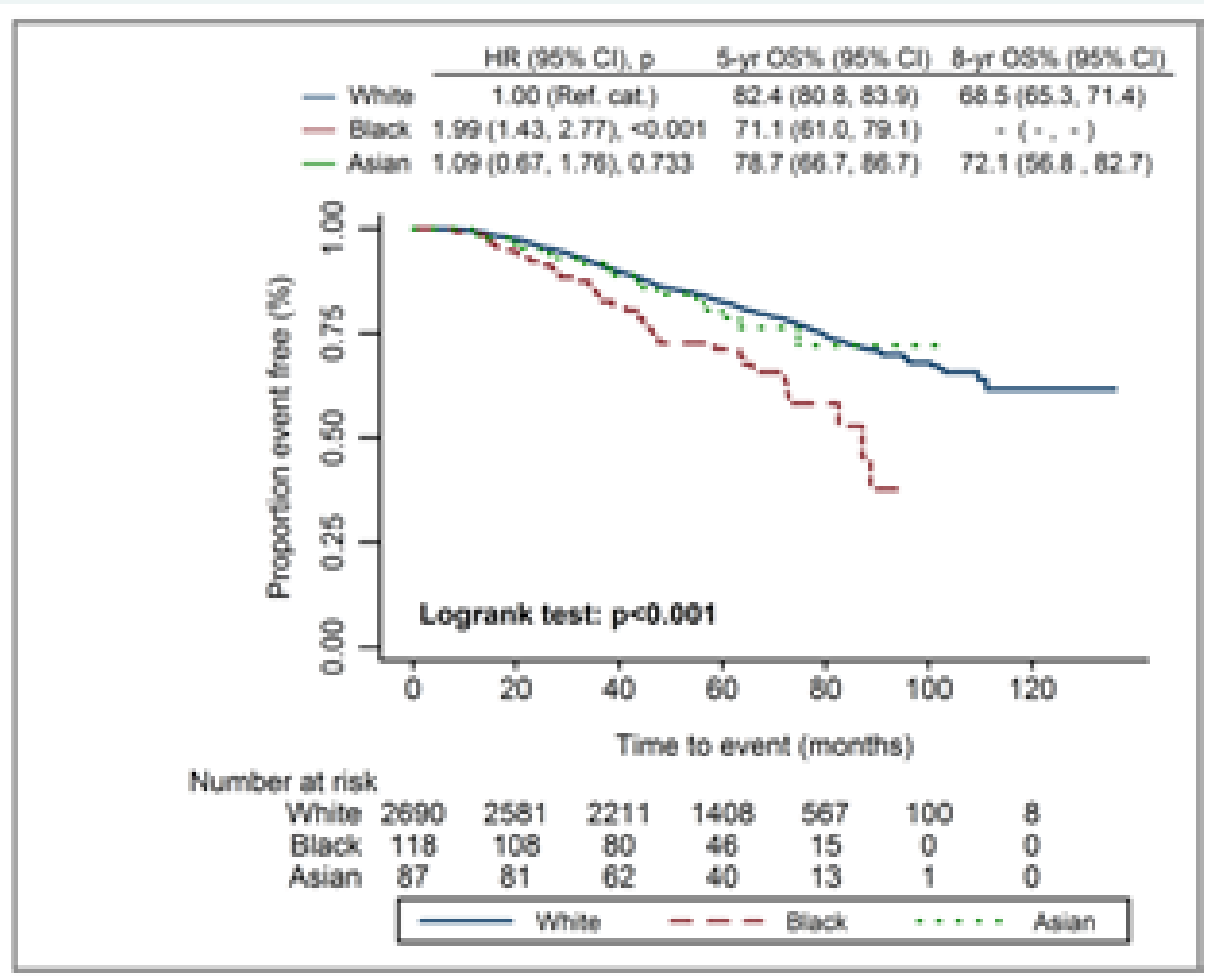
Overall survival



Copson et al. *BJC* 2014; 110 (1): 230-241

Why is obesity an adverse prognostic factor?

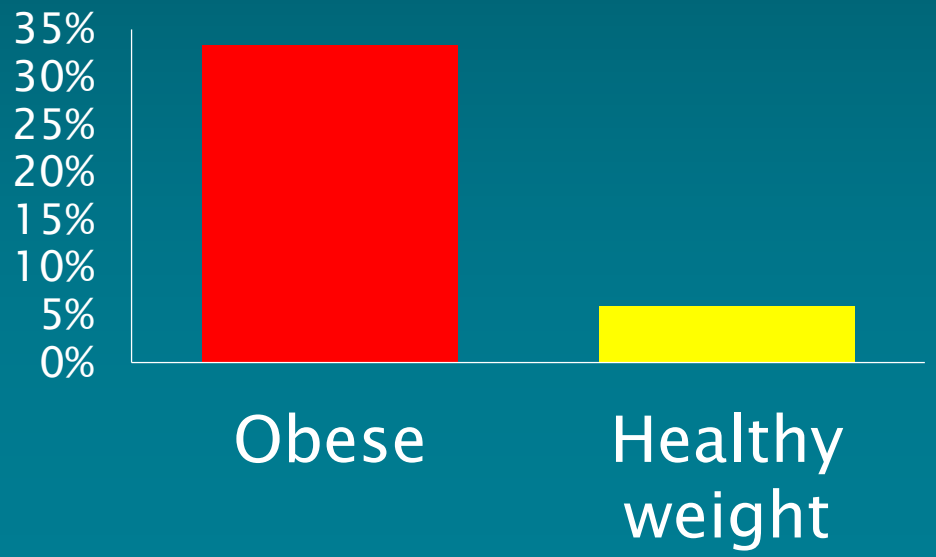
Treatment issues

- Increased surgical/ radiotherapy complications
- Hormonal therapy- efficacy/ tolerance/ adherence
- Chemotherapy- dosing/ tolerance
  - Most cytoxics prescribed by body surface area
  - Body surface area not designed for extremes
  - Dose capping traditionally common
  - Griggs et al. 2012: “40% patients underdosed”

Investigation of local adjuvant chemotherapy dosing (n=80)

- No initial dose reductions
- Significant difference in dose delays:

33.3% vs. 5.9%, p=0.0068



- Toxicities
- Access issues
- AWOL

What is "risky"about obesity?

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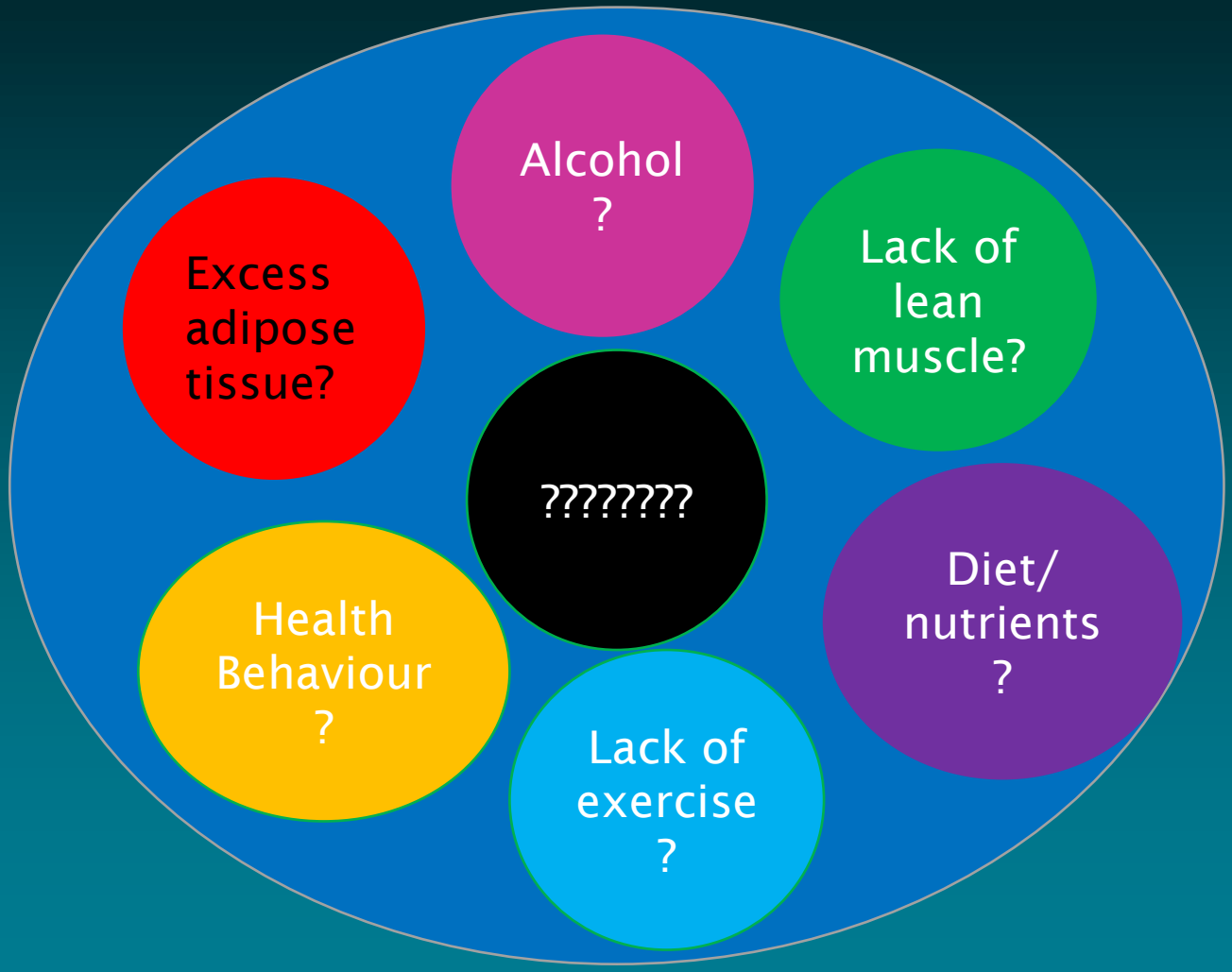


BMI and anthropometric measures cannot distinguish between lean mass and fat mass

Challenges of assessing body composition

- Gold standard body composition:
  - 4 compartment model-
    - Deuterium dilution
    - Under water weighing
    - Plethysmography
    - DEXA
  - Not suitable for routine clinical practice
- Clinical studies:
  - Anthropometric studies
  - Computerised tomography
  - DEXA

Body composition beyond BMI following a diagnosis of breast cancer

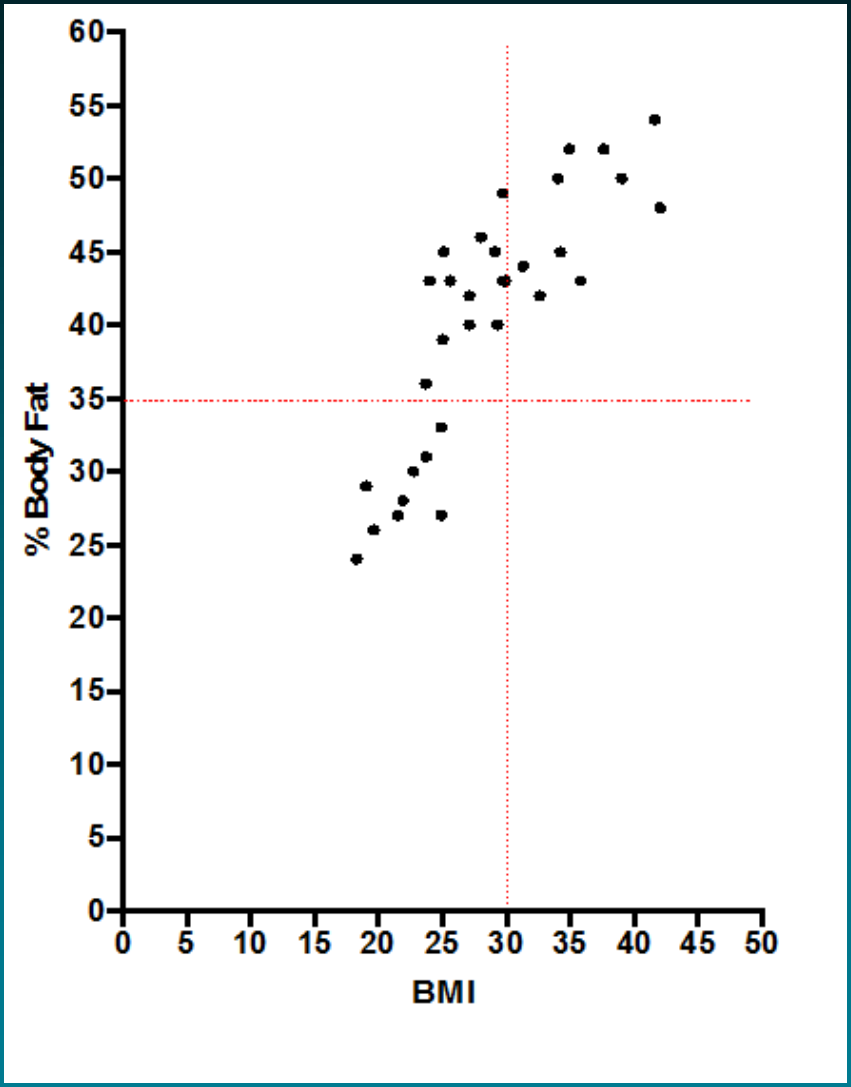
- **James et al 2015 EJC**
- 4 studies of body fatness and outcome; n=8543
  - Anthropometric measures
  - 2 studies no association WMR and outcome
  - 1 positive association WHR and poorer outcome
  - 1 positive association only with high BMI
- 2 studies of lean mass and outcome; 548 patients
  - 1 CT, 1 DEXA
  - 1 : increased mortality with sarcopaenia
  - 1: increased response to neo-adjuvant chemo with sarcopaenia

CANDO-2 Feasibility Study

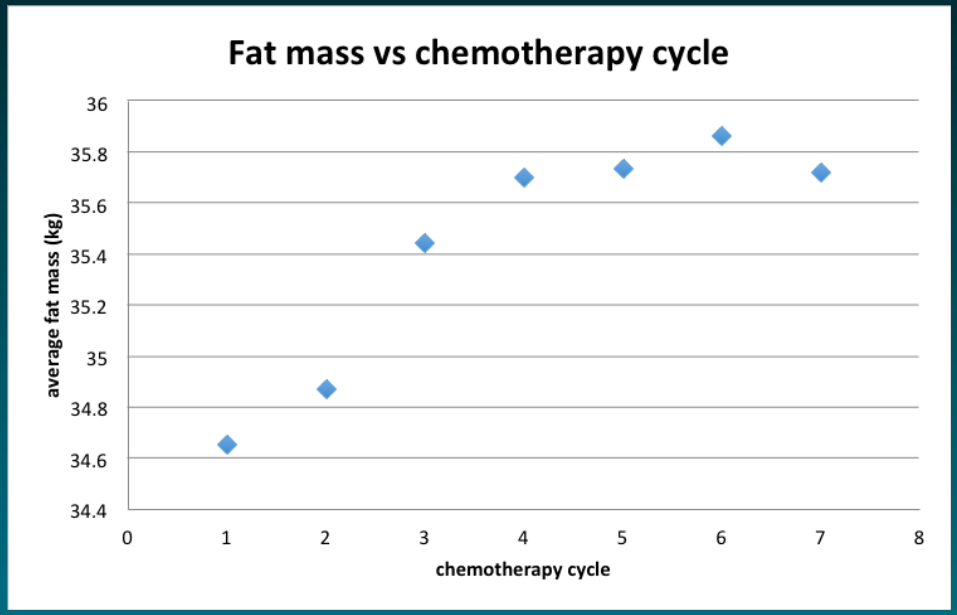
breast cancer campaign
Research that saves lives

- Demonstrate feasibility of using sBIS to obtain detailed body composition measurements in EBC patients at routine chemo clinic appmts
- Validate Sliceomatic software against sBIS
- Obtain preliminary data: chemo toxicity & body composition patterns
- Biobank serial plasma/ serum samples

BMI vs Percentage fat

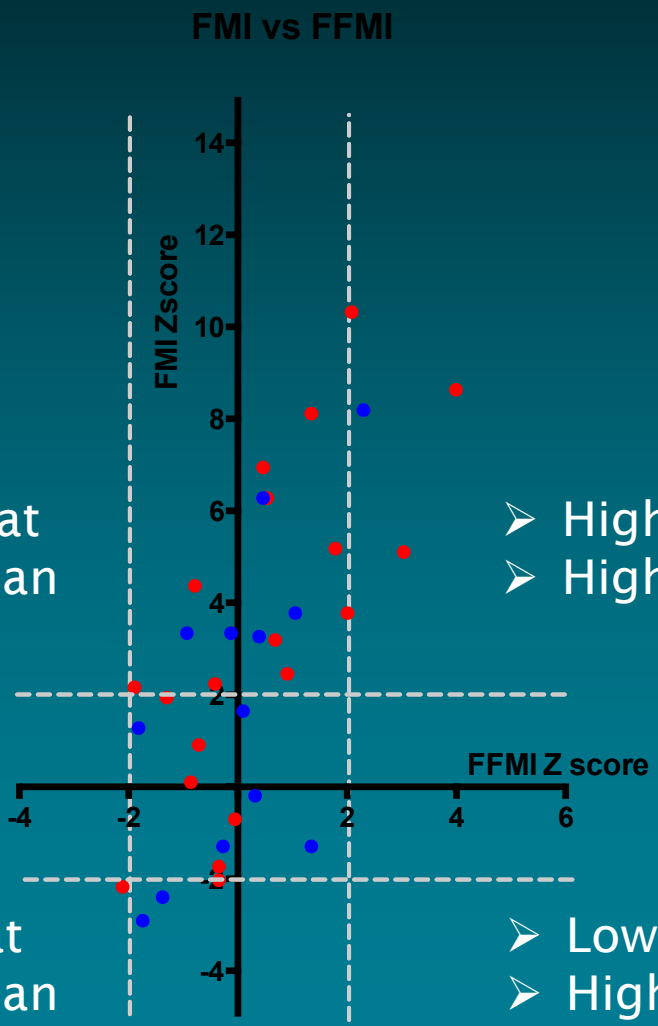


Changes in Fat Mass



- Mean increase in fat mass of 1.1 kg
- Correlation between BMI and gain of fat mass

Relationship between chemotherapy toxicity and body composition



- High fat
- Low lean

- High fat
- High lean

- Low fat
- Low lean

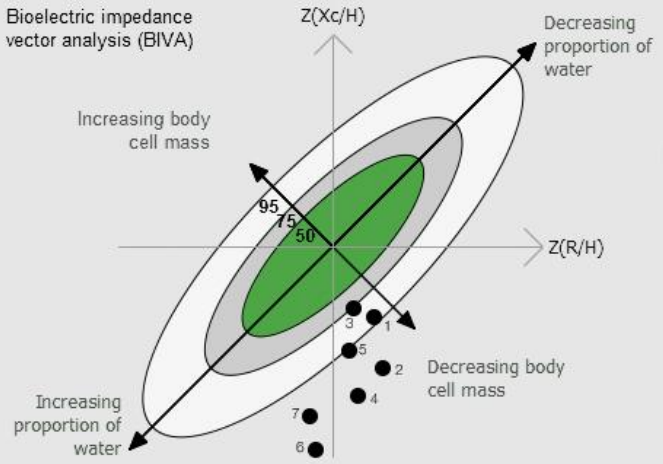
- Low fat
- High lean

Red dots = patients with Grade 3+ toxicity

Blue Dots = patients with no record of Grade 3+ toxicity

Comparison of body composition data from sBIS and CT

vs



Summary:

- Obesity is associated with reduced breast cancer specific and overall survival
- Cohort studies indicate that obesity is associated with a number of known poor prognostic factors in early breast cancer; it is possibly an independent risk factor for poorer survival
- However, much work is needed to fully investigate body composition patterns and other nutritional/ metabolic markers in order to fully define the true nature of this risk factor in early breast cancer patients

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Acknowledgements:

- Tom Maishman
- Bryony Eccles
- Louise Dent
- Ramsey Cutress
- Sue Gerty
- Lorraine Durcan
- **Diana Eccles**

- The POSH patients

- NIHR Southampton BRC- Nutrition

Work supported by :

- Cancer Research UK
- Wessex Cancer Fund
- Breast Cancer Campaign
- National Cancer Research Network







CANCER RESEARCH UK

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Research that saves lives

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Thank you