

**Supplementary study protocol**  
**Weight Gain Study Protocol, version 1 created 04/03/05**

**Hypothesis:** gains in weight and central obesity assessed at one year after diagnosis may have detrimental effects on 2-year disease free survival amongst women with and without hereditary breast cancer.

**Background:**

There is some evidence that the development of breast cancer amongst women with a family history may be in part due to shared epigenetic factors which also promote the development of central adiposity (Sellers et al 1992; Olson et al 2001). Gains in weight during the first year of treatment, and the amount of central fat (waist circumference) one year after treatment may also be relevant to the prognosis of premenopausal women with and without a hereditary breast cancer but the effects of these body size parameters on prognosis amongst women with and without hereditary breast cancer are not known.

General and central adiposity have been shown to be independent prognostic factor predicting disease free and overall survival amongst breast cancer patients irrespective of baseline tumour characteristics particularly amongst pre/ peri-menopausal (rather than post menopausal) (Gladieff et al, 2004, Borugian et al 2003 ). Likewise weight gain is a well-documented unwanted side effect of treatments for early breast cancer which is also thought to be an adverse prognostic factor amongst premenopausal women. (Camoriano et al 1990 ;Kroenke et al 2005). General and central adiposity may lead to poorer survival via their many adverse hormonal (hyperinsulinaemia and low sex hormone binding globulin and insulin like growth factor binding protein 1 (Goodwin et al 2002) and inflammatory effects.

**Methods:**

We plan to assess the independent effects of weight gain over the first year of treatment and waist circumference and waist: hip ration at one year on subsequent 2 year disease in 1000 women from the POSH study.

Body size measurements

Weight at the time of commencing treatment is already recorded amongst women recruited in the POSH study. In addition women subsequently recruited to the POSH study will be weighed and have their waist and hips measured, one year after diagnosis using standardised techniques (Seiddell, 1991) by staff within the medial oncology departments. Changes in weight over the year since commencing treatment will be determined from weight at one year and weight recorded when treatment was commenced. Any changes in smoking behaviour or menopausal status over the year since commencing treatment will also be recorded at one year.

### **Data analysis:**

The planned analysis would examine the effects of weight gain (and waist, and waist; hip ratio) using Cox regression adjusted for other cofounders which may influence disease free survival, i.e. stage of disease, receptor status age of subject, BRCA carrier status, treatment, menopausal status smoking behaviour, alcohol intake. We predict that 1000 women will allow a 7% difference in 2 year disease free survival to be determined between women who have experience the most weight gain as compared to women who have experienced the least weight gain with 85% power.

### **References**

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