Author’s response to reviews

Title: Weight before and after a diagnosis of breast cancer or ductal carcinoma in situ: A national Australian survey

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Response to Reviewer’s comments

Thank you for your kind review of our manuscript. We have responded to your comments below and feel confident that the manuscript is now significantly improved. We have also edited the paper for further readability.

Reviewer reports:

Amy Downing (Reviewer 3): I am reviewing this paper with an emphasis on the statistics, as some of the previous reviewers indicated they did not feel able to assess this aspect. Overall, this is an interesting study but it is hampered by two major limitations - the low response rate and the lack of control data. Whilst the response rate is acknowledged as a limitation, the authors need to be very cautious in their claims. Throughout the whole manuscript there is no mention of, or comparison to, control or general population data. It is impossible to properly interpret the results without this context.

Major comments:

1. In the introduction the authors refer to a paper by Vagenas et al (ref 8). This was a prospective cohort study of 287 women, assessing weight at several time points and using a control group for comparison. The current study included a few more cases (309) but
with a more limited methodology. The authors need to make a stronger case as to how these results improve on previous research.

Thank-you for this comment. We have added the following sentence to the conclusion (line 365) indicating that this is the first study to provide national data: “This is the first national survey of Australian women to describe weight gain after diagnosis of BC.” We have also included more results from another population study from Shanghai and highlighted the differences between the two studies in the discussion and made further comparison to other studies. In addition, we have highlighted the importance of this issue following the release of a national statement from Australia’s peak cancer body, the Clinical Oncological Society of Australia.

We have rewritten the Discussion to reflect the significance our findings (notwithstanding the limitations of a cross-sectional and self-report survey) which suggest that the amount of weight gain may be greater than previously thought.

“The proportion of women who were overweight or obese in our study is consistent with those from a prospective study of 287 women conducted in Queensland, Australia which compared weight gain after diagnosis of early BC. By 6 years, 68% of women in the cohort were overweight or obese, [8] which is remarkably similar to our findings. The authors of the cohort study compared the weight gain in the BC cohort with age-matched controls and reported a significant difference, with only 50% of age-matched controls being overweight or obese. Median weight gain between 6 and 72 months was 0.7kg, and mean BMI increase was 0.2kg/m2. One other population study has been published from Shanghai on obesity and clinical outcomes of 4561 Chinese women [9]. In that study, mean weight gain at 18 months post-diagnosis was 1.7kg. Mean weight gain in our study was significantly higher at 4.5kg which could be explained by the longer time since diagnosis in our study. Further, the mean weight gain in women who had gained weight overall is substantially higher than what is reported in the Australian cohort study (9.07kg vs 5.3kg). Our study provides additional data on weight gain after BC in Australia, over a wider time frame and location and with a larger sample size, and suggests that the problem of weight gain after BC may be larger than previously anticipated.

A large international review found that 50-96% of early stage BC patients experience weight gain during treatment in the range of 1.7 kg to 5.0 kg in the 18 months following treatment [15]. Of those who gained weight, 27% gained 2 kg to 5 kg and 24% gain 5 kg or more in the 18 months following treatment. This compares to our study where 50.55% reported gaining 5 kg or more mainly in the first 18 months after treatment, again suggesting that weight gain after BC is a greater problem than previously thought. “

We have added the following recommendation to the Discussion, page 18 lines 488-9

“All people with cancer should progress towards and, once achieved, maintain participation in at least 150 minutes of moderate intensity or 75 minutes of vigorous-intensity aerobic exercise (e.g. walking, jogging, cycling, swimming) each week; and two to three resistance exercise (i.e. lifting weights) sessions each week involving moderate-to-vigorous-intensity exercises targeting the major muscle groups. In women with breast cancer, there appears to be a window of
opportunity within the first 18 months to initiate weight management interventions in order to prevent excessive weight gain. “

2. The group which was invited to participate were members of a breast cancer network who had agreed to receive emails about research studies (2% of all members). This is a self-selected group who are likely to have particular characteristics. On top of this, only 15% chose to participate. This severely limits generalisability to breast cancer patients as a whole. Is any comparative data available to show how similar or different this sample of women was to all BC patients?

Unfortunately, there is no comparative data for employment and education for BCNA Survey and Review Group respondents that we could locate although we did run analyses comparing demographics of BCNA and non BCNA respondents. (See page 8 lines 163-165). Additionally, the evidence from data on incidence of breast cancer indicates that incidence rises with socioeconomic advantage, with the highest for women living in the highest socioeconomic areas (AIHW report). As the women in our sample were predominantly well-educated (60% with a University education) and employed or self-employed (55%) we feel that it is reasonable to generalise our data to women with BC notwithstanding the limitations already outlined. Further the proportions of women who gained weight are similar to that reported in an Australian cohort study (which was limited to one state in Australia).

We have inserted these sentences into page 21 lines 603-607 in the Discussion:

“Notwithstanding these limitations, the demographics in our sample (who were predominantly well-educated and either employed or self-employed) are not inconsistent with national data indicating that the incidence of breast cancer is highest in the areas with highest socioeconomic advantage. Additionally, the demographics of the BCNA respondents and non-BCNA respondents were similar. “

We have also added results from Pearson’s Chi-squared test for the comparison of employment between BCNA and non-BCNA respondents to page 8 lines 224-5.

3. In order to interpret these results properly there needs to be some comparison with women from the general population. What % of women would be expected to gain weight (and how much?) through the natural ageing process and after going through menopause etc? How much of the weight gain seen is 'extra' to what would be expected?

We have now compared rate of weight gain against normative data sourced from the AusDiab study as follows:

We have added the following to our Methods section (pages 8-9, lines 188-205)

“We calculated the mean weight gain per year in our sample as total weight gain divided by time since diagnosis in years. We removed one outlier who reported gaining 10.5kg per year over two
years and reported rate of weight gain across age groups in five-year brackets (see Figure 3 and table 5).

Comparing rate of weight gain against normative data

To compare weight gain in our sample against normative data in the Australian population, we used data from the AusDiab study. The AusDiab study is a large national, longitudinal population-based study involving >11,000 adults aged 25 years and older. Baseline data collection for the AusDiab study occurred during 1999–2000, with a subsequent 5-year followup (during 2004–2005) {Barr, 2006 #4394}. We calculated the mean weight gain per year that exceeded the amounts reported in the AusDiab study for females over five years (700g for 25-34yo, 500g for 35-44yo, 380g for 45-54yo, 140g for 55-64yo, and 0g for 65-74yo) and compared the numbers of women who gained in excess of the rates reported in the AusDiab study across the age groups using Pearson’s chi-squared testing.

We have added the following to our Results section (page 14, lines 327-337):

“Rate of weight gain, and comparison with normative data

On average, women gained 0.64kg per year (n=270, SD=1.76, range -8 to 10.5) (see Table 5). For women aged 25-74 years (the age range for which we have normative data), the mean weight gain in excess of age-matched controls was 0.48 kg per year (n=235, SD= 1.67, range -8.38 to 7.62). Overall, two thirds (69.8%) of women in our sample gained in excess of normative weight gain in the AusDiab study, including 25.1% of women who gained >1kg per year in excess of normative rates of weight gain. There was no difference between age groups with regard to the number of women who gained in excess of normative weight gain (X2, (n=235) = 6.6929, p=0.153). See Figure 3 for mean weight gain in excess of normative data for each age group. There was only one woman in the 25-34 age group; to protect confidentiality we did not include her data in Table 5 or Figure 3.

A sentence “Additionally, it would be of interest to look at change in weight over time and according to menopausal status in matched controls. As such this will be looked at in future studies“ has been added to the discussion. Indeed we are in the process of obtaining data from a cohort study of breast cancer patients which will enable collection of such data.”

Please also refer to Table 5 and Figure 3 which are new.

We have added the following to our Discussion section:

“The majority of women gained weight in excess of the rates reported in age-matched controls without breast cancer. This equated to an average of an additional 2.42 kg over five years.” – page 14, lines 373-5.

And
“Similarly, when compared to age-matched controls from the AusDiab study, 69.8% of women in our survey gained in excess of normative weight gain, indicating that the weight gain experienced within our sample is unlikely to be explained by weight gain that would normally be experienced as women age and progress through the menopausal transition.” - page 17-18 lines 462-477

And

“We acknowledge that the inability to provide matched controls in this survey is a limitation. However, we were able to retrospectively match women by age to controls from the 2005 AusDiab study and found that women gained in excess of normative data, although a limitation of our comparison is that we could not locate more recent data on normative rates of weight gain.” - page 20 lines 556-9.

4. The statistics are descriptive only, however they seem appropriate. It would be useful to include the results for concern about weight gain in one of the tables, perhaps could be added to Table 3?

Thank you for this suggestion. We have considered it, however Table 3 describes the weight and BMI changes in our respondents, and is already quite long. We think that concern about weight (by BMI categories) warrants a separate description.

5. In the first line of the discussion the authors state 'this is the first nationally representative survey conducted in Australia' - in my opinion, the sampling process and the response rate do not support this and this wording should be changed.

We have changed this now to read “first national survey” – page 15 Line 365

6. Again, with reference to other studies, how does this study improve on what has been shown before?

As previously noted, we believe this adds to the literature as there are no other national surveys. We note that there has been one other prospective study in Queensland Australia and a Cancer Registry study from Shanghai which we have now included. Our sample size is larger than the Queensland cohort study’s. We have found that the amount of weight gain exceeds previous findings and highlighted this in the discussion. Further, new guidelines about exercise after cancer treatment have now been released in Australia from the Clinical Oncological Society of Australia and hence understanding the magnitude of weight gain for the most common cancer in women at a population level is important for clinicians and patient’s alike.

7. The authors go on in the discussion on to state that the respondents were from a higher socioeconomic group, more highly educated and mainly Caucasian, so contradicting their earlier point that this is a representative survey.
Thank you – this point was made in light of comparison of our data to normative proportions of obesity and overweight in those in higher socio-economic classes. (page 17, lines 456-9). We have also now explained that we consider our sample to be consistent with national data indicating that breast cancer is highest with highest socioeconomic advantage (page 21, lines 603-8)

8. ‘Strengths include a higher than expected response rate’ - if it was expected to get a 10% response it does question the use of this group as a methodology.

BCNA is the largest consumer advocacy group in Australia for people with breast cancer, and therefore we considered it appropriate to involve its members in our survey. BCNA have a policy of limiting requests for research to those who have volunteered to receive these requests. Using this group allowed us to access women who were willing to contribute to research on breast cancer, while protecting other women from repeated requests from research. We consider this an appropriate and ethical strategy. In our Methods section page 5 lines 114-122, we had described our rationale which includes the statement “The Review and Survey Group (n=1857) represents approximately 2% of all BCNA members and is one of the largest breast cancer consumer groups available for research in Australia, representing an important source of feedback for the research community.”

9. There is no mention anywhere about the % of women who lost weight or remained stable. Yes this information is in the tables but I think it is important to point out for added context.

Thank you for this suggestion. A sentence has been added to the results and discussion describing such findings and noting that it would be of interest to enquire about the reasons for weight loss.

Page 12 Line 277-8 “Of note, a small proportion of women lost weight whereby 5.55% of women went down at least one BMI category (Table 3).”

And

Page 15 lines 375-377 “A very small proportion of women (5.55%) changed from a higher to lower BMI category. It would be of interest to explore such findings to enquire whether this is a result of intended weight loss or treatment related effects. “

10. It appears that information on exercise was collected as part of the survey. It would be very interesting to know what % (before and after) took regular exercise. It seems that detailed info on lifestyle habits was collected but not reported (although the authors state this will be in a follow-on paper). Inclusion of some of this data into the current paper may give it the added 'edge' needed.
Thank you for this suggestion. We agree that this information is very interesting and relevant to this area of research. As indicated in methods, detailed information on lifestyle habits was collected and will be reported in a follow-on paper. This current paper focuses on describing the pattern of weight gain after breast cancer.

11. Tables - I am worried about the small numbers being presented in the tables - a patient could feasibly identify themselves. It is standard practice in many organisations to suppress small numbers (say \(<5\)) or to combine some categories.

Thank you for this suggestion. The tables have been changed to reflect \(<5\) when there are fewer than 5 participants.