

Weight Change of Younger and Older Early Breast Cancer Patients – A Meta Regression

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Abstract

Introduction: Weight gain has a major impact on the quality of life of breast cancer patients. Post treatment weight gain can impact on primary endpoints such as recurrence, death, self identity and the ability to return to work. Parameters thought to impact on weight gain include menopausal status, age and chemotherapy regimen. Using meta-regression, we studied the effect of age on weight change, by menopausal status and chemotherapy regimen.

Methods: 24 studies were identified, and extracted for weight change, mean/median age, menopausal status and chemotherapy regimen. A meta-regression was performed, using a random-effects DerSimonian and Laird model for high heterogeneity and fixed-effects inverse-variance model for low heterogeneity. Subgroup analyses were conducted, by menopausal status and chemotherapy regimen. P-values less than 0.05 were considered statistically significant.

Results: There exists no relationship between weight change and age ($\beta = 0.00$; $p = 0.987$). Stratifying by menopausal status and chemotherapy regimens, there likewise was no relationship.

Conclusion: Management of weight gain due to chemotherapy has been focused on relatively young women where a higher mortality and recurrence has been found. However, our results suggest that age should not be used to differentiate care in these patients.

Introduction

For patients receiving chemotherapy for early-stage breast cancer, weight gain has been frequently reported^{1,2}. This weight gain can negatively impact quality of life and self-esteem. Mechanisms include increased edema, with decreased physical activity leading to fatigue. Important changes in body composition (BMI) is especially pronounced in younger women, who become postmenopausal due to chemotherapy. Despite less weight gain with more recent chemotherapy regimens, this change in BMI continues to impact breast cancer prognosis and development of other medical conditions, such as heart disease, which is a significant cause of mortality in breast cancer survivors³⁻⁶; Thivat *et al*⁷ report that a 5% or greater weight change is associated with increased risk of recurrence (RR: 2.28, 95% CI: 1.29–4.03) and death (RR: 2.11, 95% CI: 1.21–3.66).

Prevalence of weight gain has been reported to between 50–96%, and weight gain can vary from, on average, 1.4kg to 6.2kg⁸. van den Berg *et al*⁸, in a systematic review and meta-analysis, found that body weight increased by 2.7kg during chemotherapy. Their sensitivity analyses by study design, menopausal status, chemotherapy regimen and year of publication showed variation in weight gain. However, their review cited high heterogeneity, suggesting that there may be a confounder in their analysis.

Age has previously been reported to affect weight gain, in a large population-based cohort study of 4,561 patients. Chen *et al* reported that younger breast cancer patients experienced greater weight change⁹. Based on their results, one may infer that studies with younger patients will observe a greater weight

change. The observed variations reported by van den Berg *et al*^β, by chemotherapy regimen and menopausal status, may therefore be a confounded observation, by age. Clarifying this issue is important, as it will inform whether age of patients should be considered, when enacting interventions for weight change. Additionally, it will clarify whether menopausal status and chemotherapy regimen still has an effect on weight change, after accounting for the potential confounder of age. A meta-regression can be used in this setting, to investigate the effect of age in the causal pathway and provide clarification on whether age may have been a contributing factor to high heterogeneity in the van den Berg *et al*^β meta-analysis.

To investigate whether age has an effect on weight change, we conducted a meta-regression for studies reporting on chemotherapy use in early-stage breast cancer patients.

Methods

We searched the databases of Ovid Medline, Embase and Cochrane Central Register of Controlled Trials for studies reporting on weight change in early breast cancer patients, using the MeSH headings of “breast neoplasms”, “neoplasm staging” and “body-weight trajectory”. We identified the same 25 studies for inclusion as those reported by van den Berg *et al*^β in their systematic review were included in this analysis. We could not find the full-text for the article written by Foltz¹⁰, which was one of the 25 papers included by van den Berg *et al*^β. Therefore, 24 papers^{11–34} were included in this analysis as pertinent details from the full text article are required for meta-regression. The effect size of weight gain for each study was extracted and cross-referenced with those reported by van den Berg *et al*^β. The age of patients included in the study, as reported using measures of central tendency (mean or median), was noted. Additionally, the menopausal status of patients enrolled in studies were recorded, either as reporting exclusively on (1) premenopausal patients, (2) postmenopausal patients, and (3) premenopausal and postmenopausal patients. Finally, we recorded whether patients received (1) CMF chemotherapy only, (2) CMF chemotherapy, alongside other, or (2) other chemotherapy treatment, and not CMF chemotherapy.

A random-effects DerSimonian and Laird model was used when heterogeneity was high ($I^2 > 50\%$) and fixed-effect inverse-variance model ($I^2 < 50$) was used, to meta-regress effect size relative to age of patients. Subgroup analyses were conducted, by menopausal status of patients and by chemotherapy treatment. The threshold for statistical significance was specified, a priori, at $\alpha = 0.05$. All analyses were conducted using Stata 16.1.

Results

The average age in trials ranged from 39.9 years to 55 years. Six studies^{13,16,17,25,28,32} reported on premenopausal patients, four^{11,20,22,24} on postmenopausal patients, and fourteen^{12,14,15,18,19,21,23,26,27, 29–31,33,34} reported on both premenopausal and postmenopausal patients. Seven^{11,20,22,24,25,31,32}, nine^{16,17,}

20–23,29,30,34 and twelve studies^{12–15, 18,20,22, 25–28,33} reported on CMF-only, CMF-containing and non-CMF regimens, respectively; several studies reported separately, by chemotherapy regimen.

Across all studies, there exists no relationship between weight change and age – $\beta = 0.00$ and $p = 0.987$ (Fig. 1). In subgroup analyses of premenopausal and postmenopausal patients, there also exists no relationship – $\beta = 0.05$ and $p = 0.150$ for premenopausal patients, and $\beta = 0.09$ and $p = 0.588$ for postmenopausal patients (Fig. 2). When analyzing separately by chemotherapy regimen, there likewise was no relationship between weight gain and age (Fig. 3).

Discussion

To our knowledge, this is the first meta-regression reporting on weight change as a function of age. We report on 24 studies, with a total sample size of 2,586 patients. There is no relationship between age and weight change among early-stage breast cancer patients undergoing chemotherapy, which prevails in all subgroup analyses. Age is not a confounder in the relationships between chemotherapy regimen and weight change, and menopausal status and weight change.

This study was able to address the myth that weight gain is a larger problem for younger women, due to chemotherapy-induced menopause. This study reports otherwise, that both younger and older women experience similar degrees of weight change.

This study also provides further guidance on clinical decision making. Patients often ask about weight gain and the answer may influence their selection of chemotherapy regimen or even willingness to accept treatment. Physicians query weight gain as well as it has a significant impact on recurrence rates and quality of life. This study provides a means to inform patients with accurate data and to guide physicians in focussing not on age, but rather on other weight gain predictors. Since age is not an independent risk factor for weight gain, decisions on which patients require more intensive intervention for preventing weight gain should be based on evidence from studies exploring body composition, metabolism and insulin resistance instead.⁴ Given studies demonstrating higher morbidity and mortality among breast cancer patients with higher BMI, patients of all ages, not just younger patients, should be encouraged to maintain a healthy weight following their breast cancer diagnoses. Furthermore, as noted in the prior review by van den Berg *et al*⁸, different magnitudes of weight gain were noted by menopausal status and chemotherapy regimen⁸; these factors should be heavily considered irrespective of age, when considering intervention options.

A limitation of this study, like other evidence synthesis studies, is that its validity is reliant on the validity of included studies. As reported by van den Berg *et al*⁸, some included studies were not of the highest quality, as assessed using the Newcastle-Ottawa scale. As well, one may have concerns about reporting bias, where only certain age groups are reported in the literature. However, included studies had a wide range of average ages, spanning 15 years.

In conclusion, there is no relationship confounding effect of age on weight change in early-stage breast cancer patients. This was observed, among both premenopausal and postmenopausal patients, as well as patients receiving CMF chemotherapy and other chemotherapy regimens.

Declarations

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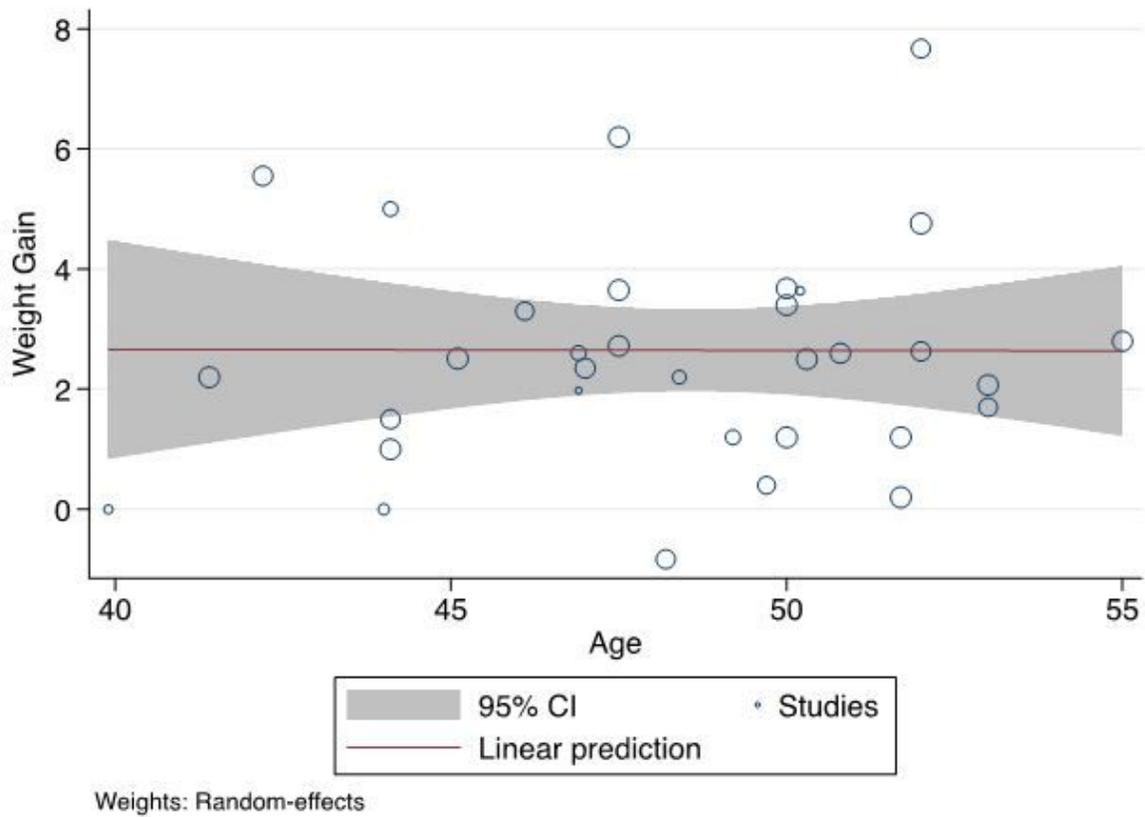
References

1. Cheney CL, Mahloch J Fau - Freeny P, Freeny P. Computerized tomography assessment of women with weight changes associated with adjuvant treatment for breast cancer.
2. Rock CL, Demark-Wahnefried W. Nutrition and survival after the diagnosis of breast cancer: a review of the evidence. *J Clin Oncol* 2002;20:3302-16.
3. Vance V, Mourtzakis M Fau - McCargar L, McCargar L Fau - Hanning R, Hanning R. Weight gain in breast cancer survivors: prevalence, pattern and health consequences.
4. Makari-Judson G, Braun B, Jerry DJ, Mertens WC. Weight gain following breast cancer diagnosis: Implication and proposed mechanisms. *World journal of clinical oncology* 2014.
5. Guo A, Zhang KW, Reynolds K, Foraker RE. Coronary heart disease and mortality following a breast cancer diagnosis. *BMC Med Inform Decis Mak* 2020;20:88-.
6. Li YR, Ro V, Tchou JC. Obesity, Metabolic Syndrome, and Breast Cancer: From Prevention to Intervention. LID - 7 [pii] LID - 10.1007/s40137-018-0204-y [doi]. 2018.
7. Thivat E, Théronnel S, Lapirot O, et al. Weight change during chemotherapy changes the prognosis in non metastatic breast cancer for the worse. *BMC Cancer* 2010;10:648.
8. van den Berg MMGA, Winkels RM, de Kruif JTCM, et al. Weight change during chemotherapy in breast cancer patients: a meta-analysis. *BMC Cancer* 2017;17:259.

9. Chen X, Lu W, Gu K, et al. Weight change and its correlates among breast cancer survivors. *Nutr Cancer* 2011;63:538-48.
10. Foltz AT. Weight gain among stage II breast cancer patients: a study of five factors. *Oncology nursing forum* 1985;12:21.
11. Aslani A, Smith RC, Allen BJ, Pavlakis N, Levi JA. Changes in body composition during breast cancer chemotherapy with the CMF-regimen. *Breast cancer research and treatment* 1999;57:285-90.
12. Basaran G, Basaran G, Turhal NS, et al. Weight gain after adjuvant chemotherapy in patients with early breast cancer in Istanbul Turkey. *Medical oncology (Northwood, London, England)* 2011;28:409-15.
13. Biglia N, Cozzarella M, Ponzzone R, et al. Personal use of HRT by postmenopausal women doctors and doctors' wives in the north of Italy. *Gynecological endocrinology* 2004;18:165-74.
14. Campbell KL, Lane K, Martin AD, Gelmon KA, McKenzie DC. Resting Energy Expenditure and Body Mass Changes in Women During Adjuvant Chemotherapy for Breast Cancer. *Cancer nursing* 2007;30:95-100.
15. Courneya KS, Segal RJ, Mackey JR, et al. Effects of Aerobic and Resistance Exercise in Breast Cancer Patients Receiving Adjuvant Chemotherapy: A Multicenter Randomized Controlled Trial. *Journal of clinical oncology* 2007;25:4396-404.
16. Demark-Wahnefried W, Hars V, Conaway MR, et al. Reduced rates of metabolism and decreased physical activity in breast cancer patients receiving adjuvant chemotherapy. *The American journal of clinical nutrition* 1997;65:1495-501.
17. Demark-Wahnefried W, Peterson BL, Winer EP, et al. Changes in Weight, Body Composition, and Factors Influencing Energy Balance Among Premenopausal Breast Cancer Patients Receiving Adjuvant Chemotherapy. *Journal of clinical oncology* 2001;19:2381-9.
18. Freedman RJ, Aziz N, Albanes D, et al. Weight and Body Composition Changes during and after Adjuvant Chemotherapy in Women with Breast Cancer. *The journal of clinical endocrinology and metabolism* 2004;89:2248-53.
19. Goodwin PJ, Ennis M, Pritchard KI, et al. Adjuvant Treatment and Onset of Menopause Predict Weight Gain After Breast Cancer Diagnosis. *Journal of clinical oncology* 1999;17:120-9.
20. Goodwin PJ, Panzarella T, Boyd NF. Weight gain in women with localized breast cancer—a descriptive study. *Breast cancer research and treatment* 1988;11:59-66.
21. Harvie MN, Campbell IT, Baildam A, Howell A. Energy Balance in Early Breast Cancer Patients Receiving Adjuvant Chemotherapy. *Breast cancer research and treatment* 2004;83:201-10.
22. Heasman KZ, Sutherland HJ, Campbell JA, Elhakim T, Boyd NF. Weight gain during adjuvant chemotherapy for breast cancer. *Breast cancer research and treatment* 1985;5:195-200.
23. Heideman WH, Russell NS, Gundy C, Rookus MA, Voskuil DW. The frequency, magnitude and timing of post-diagnosis body weight gain in Dutch breast cancer survivors. *European journal of cancer (1990)* 2008;45:119-26.

24. Huntington MO. Weight gain in patients receiving adjuvant chemotherapy for carcinoma of the breast. *Cancer* 1985;56:472.
25. Ingram C, Brown JK. Patterns of Weight and Body Composition Change in Premenopausal Women With Early Stage Breast Cancer: Has Weight Gain Been Overestimated? *Cancer nursing* 2004;27:483-90.
26. Jeon YW, Lim ST, Choi HJ, Suh YJ. Weight change and its impact on prognosis after adjuvant TAC (docetaxel–doxorubicin–cyclophosphamide) chemotherapy in Korean women with node-positive breast cancer. *Medical oncology (Northwood, London, England)* 2014;31:1-10.
27. Kumar N, Allen KA, Riccardi D, et al. Fatigue, Weight Gain, Lethargy and Amenorrhea in Breast Cancer Patients on Chemotherapy: Is Subclinical Hypothyroidism the Culprit? *Breast cancer research and treatment* 2004;83:149-59.
28. Kutynec CL, McCargar L, Barr SI, Hislop TG. Energy balance in women with breast cancer during adjuvant treatment. *Journal of the American Dietetic Association* 1999;99:1222-7.
29. Lankester KJ, Phillips JE, Lawton PA. Weight Gain During Adjuvant and Neoadjuvant Chemotherapy for Breast Cancer: an Audit of 100 Women Receiving FEC or CMF Chemotherapy. *Clinical oncology (Royal College of Radiologists (Great Britain))* 2002;14:64-7.
30. Makari-Judson G, Judson CH, Mertens WC. Longitudinal Patterns of Weight Gain after Breast Cancer Diagnosis: Observations beyond the First Year. *The breast journal* 2007;13:258-65.
31. McInnes JA, Knobf MT. Weight gain and quality of life in women treated with adjuvant chemotherapy for early-stage breast cancer. *Oncology nursing forum* 2001;28:675.
32. Rio GD, Zironi S, Valeriani L, et al. Weight Gain in Women with Breast Cancer Treated with Adjuvant Cyclophosphomide, Methotrexate and 5-Fluorouracil. Analysis of Resting Energy Expenditure and Body Composition. *Breast cancer research and treatment* 2002;73:267-73.
33. Trédan O, Bajard A, Meunier A, et al. Body weight change in women receiving adjuvant chemotherapy for breast cancer: A French prospective study. *Clinical nutrition (Edinburgh, Scotland)* 2009;29:187-91.
34. Winkels RM, Beijer S, van Lieshout R, et al. Changes in body weight during various types of chemotherapy in breast cancer patients. *e-SPEN journal* 2013;9:e39-e44.

Figures

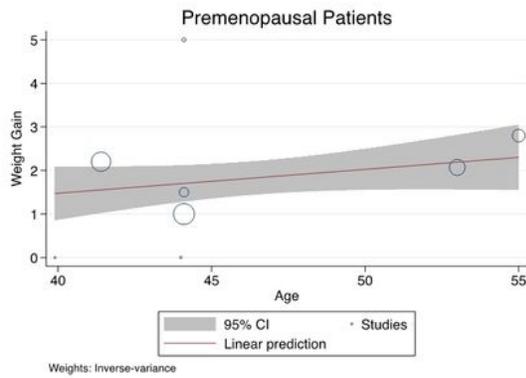


Note: Each circle indicates an individual study's results. The size of the circle denotes the weighting, in the meta-regression model.

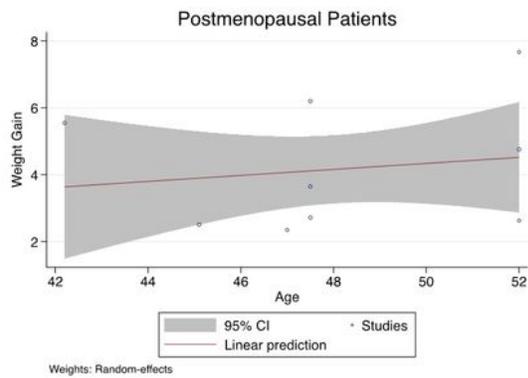
Figure 1

Weight Change, as a Function of Age, in All Early Breast Cancer Patients ($\beta = 0.00$; $p = 0.987$) Note: Each circle indicates an individual study's results. The size of the circle denotes the weighting, in the meta-regression model.

2.1



2.2



2.3

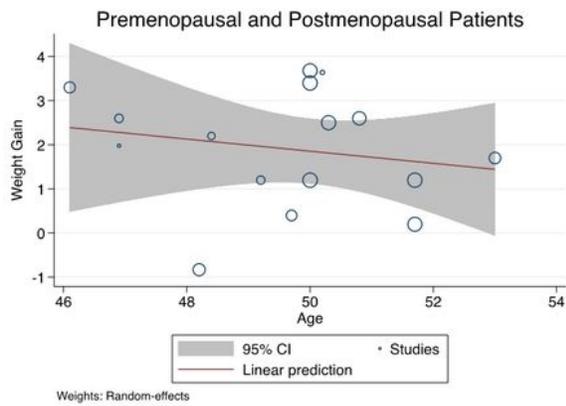
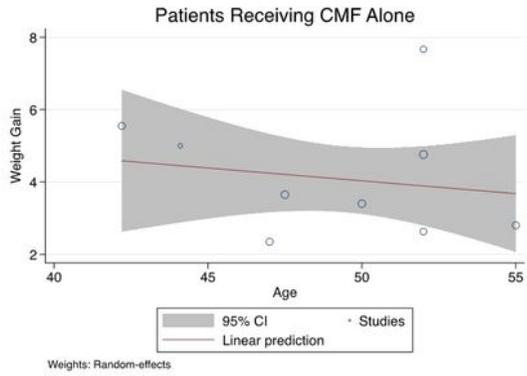


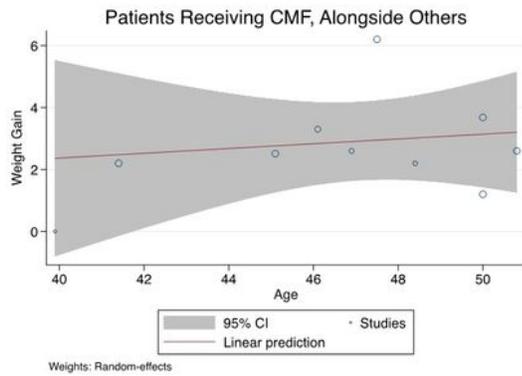
Figure 2

Weight Change, as a Function of Age, for 2.1 Premenopausal Patients ($\beta = 0.05$; $p = 0.150$) 2.2 Postmenopausal Patients ($\beta = 0.09$; $p = 0.588$) 2.3 Premenopausal and Postmenopausal Patients ($\beta = -0.14$; $p = 0.546$)

3.1



3.2



3.3

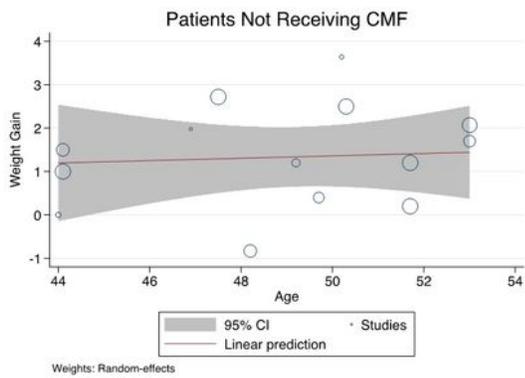


Figure 3

Weight Change, as a Function of Age, for 3.1 Patients Receiving CMF Alone ($\beta = -0.07$; $p = 0.562$) 3.2 Patients Receiving CMF, In Addition to Others ($\beta = 0.08$ $p = 0.707$) 3.3 Patients Not Receiving CMF ($\beta = 0.02$; $p = 0.807$)