

## Research Article

# Weight changes and associated factors among breast cancer patients receiving chemotherapy at a referral hospital in Kenya

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**Background:** Breast cancer patients experience weight changes during treatment, which adversely affect prognosis. However, cancer treatment in Kenya mainly focuses on tumor eradication with limited attention on weight management interventions.

**Objectives:** To determine weight changes and associated factors among breast cancer patients receiving the first three cycles of chemotherapy at Kenyatta National Hospital.

**Methodology:** A prospective cohort design was adopted. One hundred and forty two female participants aged 18-70 years diagnosed with stage 1, 2 and 3 breast cancers were followed up for three months during treatment. Data was collected after every visit using a structured questionnaire, individual dietary diversity tool and anthropometric assessments. Clinical data was extracted from participant's medical records. Frequencies, proportions, measures of central tendency and chi square tests were utilized in analysis.

**Results:** The majority of patients (59.2%) had stage 2 breast cancers. The prevalent type of cancer was ductal carcinoma (97.9%). Most of the patients were on adjuvant chemotherapy (66.9%). The mean weight (SD) was 66.6(13.6) kg, 65.9(13.4) kg and 66.1(13.2) kg at first, second and third cycles respectively. Overall (between the first and thirteenth cycle), the mean weight change (SD) was 0.4(1.6) kg. Majority (48.4%) gained weight and among them, 24.2% gained 2kg and 18.3% gained 1kg. Amongst the patients who lost weight, 19.2% and 11.7% lost 1kg and 2 kgs respectively. Weight gain was significantly ( $p<0.05$ ) associated with being married and Body Mass Index (BMI) at baseline. On the other hand, weight loss was significantly ( $p<0.05$ ) associated with diarrhea.

**Conclusion:** Weight changes were observed among the patients with majority of them experiencing weight gain than weight loss hence a need for early initiation of weight management interventions after diagnosis of breast cancer.

**Key words:** Breast cancer, weight gain, chemotherapy

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## 1. Introduction

According to the International Agency for Research on Cancer (IARC), breast cancer is the 2<sup>nd</sup> leading cause of cancer specific mortality in developing countries (Ferlay et al, 2015). In Kenya, one in every two women

diagnosed of cancer either present with cervical or breast cancer (Korir et al, 2014). A study carried out in Kenyatta National Hospital showed breast cancer (55%) as the most prevalent cancer among females (Muthike Caroline, 2013). Excess Body weight has been proven a risk factor and main prognostic factor for breast cancer.

Cytotoxic treatments like chemotherapy cause weight gain and alter the metabolic status of breast cancer patients (Bicakli et al, 2016). Agreeably, weight gain is a common problem among breast cancer patients who receive adjuvant chemotherapy and this increases the risk of metabolic syndrome among premenopausal patients (Bicakli et al, 2016; Demark-Wahnefried, Campbell & Hayes, 2012). Similarly, observational studies indicate that breast cancer mortality is 33% higher in obese than non-obese survivors (Calle, et al, 2003)

Weight gain rather than weight loss often occurs after breast cancer diagnosis (Yaw et al, 2011). Elevated weight gain has been associated with higher risk of metabolic diseases which in turn result in poor quality of life, leading to decreased overall survival (Calle et al, 2003). Factors that predispose breast cancer patients to weight gain include; early menopause as a result of chemotherapy that leads to changes in body composition, use of corticosteroids in management of nausea during chemotherapy, increased levels of fatigue and lethargy and the intense craving of energy rich foods during chemotherapy sessions (Melinda, 2015). This eventually leads to overweight and obesity which puts the patient at risk of diabetes, high blood pressure and heart diseases that decrease the quality of life or eventually lead to death (PDQ Supportive and Palliative Care Editorial Board, 2002). In overweight and obese patients, the risk of breast cancer recurrence is high because of the excess adipose tissue which indirectly activates tumor proliferation and release of circulating estrogen that accelerate proliferation of cancer cells (Calle et al, 2003; PDQ Supportive and Palliative Care Editorial Board, 2002).

On the other hand, weight loss during cancer treatment affects the severity and progress of disease leading to complications and mortality. Upto 45% of cancer patients experience weight loss greater than 10% usual body weight (Tilton, 2011). The Kenya National Guidelines on the management of Cancer 2012 indicate that underweight is a common problem in cancer prognosis that results to adverse outcomes with increased morbidity and mortality as well as decreased quality of life (Ministry of Health, 2013). Weight loss, the most common secondary diagnosis in cancer patients occurs as a result of chemotherapy and tumor induced side effects such as anorexia, early satiety, altered taste and smell, physical inability to ingest and digest food, mal absorption of macro and micro nutrients and cancer reduced abnormalities such as glucose intolerance, insulin resistance and increased lipolysis (PDQ Supportive and Palliative Care Editorial Board, 2002). These results to wasting, body weakness, immune suppression, reduced protein synthesis, poor quality of life and eventually death. Furthermore cancer induced abnormalities in metabolism also lead to cachexia (where the rate of catabolism is higher than anabolism due to the changes in metabolism induced by the tumor and chemotherapy). However breast cancer patients present more with weight gain than weight loss (Ministry of Health, 2013).

Weight management among breast cancer patients on chemotherapy is key to achieving better response to treatment, good quality of life and better survival rates. The risk of weight gain or weight loss is high among

breast cancer patients and this has a negative effect on the treatment outcomes. Kenya National Cancer management guidelines point towards maintaining ideal weight during cancer treatment. However this has not been implemented among most cancer patients in Kenya. Poor prognosis and a rise in mortality and breast cancer recurrence among female patients in Kenya is gradually becoming a common occurrence. In 2012, 44% of 4,465 registered breast cancer cases in Nairobi died (Korir et al, 2014). In addition, despite the known effects of weight on treatment outcomes of breast cancer patients, cancer experts focus mainly on removing the tumor with limited attention on other health related interventions such as weight management that could potentially be contributing to breast cancer recurrence and deaths. The overall goal of this study was to determine the weight changes and associated factors among early stage breast cancer patients receiving the first three cycles of chemotherapy at Kenyatta National Hospital.

## 2. Methods

### 2.1 Study Site

The study adopted a prospective cohort study design where participants were followed up for 3 months during which they completed the first three cycles of chemotherapy. The study was carried out at the oncology outpatient clinic in Kenyatta National Hospital where all the cancer outpatients receive their chemotherapy.

### 2.2 Study population and Eligibility Criteria

The study targeted all female breast cancer outpatients receiving chemotherapy at Kenyatta National Hospital.

Female patients aged 18 - 70 years, diagnosed with stage 1, 2 and 3 breast cancer who had enrolled for or had received their first cycle of chemotherapy and gave consent were included in the study. The study excluded patients who did not consent

### 2.3 Sample size and sampling methods

Systematic random sampling was used to select 142 participants identified from medical records and every third patient selected from the list. Participants were interviewed and assessed on the dates they came for chemotherapy sessions.

### 2.4 Data collection and Research variables

A structured questionnaire was used to collect data on socio-demographic information and factors affecting changes in weight. Data on dietary practices was collected using an individual dietary diversity tool adopted from Food and Agriculture Organization (FAO, 2013). A cancer abstract form adopted from Nairobi Cancer Registry (Korir et al, 2014) was incorporated in the tool and used to extract clinical data (type of breast cancer, stage of cancer type of chemotherapy and drugs administered) from patients' medical records. Participants' weight and height were assessed after every cycle. Using the FAO 2013 standardized individual dietary diversity score tool, the respondents were asked whether they had consumed foods from 14

food groups in the last 24 hrs after every cycle to determine level of diet quality consumed. The food groups were categorized based on the FAO guidelines as follows;

Cereals	Organ meats
Fruits rich in Vitamin A	Legumes and nuts
Eggs	Sugar and honey
Fish	Other roots and tubers
Fats and oils	Other meats
Roots/tubers & vegetables with orange flesh	Other fruits and vegetables
Dark green leafy vegetables	Milk and dairy Products

This standardized tool uses a recommended reference period of the previous 24 hrs because it is less subject to the recall error, less cumbersome for the respondent and also conforms to the recall time period used in many dietary diversity studies (Arimond, 2004; Kennedy, 2007; Steyn, 2006). Additionally analysis of 24 hr based data is easier compared to longer reference periods that result into less accurate information due to imperfect recall. Data was double entered into MS-Access database, data cleaning and validation was performed and later the data exported to SPSS version 20.0 for analysis

## 2.5 Data Analysis

Weight of study participants was assessed using digital weighing scales after every chemotherapy cycle. Body Mass Index (BMI) was calculated from the weight and height data collected after every cycle of chemotherapy. The participant's nutrition status as defined by BMI was then determined by classifying calculated BMI as underweight, normal and overweight & obesity using the WHO cut off points as shown below:

Underweight	- Below 18.5 kg/m <sup>2</sup>
Normal	- 18.5-24.9 kg/m <sup>2</sup>
Overweight and Obesity	- >25.0kg/m <sup>2</sup>

Changes in weight were determined by computing differences in weight between the first and second cycle (midline weight change) and differences in weight between the first and third cycle (overall weight change). These weight changes were further categorized into: Weight gain (positive change), Weight loss (negative change) and No change (weight change is zero).

Diet diversity scores were used to determine diet adequacy and diet variety consumed by the participants. The levels of adequacy of dietary diversity were derived using mean individual dietary diversity scores based on the FAO guidelines (FAO, 2013). A score of 1 was given to each food group consumed and total scores recorded. The diversity scores were further classified into; adequate dietary diversity and inadequate dietary diversity. A score of 14 was

considered adequate dietary diversity while a score less than 14 was considered inadequate dietary diversity score.

Descriptive statistics were used to summarize categorical variables and measures of central tendency used for continuous variables. Student T test was used to compare mean differences between weight changes among participants. Pearson's Chi-square test was used to test strength of association between categorical variables. The threshold for statistical significance was set at  $\alpha = 0.05$  and a two-sided p value at 95% confidence intervals (CI) reported for corresponding analysis.

## 2.6 Ethical Considerations

The protocol was submitted to Institutional Research and Ethics Committee (IREC) of Moi University Approval number **FAN: IREC 1473** and the Kenyatta National Hospital /University of Nairobi Ethics and Review Committee for ethical approval, number **P164/03/2015**. Participation was fully voluntary and confidentiality was observed at all times. Only patients who provided written consent were included in the study. Data was kept confidential and was only available to the research team. No identifiable details of the participants were disclosed during the study period. There were no foreseeable physical risks associated and no direct material benefits to the study participants.

## 3. Results

The mean (SD) age of patients was 48.6 (11.9) years. More than half of participants (58.5%) were at premenopausal age and unemployed (58.5%) as shown in **Table 1**.

### Diagnosis and the type of drugs used

Over half of the participants (59.2%) had stage 2 breast cancer. The majority was diagnosed with ductal carcinoma (97.9%) and was receiving adjuvant chemotherapy (66.9%). With respect to chemotherapy drugs, participants were on a combination of drugs including anthracyclines (adriamycin and epirubicin), taxanes, (paclitaxel, taxol, docetaxel,), corticosteroids (dexamethasone, prednisolone and methyl prednisolone), alkylating agents (cyclophosphamide), antimetabolites (5-fluorouracil), and platinum drugs (carboplatin). Amid drug combinations, the top most received drugs were alkylating agents (39.7%) followed by anthracyclines (27%) and corticosteroids (10.5%) as shown in **Table 2**.

### Weight and Body Mass Index of Participants

The mean weight (SD) of participants was 66.6 (13.6) kg, 65.9 (13.4) kg and 66.1 (13.2) kg during first, second and third cycle.

The mean (SD) BMI was 25.8 (4.9), 25.7 (4.9) and 25.5 (5.0) at first, second and third cycles of chemotherapy. During first cycle, the highest proportion (53.5%) of participants were overweight and obese. This data is shown in **Table 3**.

**Table 1:** Socio Demographic Characteristics of study participants

Variable		n	%
Age (n= 142)	<b>Mean</b> 48.6 SD( $\pm$ 11.9) <b>Median</b> 48.00 <b>Range</b> 55(26 - 70)		
	Premenopausal	83	58.5
	Postmenopausal	59	41.5
Occupation	Employed	59	41.5
	Unemployed	83	58.5
Marital Status	Married	101	71.1
	Single	21	14.8
	Divorced	6	4.2
	Separated	4	2.8
Religion	Christian	141	99.3
	Muslim	1	0.7
Level of Education	No formal education	20	14.1
	Primary school	53	37.3
	Secondary school	53	37.3
	College	16	11.3

**Table 2:** Patient Clinical Information

Variable	Description	1st cycle n(%)	2nd cycle n(%)	3rd cycle n(%)
Type of cancer	Ductal Carcinoma	139 (97.9)	126 (97.7)	118 (97.5)
	Lobular Carcinoma	2 (1.4)	2 (1.6)	2 (1.7)
Stage of the cancer	Stage 1	17 (11.9)	19 (14.7)	18 (16.5)
	Stage 2	84 (59.2)	72 (55.8)	64 (52.9)
	Stage 3	41 (28.9)	38 (29.5)	37 (30.6)
Type of chemotherapy	Neo-adjuvant	45 (31.7)	42 (32.6)	37 (30.6)
	Adjuvant	97 (68.3)	87 (67.5)	84 (69.4)
Type of drugs	Anthracyclines	121 (27.0)	117 (27.3)	105 (24.9)
	Taxanes	35 (7.8)	24 (5.6)	26 (6.2)
	Corticosteroids	47 (10.5)	43 (10.0)	47 (11.2)
	Alkylating agents	178 (39.7)	172 (40.2)	163 (38.7)
	Others	23 (5.1)	11 (2.5)	14 (3.2)
	Antinausea	44 (9.8)	61 (14.3)	66 (15.7)

**Table 3:** Anthropometry characteristics of participants

Variable	Description	Baseline (1st Chemo*)	Midline (2nd Chemo*)	Final (3rd Chemo*)
		N=142	N=129	N=120
<b>Weight</b>	Mean(SD)	66.6 (13.7)	65.9 (13.4)	66.1 (13.2)
	Range(Min-Max)	71 (38 - 109)	76 (39-107)	67 (40-107)
<b>BMI</b>	Mean (SD)	25.8 (4.9)	25.5 (4.9)	25.5 (5.0)
<b>BMI Categorized</b>	Underweight N (%)	3 (2.1)	3 (2.3)	4 (3.3)
	Normal N (%)	63 (44.4)	62 (48.5)	52 (43.3)
	Overweight & Obese N (%)	76 (53.5)	63 (49.2)	64 (53.3)

\*Chemo refers to chemotherapy cycles

Weight change was derived by determining the differences in weight between first and second cycle (midline weight change) and first and third (overall weight change). Between the first and second cycle, the highest proportion (29.5%) of the patients did not experience any weight change, 28.7% gained 1 kg while 20.9% lost 1 kg. In addition, 14.7% of participants gained 2 kg as indicated in **Figure 1**.

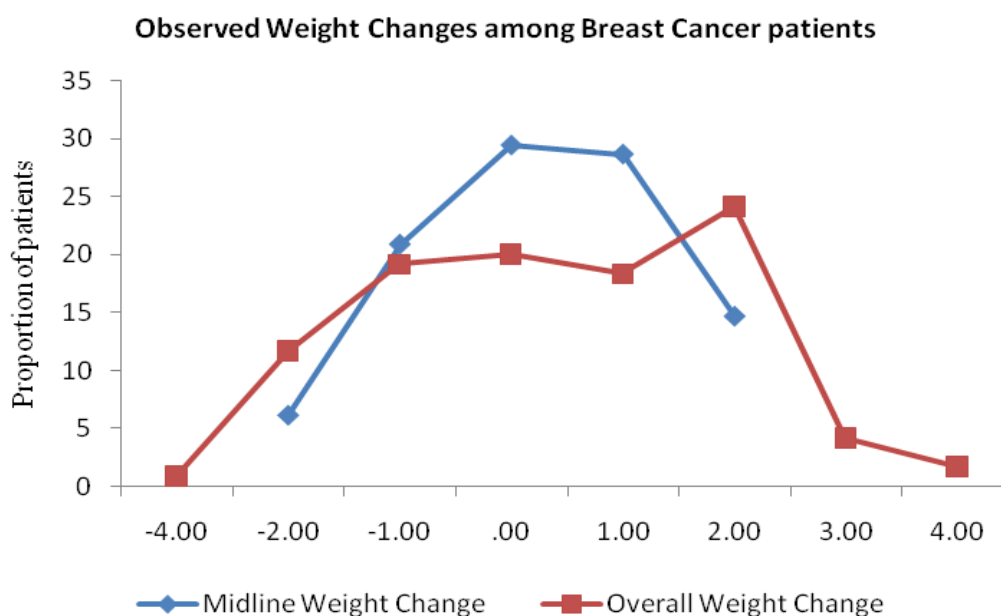
Between the first and the third cycle, majority (24.2%) of the patients gained 2 kg, 18.3% gained 1 kg, 4.2% gained 3 kg and 1.7% gained 4 kgs. Among those who lost weight, 19.2% lost 1 kg, 11.7% lost 2 kgs while 0.8% lost 4 kgs as indicated in **Figure 1**. The mean (SD) midline weight change was a gain of 0.2 kg (1.1) while mean (SD) overall weight change was a gain was 0.4 kg (1.6) among the cancer patients. A paired sample t test showed no significant difference between weight change at midline and overall weight change at 95% confidence interval as shown in **Table 4**.

Weight change was further classified into three groups; weight gain (positive weight change), no change and

weight loss (negative weight change). At midline (between the first and second cycle), 27.1% lost weight while close to half of the patients (43.4%) gained weight. At end line (between the first and third cycle), 31.7% lost weight, 48.3% reported positive weight change, while 20.0% reported no change.

#### Factors associated with weight changes

Chi square tests were used to determine factors associated with both weight gain and weight loss. The study results showed that participants who were married significantly gained weight compared to their unmarried counterparts ( $p < 0.05$ ). Body Mass Index at the start of chemotherapy was significantly ( $p < 0.05$ ) associated with weight gain with more overweight patients gaining weight compared to those who were underweight and normal as shown in **Table 5**. With regards to weight loss, the study also showed that patients who experienced diarrhea significantly ( $p < 0.05$ ) lost weight compared to their counterparts (**Table 5**).



**Figure 1:** Weight Changes observed among Breast Cancer Patients

**Table 4:** Weight changes among Breast Cancer Patients at Midline and Overall

Weight change	Midline weight change <sup>a</sup>	Overall weight change <sup>b</sup>	p-value
Mean(SD)	0.2(1.1)	0.4(1.6)	0.109
Median	0.0	0.0	

<sup>a</sup> Weight change between the 1<sup>st</sup> and 2<sup>nd</sup> cycle

<sup>b</sup> Weight change between the 1<sup>st</sup> and 3<sup>rd</sup> cycle

**Table 5:** Overall weight changes and associated factors

<b>Weight gain and associated factors</b>					
	<b>Description</b>	<b>Gained 1 kg n (%)</b>	<b>Gained 2-5 kg n (%)</b>	<b>Chi square value</b>	<b>P-value</b>
Marital Status	Married	8 (20.5)	31 (79.5)	9.579	0.048
	Single	1 (11.1)	8 (88.9)		
	Divorced	0 (0)	3 (100)		
	Widowed	2 (100)	0 (0)		
	Separated	1 (50)	1 (50)		
BMI Baseline	underweight	1 (100)	0 (0)	6.309	0.043
	Normal	6 (33.3)	12 (66.7)		
	Overweight	5 (13.9)	31 (86.1)		
<b>Weight loss and associated factors</b>					
	<b>Description</b>	<b>Lost 1 kg n (%)</b>	<b>Lost 2-5 kg n (%)</b>	<b>Chi square value</b>	<b>P-value</b>
Diarrhoea	Yes	7 (46.7)	8 (53.3)	5.625	0.018
	No	2 (10.5)	17 (89.5)		

#### 4.0 Discussion

A significant change in weight during chemotherapy is reported to be associated with a poor prognosis in early breast cancer patients (Gadéa et al, 2012; Kroenke et al, 2005; Thivat et al, 2010). Weight gain is a common phenomenon in breast cancer patients associated with poor survival with reported evidence among post-menopausal women and receiving chemotherapy (Caan et al, 2012; Campbell et al, 2007; Han et al, 2006). Results from our study reported 14.6% increase in the number of participants who gained weight between the first and third cycle with an overall mean weight change of 0.4 kg and mean weight change of 0.2kg at midline. These results are in line with findings from a Korean study which recorded a mean weight change of 0.3 kg after 3 months of starting adjuvant chemotherapy among early stage breast cancer women (Han et al, 2006). Correspondingly, a study on weight change and its correlates among breast cancer women showed a mean weight gain of 1.7kg eighteen months after diagnosis (Chen et al, 2011). Another study reported an average weight gain of between 1.7-4.4 kg among breast cancer patients during early post chemotherapy years (Caan et al, 2012). Our results were also comparable to the Women's Healthy Eating and Living Study (WHEL) which observed 2.7 kg of mean weight gain among 1116 women with stage I-IIIa breast cancer, 60% of whom reported weight gain within 4 years of diagnosis (Rock et al, 1999).

In breast cancer, weight gain is caused by premature menopause as an adverse effect of chemotherapy which results to slowed metabolic rate hence more body fat is gained than lean mass. A strong positive correlation between pre-chemotherapy weight and midpoint and overall weight changes was experienced by participants. These results are comparable with findings from most studies carried out to compare weight changes and pre diagnosis weight (Demark-Wahnefried et al, 2012; Goodwin et al, 1999; Irwin et al, 2005)

More participants who were married experienced weight gain compared to counterparts and this was statistically significant ( $p < 0.05$ ). The results are similar with findings from studies that indicate that married cancer patients were less likely to have more advanced cancer compared to the time at diagnosis, are more likely to receive proper treatment and nutritional care and less likely to die compared to their unmarried counterparts (Schwartz, 2014) and experience higher survival rates. These results contrast with a Turkish study which did not find marital status a factor of weight gain in breast cancer patients (Basaran et al, 2011). Similarly another Chinese study found out that education, income and marital status were not significantly associated with weight change (Chen et al, 2011). As much as married cancer patients were reported to gain weight, there is need to carry out nutritional education and counselling on the dangers of excessive weight gain during cancer treatment, appropriate dietary practices and the importance of physical activity to achieve better treatment outcomes

With Regards to BMI, our study indicated that more overweight and obese patients at the start of chemotherapy gained weight compared to their counterparts. Our results concur with a study carried out by Vagenas et al (2011) which revealed that weight gains of over five kilograms were observed between six and sixty months post-surgery among obese patients. At six-month post-surgery, more than half of women (57%) who participated in the study were overweight or obese, and by six-years post-breast cancer 68% of women were overweight or obese. According to NH Comprehensive Cancer Collaboration (2011), treatment regimen, tamoxifen use, fatigue, decreased physical activity, decreased lean body mass, decreased resting energy expenditure, increased consumption of foods to cope with nausea, or treatment-related increase in appetite are attributed to weight gain amongst breast cancer patients. There is therefore need to ensure weight management interventions are initiated among patients at the start of treatment.

On the other hand, diarrhea was significantly associated with weight loss among breast cancer patients. A meta-analysis of risk of gastrointestinal complications in breast cancer patients treated with neratinib indicated an increased risk of diarrhea 89%(95%CI=77-95%) among breast cancer patients though significant increase in patients taking neratinib compared to those in the control group(Jiang et al, 2017). In a study on prevention of 5- Fluorouracil induced diarrhea, those who received synbiotics were less likely to suffer diarrhea(Osterlund et al, 2007).Diarrhea in cancer patients occurs as a side effect of treatment or the cancer itself(Cancer Research UK, 2017). A number of chemotherapy drugs irritate the lining of the digestive system which occurs days after treatment. In addition to killing cancer cells, Chemotherapy also tends to kill fast growing cells like those of the intestine causing damage leads to diarrhea (Mayo Clinic, 2015). Diarrhea is a factor for significant unintentional weight loss defined as >5% loss of the usual body weight in the last 6-12 months among cancer patients. However, minimal studies have been carried out to explain the correlation between diarrhea and weight loss specifically among breast cancer patients. In Kenya, there is therefore need for oncologists managing breast cancer patients to identify cases of diarrhea among these patients to ensure adequate measures are put in place to address it early and prevent it.

### Study Limitations

Due to financial constraints, the study adopted a prospective cohort study design where patients were followed up for a period of 3 months instead of 6 months during which their cycles are completed. Kenyatta National Hospital does not assess patient tumor grading and staging of the cancer after every cycle hence the study did not consider changes in the severity of cancer in relation to weight changes that occurred.

### 5.0 Conclusion

Majority of breast cancer patients were overweight and obese at diagnosis and most of them experienced weight gain compared to their counterparts. There is an increase in number of breast cancer patients who gain weight with continued chemotherapy. A higher number of patients who were married experienced weight gain than their unmarried counterparts. Diarrhea is associated with weight loss among breast cancer patients on chemotherapy. There was no association between age and weight gain as indicated in previous studies with larger sample sizes and longer follow ups periods

Weight management interventions should be integrated in management of breast cancer patients.

### Conflict of Interest declaration

The authors declare no conflict of interest.

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