

# Prevalence and Determinants of Adherence to Oral Adjuvant Endocrine Therapy among Breast Cancer Patients in Singapore

Eskinder Eshetu Ali<sup>1</sup>, Ka Lok Cheung<sup>1</sup>, Chee Ping Lee<sup>2</sup>, Jo Lene Leow<sup>2</sup>, Kevin Yi-Lwern Yap<sup>1</sup>, Lita Chew<sup>1,2</sup>

<sup>1</sup>Department of Pharmacy, Faculty of Science, National University of Singapore, <sup>2</sup>Department of Pharmacy, National Cancer Centre Singapore, Republic of Singapore



**Corresponding author:** Lita Chew, MMed Science

Assistant Professor, Department of Pharmacy, National Cancer Centre Singapore

11 Hospital Drive, Singapore 169610

Tel: 6436 8137; Fax 62202573

E-mail: lita.chew@nccs.com.sg

Received: August 10, 2016, Accepted: April 17, 2017

## ABSTRACT

**Objective:** The success of oral adjuvant endocrine therapy (OAET) is greatly influenced by patients' level of adherence to treatment. The objective of this study is to measure the prevalence and determinants of adherence to OAET among breast cancer patients in Singapore.

**Methods:** A cross-sectional survey of patients supplemented by analysis of their prescription records was used to collect data. Adherence to OAET was assessed using the Morisky Medication Adherence Scale-4 items and evaluation of refill gaps. Univariate and multivariate analyses were done to evaluate the association between patients' characteristics and adherence to OAET. **Results:** A total of 157 women who have started OAET at least 6 months before the time of interview participated in the study, of which less than half (64 patients, 40.8%) of the patients had high adherence. Univariate analysis identified patients who were 57 years or older ( $P = 0.027$ ),

unemployed ( $P = 0.027$ ), on aromatase inhibitors ( $P = 0.023$ ), on three or more concurrent medications ( $P = 0.001$ ), and had one or more comorbidities ( $P = 0.000$ ) to be significantly more adherent. However, only the number of comorbidities was found to be an independent predictor of adherence in a multiple logistic regression analysis (adjusted odds ratio = 2.60; 95% confidence interval = 1.208–5.593;  $P = 0.015$ ). Forgetfulness was the main reason for nonadherence mentioned by 63 (67.7%) of the 93 nonadherent patients. **Conclusions:** Low level of OAET adherence was found in this study, and forgetfulness was cited as the main reason for nonadherence. Patients were generally receptive to the implementation of various strategies to assist them with their medication-taking behavior.

**Key words:** Adherence, breast cancer, hormonal therapy, oral adjuvant endocrine therapy

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DOI:  
10.4103/2347-5625.212864

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**Cite this article as:** Ali EE, Cheung KL, Lee CP, Leow JL, Yap KY, Chew L. Prevalence and determinants of adherence to oral adjuvant endocrine therapy among breast cancer patients in Singapore. *Asia Pac J Oncol Nurs* 2017;4:283-9.

## Introduction

Oral adjuvant endocrine therapy (OAET) is recommended to reduce the risk of recurrence and mortality in women who received primary treatment for estrogen or progesterone receptor positive breast cancer.<sup>[1]</sup> OAET involves the use of agents such as tamoxifen or the third-generation aromatase inhibitors (letrozole, anastrozole, and exemestane).<sup>[2]</sup> It has long been established that the use of OAET is associated with improvements in disease-free survival in hormone receptor-positive breast cancer patients.<sup>[3,4]</sup> The success of therapy depends on how patients are taking their medications for the duration of therapy. However, studies show that poor adherence to OAET is a significant clinical problem.<sup>[5]</sup>

Nonadherence to OAET could potentially lead to dire clinical and economic consequences.<sup>[6,7]</sup> An obvious consequence of a reduction in dose-intensity due to nonadherence is the loss of treatment efficacy leading to increased risk of recurrence and mortality.<sup>[7,8]</sup> Moreover, poor adherence is associated with increased costs as a result of disease complications, the need to use additional clinical interventions, and death.<sup>[9,10]</sup>

Different factors are reported to be associated with low level of adherence to OAET. These include switching of hormonal therapy, extremes of age, increasing out-of-pocket costs, treatment side effects, low recurrence risk perception, suboptimal patient–physician communication, and lack of social support.<sup>[11–13]</sup> Identifying the factors that influence adherence to OAET is important for the implementation of effective interventions.<sup>[14]</sup> While there are a number of studies on the prevalence and determinants of adherence to OAET in other parts of the world, there is a paucity of data in Asia, and Singapore is not an exception.

Breast cancer is the leading cause of cancer-related morbidity and mortality among women in Singapore.<sup>[15]</sup> The country also has one of the highest incidences of breast cancer in Asia.<sup>[16]</sup> Given the significance of the condition and the need to maintain quality of patient care, there is no doubt about the importance of ensuring adherence to breast cancer treatment. The objective of this study was to quantify the level and determinants of adherence to OAET among breast cancer patients in Singapore and to identify the reasons for nonadherence. Patients' preferences for different adherence-enhancing strategies were also assessed.

## Methods

### Study design and participants

A cross-sectional survey in combination with a retrospective analysis of patient medical and dispensing

records was conducted at a tertiary cancer center in Singapore. Patients had to be female, above 21 years old, residing in Singapore, diagnosed with breast cancer, receiving OAET for at least 6 months, and be able to provide written informed consent. Besides, patients had to be able to speak and understand English or Mandarin. Patients who did not fulfill the inclusion criteria and those with prescriptions from external or private oncologists were excluded from the study. Ethical approval was obtained from the Institutional Review Board, and all participants provided their written informed consent before participation in the study.

### Data collection

Data collection was done from December 2013 to January 2014, using face-to-face interview with a semi-structured questionnaire and review of medical records using a structured checklist. The questionnaire was prepared based on review of literature and had five sections, namely, (a) demographics, (b) therapy-related information, (c) medication adherence, (d) reasons for nonadherence, and (e) preferred strategies to help improve medication adherence. The questions on respondents' reasons for nonadherence and their suggested strategies for enhancing adherence were designed as open-ended questions. A list of prompts on the reasons for nonadherence and strategies to improve adherence were prepared to facilitate the interview process. Interviewers employed the list of prompts after obtaining patients' responses on the open-ended questions. For the structured sections of the questionnaire, interviewers were trained to follow a set of written instructions with exact phrasing of questions to minimize interviewer bias.

### Primary outcome variable

The primary outcome variable in this study was the level of adherence to OAET. The four-item Morisky Medication Adherence Scale-4 (MMAS-4) originally validated in patients with hypertension was used to determine adherence as it was validated in the broadest range of diseases.<sup>[17,18]</sup> The four items in the MMAS-4 were designed as yes or no questions. For each item, a "yes" response was scored as 0 and a "no" was scored as 1.<sup>[19]</sup> In this study, patients with a total score of 4 were deemed to have high adherence while scores of 3 points and  $\leq 2$  points, respectively, indicated moderate and low levels of adherence. To verify patients' reported level of adherence, their dispensing records were analyzed for the presence of refill gaps during the entire treatment phase from the start to the most recent tamoxifen or aromatase inhibitor received. A refill gap was defined as having a prescription refilled after the expected refill date based on previous medication supply. Medication switching

and possible surplus from previous fills were taken into account in the calculation. Accordingly, patients with refill gap were considered nonadherent.

### Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics for Macintosh, Version 23.0. (IBM Corp., Armonk, NY, USA). Statistical tests of association were done by comparing patients who had moderate or low level of adherence, as measured by MMAS-4, with those who had high adherence. The independent variables were also transformed into binary variables for the analysis. Respondents' answers to the open-ended questions were analyzed based on the preset list of prompts. Responses that were different from this list were coded and analyzed as unique categories of preferred adherence-enhancing strategies and reasons for nonadherence. Univariate analysis (Pearson Chi-square and Fisher's exact test) was performed to evaluate the effect of sociodemographic and disease- and therapy-related variables on adherence. Factors found to be statistically significant in the univariate analysis were included in the multivariate logistic regression model.  $P \leq 0.05$  was considered statistically significant.

## Results

Face-to-face interviews and medical record reviews were conducted for a total of 157 patients. The average age of participants was 56.3 (standard deviation  $\pm$  10.4) years. The majority of the participants were Chinese (135, 86.0%), married (116, 73.9%), and under a copayment or a third party payer scheme to cover expenses of their OAET drugs (116, 73.9%) [Table 1]. A total of 104 (66.2%) patients had prior chemotherapy, and slightly more than half (81, 51.6%) were currently on aromatase inhibitors. Moreover, 79 patients (50.3%) had one or more comorbidities, and 77 (49%) were concomitantly taking 3 or more medications [Table 2].

The median MMAS-4 score was 3.0 (interquartile range = 2.0). The proportions of patients with high, moderate and low levels of adherence to OAET were 64 (40.8%), 49 (31.2%) and 44 (28.0%) respectively. Record reviews also showed that 58 (36.9%) patients had no refill gap in the review period. The sociodemographic [Table 1] and clinical characteristics [Table 2] associated with high adherence to OAET were older age (57 years and older) ( $P = 0.027$ ), unemployment/being retired ( $P = 0.027$ ), being on aromatase inhibitors ( $P = 0.023$ ), having one or more comorbidities ( $P < 0.001$ ), and being on three or more concurrent medications ( $P = 0.001$ ). All the five variables that showed significant association with high adherence to OAET were entered into a multivariate logistic regression model. After adjustment for potential confounders, the

**Table 1: Univariate analysis of the association between the sociodemographic characteristics of respondents and their adherence to oral adjuvant endocrine therapy (n= 157)**

Sociodemographic characteristics	n (%)	Prevalence of high adherence (%) <sup>a</sup>	P <sup>b</sup>
Total study sample	157 (100.0)	40.8	
Ethnic background			
Chinese	135 (86.0)	40.0	0.646
Others <sup>c</sup>	22 (14.0)	45.5	
Age, years			
56 and younger	78 (49.7)	32.1	0.027
57 and older	79 (50.3)	49.4	
Marital status			
Married	116 (73.9)	41.4	0.792
Single, divorced, or widowed	41 (26.1)	39.0	
Number of children			
1 or more children	116 (73.9)	41.4	0.792
None	41 (26.1)	39.0	
Living arrangements			
Alone	13 (8.3)	15.4	0.075
With family or someone else	144 (91.7)	43.1	
Highest education level			
None, primary	49 (31.2)	42.9	0.853
Secondary school	68 (43.3)	38.2	
Polytechnic, university and above	40 (25.5)	42.5	
Employment status			
Employed	78 (49.7)	32.1	0.027
Unemployed/retired	79 (50.3)	49.4	
Type of payment			
Copay or third party pay	116 (73.9)	44.8	0.081
Fully self-pay	41 (26.1)	29.3	

<sup>a</sup>Patients who scored 4 on MMAS-4 were considered to have high adherence, <sup>b</sup>P value based on Chi-square test, <sup>c</sup>Others refers to Malay, Indians, and others. MMAS-4: Morisky Medication Adherence Scale-4 items. Use of the "MMAS"™ is protected by US and International copyright and trademark laws. Permission for use is required. A license agreement is available from: Donald E. Morisky, MMAS Research) LLC 14725 NE 20<sup>th</sup> St. Bellevue WA 98007

only variable that was found to significantly predict high adherence to OAET was the presence of one or more comorbidities (adjusted odds ratio [OR] =2.60, 95% confidence interval [CI] =1.208–5.593) [Table 3].

Patients who reported moderate or low level of adherence (93 patients, 59.2%) were asked for their reasons for nonadherence. Accordingly, forgetfulness was the reason given by 63 (67.7%) of patients followed by the long duration of therapy (18, 19.4%) and trying to avoid side effects (14, 15.1%) [Table 4]. Although all patients were asked about the strategies that they think will help in improving adherence, only 136 (86.6%) provided specific responses. From these, 83 (61.0%) suggested using pillboxes to organize daily doses as a strategy to improve adherence. Moreover, 74 (54.4%) patients suggested getting education on benefits of their medications and 70 (51.5%) suggested getting education on the nature of their illness as possible strategies to improve adherence [Table 5].

**Table 2: Univariate analysis of the association between the clinical- and medication-related characteristics of respondents and their adherence to oral adjuvant endocrine therapy (n = 157)**

Clinical- and medication-related characteristics	n (%)	Prevalence of high adherence (%) <sup>a</sup>	P <sup>b</sup>
Type of OAET taken for the past 1 month			
Tamoxifen	76 (48.4)	31.6	0.023
Aromatase inhibitors	81 (51.6)	49.4	
Side effects			
No side effects reported	75 (47.8)	45.3	0.265
One or more side effects	82 (52.2)	36.6	
Cancer stage at diagnosis			
Stage 0	10 (6.4)	50.0	0.293
Stage 1	46 (29.3)	32.6	
Stage 2	69 (43.9)	39.1	
Stage 3	32 (20.4)	53.1	
Prior chemotherapy			
No	53 (33.8)	34.0	0.216
Yes	104 (66.2)	44.2	
Years since first OAET			
≤2	73 (46.5)	47.9	0.088
>2	84 (53.5)	34.5	
Number of comorbidities			
None	78 (49.7)	25.6	<0.001
≥1	79 (50.3)	55.7	
Total number of chronic medications			
≤2	80 (51.0)	27.5	0.001
≥3	77 (49.0)	54.5	

Patients who scored 4 on MMAS-4 were considered to have high adherence, <sup>a</sup>P value based on Chi-square test. OAET: Oral adjuvant endocrine therapy; MMAS-4: Morisky Medication Adherence Scale-4 items

**Table 3: Multiple logistic regression analysis of factors associated with adherence among Singaporean breast cancer patients currently on oral adjuvant endocrine therapy (n = 157)**

Sociodemographic and clinical factors	Adjusted OR (95% CI)	P
Age (years)		
56 and younger	1.00	0.960
57 and older	1.021 (0.444-2.348)	
Employment status		
Employed	1.00	0.417
Unemployed/retired	1.359 (0.648-2.849)	
Number of comorbidities		
None	1.00	0.015
≥1	2.60 (1.208-5.593)	
Total number of chronic medications		
≤2	1.00	0.241
≥3	1.630 (0.721-3.687)	
Type of OAET taken for the past 1 month		
Tamoxifen	1.00	0.226
Aromatase inhibitors	1.615 (0.743-3.512)	

OR: Odds ratio; CI: Confidence interval; OAET: Oral adjuvant endocrine therapy

## Discussion

This study documented the level of breast cancer patients' adherence to OAET from an Asian tertiary care

cancer center. As such, the findings will help narrow the research gap on the issue of patient adherence to OAET and its determinants among Asian patients. The study also identified the underlying reasons for nonadherence and potential strategies to promote adherence to OAET.

The overall proportion of breast cancer patients who had high adherence to OAET was found to be less than half (40.8%). Although the adherence rate in this study was lower than most other studies, results were comparable with that reported by Atkins and Fallowfield.<sup>[20,21]</sup> The variations in the rate of adherence reported by different studies can be attributed to the differences in the study design, study population, and the method of measurement of adherence used.<sup>[21]</sup> In this study, level of adherence from self-reported subjective data (MMAS-4) was confirmed with the analysis of prescription refill gaps, a fairly objective approach.<sup>[22]</sup> Adherence rates inferred from both methods were comparable. This implies that patient reports of their adherence levels were reasonably reliable.

There are numerous factors that may influence adherence to OAET, and the literature sometimes shows conflicting reports regarding the direction of influence of some of the factors.<sup>[11]</sup> The univariate analysis in this study identified five factors as significantly associated to high adherence. These factors were age ( $P = 0.027$ ), employment status ( $P = 0.027$ ) [Table 1], type of OAET taken ( $P = 0.023$ ), number of comorbidities ( $P < 0.001$ ), and number of chronic medications ( $P = 0.001$ ) [Table 2]. However, only the number of comorbidities was found to be an independent predictor of high adherence in a multiple logistic regression analysis (adjusted OR = 2.60; 95% CI = 1.208–5.593;  $P = 0.015$ ). The absence of statistical significance with the other variables can partly be explained by the small sample size of the study.

Univariate analysis showed that women who were 57 years and older were significantly more likely to have high adherence to OAET ( $P = 0.024$ ). This is consistent with the different studies that have shown association of nonadherence with younger age.<sup>[5,20]</sup> Moreover, younger age (<45 years) and age ≥85 years were reported to be reliable predictors of nonadherence to adjuvant tamoxifen therapy.<sup>[23]</sup> Participants of our study were relatively younger, with age range from 25 years to 84 years. Hence, the assumption that women older than 85 years tend to be nonadherent might not apply to our study population. Besides, we found that patients who had one or more comorbid conditions and were taking three or more medications were more likely to have high adherence to their OAET. Other studies also reported similar findings, especially for the positive effect of taking more number of medications on adherence to OAET.<sup>[24,25]</sup>

**Table 4: Reasons of respondents on oral adjuvant endocrine therapy for not taking their medications as prescribed (n=93)**

Reasons for nonadherence	n (%) <sup>*</sup>
Forgetfulness	63 (67.7)
The long duration of therapy	18 (19.4)
Intention to avoid potential side effect	14 (15.1)
Feeling worse when taking medications	9 (9.7)
Patients' perception that the medication does not work for them	8 (8.6)
Having to deal with too many medications	7 (7.5)
Absence of a person to check on patient	4 (4.3)
Lack of knowledge on how the medication can help	4 (4.3)
Thinking that there is no need to take the medication	3 (3.2)
Not taking part in making decision to take the medication	3 (3.2)
Lack of understanding on what the doctor/pharmacist says regarding the medicine	3 (3.2)
High cost of the medications	2 (2.2)
Lack of understanding of instructions on the label	1 (1.1)

<sup>\*</sup>Percentages do not add up to hundred because a respondent can give more than one reason for nonadherence

**Table 5: Potential solutions suggested by respondents to facilitate adherence to oral adjuvant endocrine therapy (n=136)**

Suggested strategies	n (%) <sup>*</sup>
Using pill boxes to organize daily doses	83 (61.0)
Education on benefits of the medications patients are taking by health care professionals	74 (54.4)
Education on the nature of illness by health-care professionals	70 (51.5)
Education on side effects and how to manage them	63 (46.3)
Monitoring of patient's medication taking pattern by health-care workers at every visit	61 (44.9)
Monitoring of medication taking pattern and any related side effects by phone calls	58 (42.6)
SMS reminder system to promote timely taking of medications	49 (36.0)
Provision of illustrations (e.g., diagrams, charts) to enhance patients' understanding of their illness/medication	44 (32.4)
Involvement of patients in making clinical decisions	41 (30.1)
Provision of access to relevant support groups	26 (19.1)
Improving patient's self-discipline to improve adherence	22 (16.2)
Introducing the use of mobile phone applications that can help with medication taking	15 (11.0)
Better labeling on medication package	10 (7.4)
Others <sup>†</sup>	20 (14.7)

<sup>\*</sup>Percentages do not add up to hundred because a respondent can suggest more than one strategy. <sup>†</sup>Medication diary (8); family support (7); switch to injection (1); relax and reduce depression (1); pharmacy home delivery service (1); getting smaller medicine packaging (1); and reducing the cost of medicines (1). SMS: Short message service

The presence of comorbidities was also reported to be predictive of adherence and persistence to OAET.<sup>[23,26]</sup> This is consistent with the fact that patients with one or more comorbid conditions were found to be significantly more adherent to OAET in the multiple logistic regression analysis (adjusted OR = 2.60; 95% CI = 1.208–5.593;  $P < 0.05$ ).

The other variables, which were found to have a significant association with high adherence in the univariate analysis, were employment status and class of medicine used in

OAET. Women who were unemployed and those currently on aromatase inhibitors were more likely to have high adherence to their medications. The association between employment and nonadherence is rarely examined, and the already available data fail to show association between employment status and adherence.<sup>[5]</sup> Different studies showed that tamoxifen users were more likely to be nonadherent than those taking aromatase inhibitors, which could be attributable to differences in the side effect profiles of these agents.<sup>[27]</sup> In this regard, the findings of this study were consistent with the literature although the limited sample size and the absence of significance in the multiple regression analysis may limit the generalizability of the findings.

Patients were asked about their reasons for nonadherence, and 63 (67.7%) of the 93 patients deemed to have moderate or low level of adherence based on MMAS-4, cited forgetfulness. As much as this is a widely reported reason for OAET nonadherence, it should also be seen with caution. This is because it is likely that patients may find it easier and more convenient to report “forgetting” to take their medicines since it is a relatively more socially desirable answer than reporting an intentional action not to take them.<sup>[20]</sup> The other reasons reported by patients for OAET nonadherence were the long duration of therapy and attempts to avoid potential side effects. However, the proportions of patients citing these reasons were very low (19.4% and 15.1%, respectively) compared to those who blamed forgetfulness [Table 4].

Promotion of adherence to OAET should include teaching and counseling of patients to enhance their knowledge about the purpose and expected outcomes of medication treatment and their skills for self-management of side effects. Monitoring the adherence behavior of patients and provision of feedback are also important.<sup>[28]</sup> In line with this, patients in this study suggested a variety of strategies that they believed could be useful to improve their adherence to OAET. While the use of pillboxes to organize daily doses was the most widely suggested strategy, the rest of highly recommended strategies focused either on educational interventions to increase patients' awareness on their illness and the benefits and side effects of their medications or the use of face-to-face or telephone-based monitoring of their medication-taking patterns [Table 5].

## Limitations

Although this study has shed light on the level and determinants of OAET adherence among breast cancer patients in Singapore, the findings should be interpreted with limitations in mind. Most importantly, a small convenient sample was used. Hence, most of the factors that were known to influence OAET adherence in other studies were not found to be significant in our study. In addition,

the MMAS-4 has not been validated in patients with breast cancer despite being validated in a broad range of diseases. This might have had an influence on the data quality of this study. In this study, semi-structured interviews were used with the objective of obtaining the maximum amount of information about patients' reasons for nonadherence and their preferred strategies to improve adherence. In line with this, patients who preferred to talk in Mandarin were allowed to share their views despite using a semi-structured questionnaire prepared in English. About 40% of interviews were done this way, and this might have introduced some level of bias in the results of the study.

## Conclusion

This study documented suboptimal OAET adherence rate of 40.8% among breast cancer patients. Sociodemographic factors such as older age and being unemployed/retired and clinical- and medication-related factors such as having one or more comorbidities, being on aromatase inhibitors and being on three or more chronic medications were associated with high adherence in a univariate analysis. However, the presence of one or more comorbidities was identified as the only independent predictor of high adherence in a multivariate logistic regression analysis. The most widely cited reason for nonadherence was forgetfulness followed by the long duration of therapy and trying to avoid medication side effects. As patient education is at the heart of most interventions to enhance patient adherence, strategies developed should be targeted to increase patient medication knowledge and their skills for self-management. Different modes of delivery should also be considered, and future research should focus on establishing the effectiveness of such interventions in breast cancer patients.

## Acknowledgments

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## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

## References

- Chlebowski RT. Optimizing aromatase inhibitor integration into initial treatment strategies in postmenopausal women with hormone-receptor-positive early breast cancer. *Breast Cancer Res Treat* 2008;112 Suppl 1:25-34.
- Burstein HJ, Griggs JJ, Prestrud AA, Temin S. American society of clinical oncology clinical practice guideline update on adjuvant endocrine therapy for women with hormone receptor-positive breast cancer. *J Oncol Pract* 2010;6:243-6.
- Tamoxifen for early breast cancer: An overview of the randomised trials. Early Breast Cancer Trialists' Collaborative Group. *Lancet* 1998;351:1451-67.
- van de Velde CJ, Rea D, Seynaeve C, Putter H, Hasenburg A, Vannetzel JM, et al. Adjuvant tamoxifen and exemestane in early breast cancer (TEAM): A randomised phase 3 trial. *Lancet* 2011;377:321-31.
- Murphy CC, Bartholomew LK, Carpentier MY, Bluethmann SM, Vernon SW. Adherence to adjuvant hormonal therapy among breast cancer survivors in clinical practice: A systematic review. *Breast Cancer Res Treat* 2012;134:459-78.
- Hohneker J, Shah-Mehta S, Brandt PS. Perspectives on adherence and persistence with oral medications for cancer treatment. *J Oncol Pract* 2011;7:65-7.
- McCowan C, Shearer J, Donnan PT, Dewar JA, Crilly M, Thompson AM, et al. Cohort study examining tamoxifen adherence and its relationship to mortality in women with breast cancer. *Br J Cancer* 2008;99:1763-8.
- Makubate B, Donnan PT, Dewar JA, Thompson AM, McCowan C. Cohort study of adherence to adjuvant endocrine therapy, breast cancer recurrence and mortality. *Br J Cancer* 2013;108:1515-24.
- Geynisman DM, Wickersham KE. Adherence to targeted oral anticancer medications. *Discov Med* 2013;15:231-41.
- McCowan C, Wang S, Thompson AM, Makubate B, Petrie DJ. The value of high adherence to tamoxifen in women with breast cancer: A community-based cohort study. *Br J Cancer* 2013;109:1172-80.
- Chlebowski RT, Kim J, Haque R. Adherence to endocrine therapy in breast cancer adjuvant and prevention settings. *Cancer Prev Res (Phila)* 2014;7:378-87.
- Sedjo RL, Devine S. Predictors of non-adherence to aromatase inhibitors among commercially insured women with breast cancer. *Breast Cancer Res Treat* 2011;125:191-200.
- Wigertz A, Ahlgren J, Holmqvist M, Fornander T, Adolffson J, Lindman H, et al. Adherence and discontinuation of adjuvant hormonal therapy in breast cancer patients: A population-based study. *Breast Cancer Res Treat* 2012;133:367-73.
- Doggrell SA. Adherence to oral endocrine treatments in women with breast cancer: Can it be improved? *Breast Cancer Res Treat* 2011;129:299-308.
- National Registry of Diseases Office (NRDO). Singapore Cancer Registry Interim Annual Registry Report: Trends in Cancer Incidence in Singapore 2009-2013. Singapore: Health Promotion Board; 2014.
- Jara-Lazaro AR, Thilagaratnam S, Tan PH. Breast cancer in Singapore: Some perspectives. *Breast Cancer* 2010;17:23-8.
- Morisky DE, DiMatteo MR. Improving the measurement of self-reported medication nonadherence: Response to authors. *J Clin Epidemiol* 2011;64:255-7.
- Lavsa SM, Holzworth A, Ansani NT. Selection of a validated scale for measuring medication adherence. *J Am Pharm Assoc* 2011;51:90-4.
- Morisky DE, DiMatteo MR. Improving the measurement of self-reported medication nonadherence: Final response. *J Clin Epidemiol* 2011;64:258-63.
- Atkins L, Fallowfield L. Intentional and non-intentional

- non-adherence to medication amongst breast cancer patients. *Eur J Cancer* 2006;42:2271-6.
21. Ayres LR, Baldoni Ade O, Borges AP, Pereira LR. Adherence and discontinuation of oral hormonal therapy in patients with hormone receptor positive breast cancer. *Int J Clin Pharm* 2014;36:45-54.
  22. Osterberg L, Blaschke T. Adherence to medication. *N Engl J Med* 2005;353:487-97.
  23. Partridge AH, Wang PS, Winer EP, Avorn J. Nonadherence to adjuvant tamoxifen therapy in women with primary breast cancer. *J Clin Oncol* 2003;21:602-6.
  24. Lash TL, Fox MP, Westrup JL, Fink AK, Silliman RA. Adherence to tamoxifen over the five-year course. *Breast Cancer Res Treat* 2006;99:215-20.
  25. Barron TI, Connolly R, Bennett K, Feely J, Kennedy MJ. Early discontinuation of tamoxifen: A lesson for oncologists. *Cancer* 2007;109:832-9.
  26. Kimmick G, Anderson R, Camacho F, Bhosle M, Hwang W, Balkrishnan R. Adjuvant hormonal therapy use among insured, low-income women with breast cancer. *J Clin Oncol* 2009;27:3445-51.
  27. Baum M, Buzdar A, Cuzick J, Forbes J, Houghton J, Howell A, *et al.* Anastrozole alone or in combination with tamoxifen versus tamoxifen alone for adjuvant treatment of postmenopausal women with early-stage breast cancer: Results of the ATAC (Arimidex, Tamoxifen Alone or in Combination) trial efficacy and safety update analyses. *Cancer* 2003;98:1802-10.
  28. Irwin M. Theoretical foundations of adherence behaviors: Synthesis and application in adherence to oral oncology agents. *Clin J Oncol Nurs* 2015;19 3 Suppl: 31-5.