Adherence to adjuvant therapy in post-menopausal breast cancer patients: a review

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This review aimed to address the concept of adherence to adjuvant therapy in post-menopausal women. Thirteen studies were included in the review. Study quality was assessed using Critical Appraisal Skills Programme and CONSORT tools. Adherence to adjuvant medication was assessed using a variety of methods. Estimates of adherence rates to adjuvant therapies indicated that of the post-menopausal women prescribed adjuvant therapy, between 15% and 55% were adherent to tamoxifen from 1 to 5 years of follow-up, albeit two studies proposed adherence rates greater than 85%; these data may be flawed due to the methods of data collection. Between 31% and 73% of women were adherent to anastrozole, letrozole or exemestane from 1 year of treatment. These estimates of adherence are based on a variety of reported records including self-report. Current evidence on the assessment of adherence to adjuvant therapies in post-menopausal women indicate that the adherence rates of medication maybe suboptimal and therefore therapeutic efficacy is questionable and may increase the risk of cancer recurrence and reduce disease survival rates. Concerted research is needed to investigate adherence rates, examine patient health beliefs in the medication management of postmenopausal breast cancer patients and also develop new measures to assess adherence with medication.

Keywords: breast cancer, non-adherence, adjuvant therapy, oncology, side effects, medicines, post-menopause, older women.

INTRODUCTION

Medication-taking behaviour is an important concept particularly when the medication aims to support disease-free survival. This behaviour may be
determined by the balance between the perceived benefits and risks the patient associates with the prescribed medication. When the risks outweigh the benefits, non-adherence with medicines can result. Two forms of non-adherence are noted: intentional non-adherence and non-intentional non-adherence (Banning 2008). Both forms can occur independently and jointly. In the intentional form, patients intentionally refuse to adhere to medicine regimens often due to lack of medication education, disinterest in treatment regime, discordant health beliefs and perceptions of illness encouraging failure to accept the need for treatment, complexity of the drug regimen, but also side effects and cost (Partridge et al. 2003; Goldman et al. 2007) (Box 1). In the case of non-intentional non-adherence forgetfulness, cognitive impairment polypharmacy and psychosocial issues are commonly cited causes (Banning 2008). Age, particularly older age, may have a negative impact on adherence with medication due to presence of co-morbid conditions (Balkrishnan 1998).

Various forms of adherence with medication are noted: adherers, partial adherers, erratic and over users, dropouts and partial dropouts (Partridge et al. 2002). These different forms may relate to the dosing interval, drug regimen and perceived impact of treatment and benefit of prolonged therapy.

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**Box 1. Factors associated with poor adherence with medication**

- Complexity of medication regimen.
- Exposure to adverse effects of medicines.
- Deficient belief in value of prescribed medicines.
- Cognitive deficits and forgetfulness in relation to adhering to medication regimen and timing of medicine doses.
- Lack of awareness of therapeutic benefit of medicines.
- Poor relationship with prescriber & lack of education on importance of adherence patterns and possible risk reduction.
- Lack of awareness of possible adverse effects of medicines.
- Inadequate dialogue with prescriber on possible medication-related issues/concerns.
- Missed follow-up appointments.
- Inadequate follow-up.
Adherence rates with oral medication in oncology patients range from 20% to 100% and may depend on cancer type, age of study participants, the definition of adherence used in studies and the variety of measuring tools employed. These features can prohibit the comparability of studies and their outcomes and influence the efficacy of interventions used to assess adherence (Partridge et al. 2003; Ruddy et al. 2009). In post-menopausal women with oestrogen receptor (ER)-positive breast cancer, the ER modulator tamoxifen was, until recently, the most prescribed adjuvant endocrine therapy (Baum et al. 2002). Tamoxifen was recognised as a therapy that could reduce the risk of recurrence in the contralateral breast (Fisher et al. 1996; Jahanzeb 2007) and breast cancer mortality by up to 26% and maintain a post-treatment effect for up to 4 years [Early Breast Cancer Trialists’ Collaborative Group (EBCTCG) 2005]. This is important as the risk of recurrence of breast cancer is increased in women in 2.5 years of diagnosis (Kennecke et al. 2008). More recently, the third-generation aromatase inhibitors (AIs), anastrozole, exemestane and letrozole, have been shown to be superior to tamoxifen due to improved efficacy, rates of disease-free survival and incidence of contralateral breast cancer but also the delayed time to recurrence phase and quantity of metastases (Forbes et al. 2008; Ingle et al. 2009). Moreover, the development of non-breast malignancy such as endometrial cancer is lower with letrozole and anastrozole compared to tamoxifen (Jakesz et al. 2005). Disease-free survival appears to be greater with letrozole and anastrozole (Cella et al. 2006), but total survival remains similar especially with exemestane compared to tamoxifen (Coombs et al. 2004).

These AIs also possess a better safety profile than tamoxifen [Goss et al. 2005; Cella et al. 2006; Arimidex, Tamoxifen, Alone or in Combination (ATAC) Trialist’s Group 2008]. Although AIs such as anastrozole and letrozole produce similar side effects to tamoxifen, these may differ due to mode of action. Third-generation AIs reduce endogenous oestrogen by blocking the conversion of androgens to oestrogen via the aromatase enzyme, whereas tamoxifen competitively inhibits oestrogen binding to ERs (Baum et al. 2002; Ponzone et al. 2008).

The profile of side effects for both AIs and tamoxifen, albeit extensive, vary in intensity. Women administering adjuvant hormone therapy will experience hot flushes due to oestrogen deprivation but these may be less severe with AIs compared to tamoxifen (Coates et al. 2007). Oestrogen inhibition due to treatment with AIs and tamoxifen also increases osteoclastic activity, adversely influences bone remodelling and reduces bone density which can increase the risk
of fractures particularly in the lumbar spine and hips. Reports indicate that the fracture risk is equivalent for both AIs and tamoxifen (Jakesz et al. 2005; Arimidex, Tamoxifen, Alone or in Combination (ATAC) Trialist’s Group 2008). In addition, AIs are reported to cause pain and stiffness in joints (Coates et al. 2007).

The Early Breast Cancer Trialists’ Collaborative Group (EBCTCG) (2005) study and other studies indicated that AIs have a better profile than tamoxifen in terms of venous thromboembolic events (Jakesz et al. 2005). However, data on tamoxifen- and anastrozole-induced hypercholesterolaemia is conflicting with reported increments (Jakesz et al. 2005) and reductions in total cholesterol and lactate dehydrogenase (Tominaga et al. 2010). Moreover, oestrogen deprivation can increase menopausal symptoms such as alterations in weight, appetite, nausea, breast sensitivity, fluid retention, depression, vaginal discharge and bleeding, risk of endometrial cancer (Partridge et al. 2003; Fink et al. 2004). Perhaps, the more disturbing side effects are those involving genitourinary atrophy and its impact on sexual such as vaginal dryness and urinary function that can lead to a reduced quality of life in women (Winer et al. 2005). The plethora of side effects can possibly influence adherence with medication.

A drawback of prescribing AIs is the deficient evidence on the long-term toxicity and the optimal treatment duration (Colozza et al. 2008). Although oncologists may preferentially prescribe AIs in older women with ER-positive breast cancers due to increased efficacy and tolerability (Wong et al. 2010), adherence with medication is a prominent issue not only for AIs but also for tamoxifen irrespective of reported benefits of therapy (Chlebowski & Geller 2006). There is no guarantee of cancer-free survival (Atkins & Fallowfield 2006).

Current evidence on adherence with medication is limited (Chlebowski & Geller 2006). A recent systematic review identified that non-adherence to AIs was equivalent to that of tamoxifen circa 20–23% and 30–50% in studies over 4 years. The paucity of evidence in this area merits further investigation.

METHODS

This review aimed to provide a succinct account of the range of existing evidence that has explored and researched adherence with medication in postmenopausal
women receiving adjuvant therapy for breast cancer. This review provides insights on the range of evidence pertinent to women’s ability to adhere to adjuvant therapy.

Search strategy

The search strategy involved the use of the following databases: Pubmed, Medline, Cochrane Library, PsychoInfo, British Nursing Index and the search engine Advanced Google Scholar. Evidence was also generated from hand searching individual journals. A defined search strategy was undertaken using the following terms: postmenopausal women, older women, breast cancer, early breast cancer, adjuvant therapy, tamoxifen, anastrozole, aromatase inhibitors, breast cancer patients, adherence and compliance. Search terms were used in combination. Research studies, exploratory studies, quantitative research designs, cohort studies and randomised controlled trial (RCT) were included in the review. To include an appraisal of adherence research studies, searches were restricted to papers written in English that addressed adherence with adjuvant medication in post-menopausal breast cancer patients. The search involved papers published between January 1999 and March 2011 as it was believed that most relevant studies would be found within this period. Evidence was drawn from international and UK literature in an attempt to illustrate the complexity and depth of the subject and the global nature of the subject matter.

Selection criteria

Using a combination of the above search terms, a total of 817 papers were identified electronically and by hand searching. Abstracts and titles were scanned for relevance. Papers that did not address adherence with adjuvant therapy in post-menopausal breast cancer patients were excluded. Also replicates identified by the search engine or database were excluded. RCTs of short duration less than 3 months were also excluded as this short time scale would be insufficient to assess adherence to medication. Full-text papers not written in English were also excluded (Fig. 1).
In total, 47 papers were selected for in-depth evaluation by initial reading and appraising the relevance and research design in relation to identified research outcomes. As this study focused on older women, preference was given to studies that included women aged 50 years and older; however, in four studies the age range was variable and included women younger than 50 years (Grunfeld et al. 2005; Atkins & Fallowfield 2006; Partridge et al. 2008; Sedjo & Devine 2011). These studies were felt to be relevant and made a significant contribution to the study so were included. This decision was also supported by the paucity of studies in this area of research.
Studies were excluded if they failed to address how adherence was measured or did not clearly identify the age range of patients or accurately discuss the research design. Of these, 13 studies emerged that examined adherence with adjuvant medication in post-menopausal women and met the selection criteria. These included: one RCT, one qualitative study, seven surveys, one longitudinal study and three cohort studies. The details of individual studies are presented (Table 1).

Data analysis

In this review, the CONSORT scoring was used to analyse the quality and rigour of RCTs. Using this scoring system, RCTs were assessed for quality using the 25-item checklist. The checklist provides an indication of the factors that were considered in terms of the trial design, sample size, research outcomes and limitations (CONSORT 2010) (Table 2).

Papers were appraised using a version of the Critical Appraisal Skills Programme (CASP) (1998). Using this method, studies were excluded if they were judged to be insufficiently focused on medication adherence or did not focus specifically on post-menopausal women. The design of studies included in this exercise varied from qualitative study using an interpretive design, cohort, longitudinal studies and questionnaire and database surveys. As studies differed in their intervention, outcomes measured, time scale involved and results, no meta-synthesis was possible. For this reason, a narrative synthesis of the evidence was undertaken. This allowed a subjective analysis of the relative merits of papers specific to the aims of the review and to what extent these were addressed and their contribution to adherence research. Each paper consistently identified and discussed issues related to the measurement of and tools used to measure adherence and also provided data on adherence rates with discussion on factors that influenced adherence. From these salient aspects, three themes emerged.

RESULTS

Studies that reported on measures of non-adherence with adjuvant medication were heterogeneous in terms of their quality, duration, patient population, measurement of adherence, outcome measures employed and assessment of
follow-up. The three emergent themes included the definitions and measurement of adherence, estimates of non-adherence and factors perceived to influence non-adherence.

Definitions and measurement of adherence

Adherence was not defined in all papers. In this review, adherence to drug therapy was defined ‘as the extent to which a patient adheres to a recommended dosage and intake interval’ (Ziller et al. 2009, p. 432). Self-reported and prescription controlled adherence have been used previously as measures to assess adherence (Partridge et al. 2003, 2008; Ziller et al. 2009). Prescription controlled adherence is also referred to as the medication possession ratio. This is the quotient of actual daily doses purchased to the recommended number of days over a specified time period. The most acceptable value for quantity for number of days of filled prescriptions is 80% (Partridge et al. 2003; Ziller et al. 2009). Patients are considered to be non-adherent if the medication possession ratio is ≤80 (Partridge et al. 2003).


Estimates of non-adherence

The rates of non-adherence for women prescribed either tamoxifen or anastrozole reported in studies ranged from 10.8% to 85%. These include Atkins and Fallowfield (2006) (55%), Demissie et al. (2001) (15%), Fink et al. (2004)
(17%), Ell et al. (2009) (41%), Hershman et al. (2011) (28%), Lash et al. (2006) (31%), Güth et al. (2008) (10.8%), Owusu et al. (2008) (49%), Partridge et al. (2003) (21–32% at year 1, 32–50% by year 3), Sedjo and Devine (2011) (20.1% anastrozole, 25.3% letrozole, 30.6% exemestane and 37% tamoxifen) and Ziller et al. (2009) (20% tamoxifen and 31% anastrozole). The variation in these figures may be a reflection of the methods used to measure adherence. For example, reports on adherence to tamoxifen indicate that rates of non-adherence were most prevalent in non-Caucasian women (OR 1.62, 95% CI 1.26–2.09), women aged 75 to 84 years (OR 2.61, 95% CI 1.30–5.23) and in mastectomy patients (OR 1.64, 95% CI 1.33–2.02) (Partridge et al. 2003).

Partridge et al.’s adherence rates cited in 2003 in older women and mastectomy patients concur with more recent studies (Owusu et al. 2008). Findings indicate that 49% of women with ER-positive breast cancer are more likely to be non-adherent with medication. Of these, 20% were in the 75 to 80 age group [hazards ratio (HR) 2.02, 95% CI 1.53–2.66] or patients with a history of mastectomy (HR 1.62, 95% CI 1.18–2.22) (Owusu et al. 2008). Older women aged 75+ years also featured as a significant group that can be non-adherent with tamoxifen (Demissie et al. 2001; Partridge et al. 2003; Lash et al. 2006).

Adjuvant therapy is normally prescribed for 5 years. Two studies reported high rates of non-adherence with anastrozole in 4 years of therapy (Grunfeld et al. 2005, 46%; Partridge et al. 2008, 32–50%). More recently, Ziller et al. (2009) reported non-adherence rates for tamoxifen of 20% and anastrozole of 31% between 1 and 4 years of therapy. The rates for anastrozole concur with those of Partridge et al. (2008).

A recent questionnaire survey found that 46% of women reported non-adherence within 2 years of therapy (Grunfeld et al. 2005). This concurs with previous reports that by 4 years of treatment, non-adherence rates were as high as 50%. More recent reports indicate that mean adherence decreased each year from 78% in year 1 to 66–50% by year 3 (Partridge et al. 2008). These data concur with the percentage reduction in adherence rates (17%) identified after the first and second years of therapy (Fink et al. 2004) and also an annual 10% reduction in adherence rate (Güth et al. 2008; Owusu et al. 2008). Reasons attributed to the annual reduction in rates include: side effects, the extension of menopausal symptoms, fear of adverse effects and the development of non-breast cancer second tumours (Demissie et al. 2001; Grunfeld et al. 2005). Relevant incidence
data for the discontinuation of tamoxifen therapy due to development of side effects (HR per side effect 1.2, 95% CI 0.97–1.5) were: quantity of existing medications (HR 0.90, 95% CI 0.81–0.99) and addition of new medications (HR 1.2, 95% CI 1.0–1.4) (Lash et al. 2006).

Factors influencing non-adherence

Alternative contributing factors to non-adherence with medication included a lack of interest and a dislike of taking medicines. In such cases, younger women and those aged under 57.6 years were intentionally non-adherent with their medication, often refusing to adhere to treatment regimens. This concurs with published data (Partridge et al. 2003; Atkins & Fallowfield 2006). The occasional and intermittent skipping of drug doses was often related to lower health scores, implied reduced locus of control in relation to health concerns (Atkins & Fallowfield 2006). Women also perceived a lack of benefit from medicines which outweighed the risks associated with treatment (20% of women), forgetfulness (18% of women) (Grunfeld et al. 2005) but also negative health beliefs about the value and importance of therapy (3.0, 95% CI 1.6–5.6) (Fink et al. 2004). Non-adherence with medication was also common in women with up to four positive lymph nodes (OR 2.5, 95% CI 1.0–6.3) (Fink et al. 2004). In this study, the characteristics of women differed from most cited studies; women were predominantly Caucasian, well educated, mean age of 60 years, three to four co-morbidities and negative health beliefs. These factors may have had an impact on non-adherence data. Sedjo and Devine (2011) also reported a higher rate of non-adherence in women with secondary breast cancer and existing co-morbidities such as depression, heart disease and diabetes but also in younger women.

Only one study acknowledged the form of non-adherence experienced by patients (Atkins & Fallowfield 2006). The mean age of non-adherent women was 59.4 ± 11.534 years. Non-adherence with tamoxifen was identified in 55% of patients. Of these, 15% were intentionally non-adherent and 85% non-intentionally non-adherent. By comparison of the patients prescribed anastrozole, 61% were non-adherent with medication. Of these, 18% of patients were intentionally non-adherent and 82% non-intentionally non-adherent. In summary, 83% of the non-intentional non-adherers forgot to take their medication compared to 17% of the intentional non-adherers who chose not to administer their prescribed medication (Atkins & Fallowfield 2006).
DISCUSSION

In the studies examined, the ability of post-menopausal breast cancer patients to adhere to adjuvant therapy varied. Adherence rates for tamoxifen varied from 15% to 85% (50–77%) [Demissie et al. 2001 (83%); Partridge et al. 2003, 2008 (50–85%); Fink et al. 2004 (83%); Grunfeld et al. 2005; Atkins & Fallowfield 2006 (45%); Lash et al. 2006 (69%); Owusu et al. 2008 (51%); Hershman et al. 2011 (39.2%); Sedjo & Devine 2011 (63%); Ziller et al. 2009 (80%)]. Rates for anastrozole ranged from 27.7% to 81% [Atkins & Fallowfield 2006 (39%); Partridge et al. 2008 (72–81%); Ziller et al. 2009 (69%); Hershman et al. 2011 (27.7%); Sedjo & Devine 2011 (69.4–79.3% for AIs)]. The data for tamoxifen concur with reported estimates identified in clinical trials of less than 4-year duration; however, the adherence rate estimate for anastrozole varies from published accounts (Chlebowski & Geller 2006). In trials and studies of 4 years and longer, non-adherence rates with tamoxifen increased to 30–50% (Hershman et al. 2011). These data concur with published studies (Partridge et al. 2003). What is unclear is whether clinical trial data also pertain to specific categories of older women, for example, those aged 75 years and older. The difference in adherence rates for tamoxifen and anastrozole may be due to the onset of, and severity of, drug-related side effects. Cella et al. (2006) found that women treated with anastrozole reported less dizziness and vaginal discharge compared to tamoxifentreated groups of women.

In this review, the annual percentage reduction in adherence ranged from 10% to 23% [Partridge et al. 2003, 2008; Fink et al. 2004 (10.8%); Owusu et al. 2008; Güth et al. 2008 (10%); Sedjo & Devine 2011]. This range is particularly high and the validity of the results may be subjected to potential flaws, especially the deficient detail on how adherence was measured and the relative accuracy of measurement. Studies in this review can be differentiated on the basis of their measurement of adherence and their accompanying validity, particularly those studies that employed self-assessment measures such as patient recall, medical records, pharmacy records, telephone interviews, retrospective documentary analysis, prescriber recall assessment but also patient interviews (Demissie et al. 2001; Partridge et al. 2003, 2008; Fink et al. 2004; Grunfeld et al. 2005; Atkins & Fallowfield 2006; Lash et al. 2006; Güth et al. 2008; Ziller et al. 2009). Ziller et al.’s retrospective study employed a self-assessment measure in the form of a questionnaire to measure non-adherence supported by medical records and...
prescriber recall assessment. Findings indicate incongruence between what patients recall as 100% adherence and prescription refill records of 80% of patients on tamoxifen and 69% on anastrozole (Ziller et al. 2009). Limitations of using patient and prescriber recall as data collection tools is the subjective nature of the process with a tendency to over-estimate adherence; increased possibility of the ‘Hawthorne effect’ on outcome of data collected, subjective memory lapse and the veracity of responses may endorse data inaccuracies as participants may have no desire to acknowledge non-adherence due to choice (Horne & Weinman 1999). Measuring medication adherence is restricted due to the lack of gold standard measurement tool (Banning 2009). Novel approaches to measuring adherence with medication are needed.

Given the support for use of AIs anastrozole, letrozole and exemestane to treat early-stage breast cancer in postmenopausal women (Jakesz et al. 2005; Coates et al. 2007; Carpenter 2008; Colozza et al. 2008), more attention is needed to address adherence with medication in this group of patients. Although oncologists may recognise that adherence and patient persistence with medication is a problem, patient assessment in these issues is ad hoc (Davidson et al. 2007).

Current adherence research acknowledges that communication is an important aspect of the prescriber/patient consultation (Silliman et al. 2002). Improvements can be made on patient medication management, discussion of the long-term benefits of medicines, recognition of, and discussion on, drug-induced side effects, both current and additional medicines and impact of patient lifestyle on efficacy of medicines (De Jong et al. 2008). Also worthy of consideration is the acknowledgement of patient’s health beliefs; the impact of a dislike of taking medicines particularly in younger women, and locus of control and their impact on medication-related decision making are important attributes of medication adherence (Siminoff & Fetting 1991; Braddock et al. 1997). These issues are especially important in intentionally non-adherent patients where perceptions of having less influence over health decisions and an underpinning lower internal locus of control may foster non-adherent behaviour (Horne & Weinman 1999). Patients with positive views about medication are more likely to continue with their therapy (Lash et al. 2006; Ruddy et al. 2009; Hadji 2010). This requires a good rapport between the patient and the prescriber supported by continuous follow-up procedures (Fink et al. 2004).
Box 2. Measures to improve adherence

Promote better interaction and dialogue with breast cancer patients through openness and communication.

Encourage the development of a therapeutic alliance with breast cancer patients in order to promote improved communication.

Enhance collaborative decision making by providing patients with choices regarding drug therapies available to them.

Provide breast cancer patient with informed medication management education on the risks and benefits of prescribed medicines but also the importance of adhering to regimens.

Provide regular follow-up appointments that are at a time that suit patients.

Additional measures that can be implemented to improve adherence with medication include: improving medication education with specific reference to medication-related side effects, and their recognition (Davidson et al. 2007; Body 2010) (Box 2). The development of side effects is an indication of adherence. It is also important to discuss the benefits associated with tamoxifen therapy, for example, protection against fractures involving weight-bearing joints which should be supported by dietary advice and possible supplementation with calcium, vitamin D and bisphosphonates (Gail et al. 1999; Hadji 2010). Also it is important to consider the potential risks of increased risk of deep venous thrombosis, pulmonary embolism, endometrial cancer as these conditions increase with age (Gail et al. 1999). Patient education to improve adherence is an important aspect of treatment and an area of ongoing research.

Patients should be involved in conversations on treatment and in shared decision making in relation to the selection of medicines. This will enhance adherence through informed decision making the acknowledgement of treatment preference and selection of medicines from an informed stance. There is also a need to consider the psychological adjustments that women have to make. Women may have successfully completed chemotherapy and surgery but are reminded on a daily basis that the risk of recurrence requires them to administer medication even though they may feel healthy (Atkins & Fallowfield 2006). In this instance, counselling can be offered as appropriate (Body 2010).

Adherence with medication can also be adversely influenced by financial commitments. In the USA, the cost of medicines is a key concern with many
women having difficulties purchasing their medicines (Goldman et al. 2007). Limitations of this review are noted. It is important to note that when researching adherence with medication, one needs to consider that in clinical trial data reported rates of adherence may be higher than those reported in clinical settings and contribute to therapeutic failure (Hadjì 2010). The studies included in the review employed a variety of research designs; the cohort study approach was the most common design used and time scales varied from 1 to 5 years. The shorter time scales (1–2 years) may provide an inaccurate picture of adherence history. Data collection approaches differed, and included questionnaire, medical records and self-report measures. The efficiency of these data collection approaches have drawbacks of poor response rates, retrospective and possibly incomplete accounts of records, and possible overestimations of adherence rates. Only Lash et al. (2006) attempted to triangulate the results using both questionnaire and interview approaches to authenticate the data. Although there is no gold standard approach to measure adherence, studies should employ a combination of data collection measures to provide an accurate assessment of adherence patterns.

In addition, there is also a need to examine the impact of social factors that may adversely influence adherence such as the time required by medical professionals to adequately explain important drug regimens to women, the significance of the use of language during consultations and the impact of poverty, time management and social pressures and how they influence adherence with medication (Davidson et al. 2007).

It is also important to review the profile of women most likely to not adhere to adjuvant therapy. Research to date suggests that older women can be segmented in relation to adherence patterns. Women with poorer adherence rates tend to be aged 55–64 years and >75 years with ER-positive breast cancer (Demissie et al. 2001; Partridge et al. 2003; Fink et al. 2004; Guth et al. 2008). Even though women aged 75+ years are more likely to have good emotional health, may report less drug-related side effects and may engage with physicians to discuss drugs and drug-related effects, they are equally likely to be non-adherent with medication (Demissie et al. 2001). Profiling of women is difficult due to the deficiencies in measuring adherence and the absence of models to explain adherence (Fink et al. 2004).

CONCLUSION
From a global perspective, breast cancer is the most common cancer in post-menopausal women and requires continuous treatment. A key message from this review is that the administration of adjuvant therapies in postmenopausal women is suboptimal. The reasons why some women fail to adhere to their hormonal medication is unclear. There is a paucity of research on the incidence and patterns of non-adherence with long-term adjuvant therapy in post-menopausal women (Hadji 2010). This area of research requires more concerted action to identify current trends in non-adherence with adjuvant therapies, to clarify patient health beliefs, perceptions of illness and support strategies needed, but also to increase disease-free survival of post-menopausal breast cancer patients through the promotion and maximisation of the benefits to be gained from adherence with adjuvant therapy.

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Arimidex, Tamoxifen, Alone or in Combination (ATAC) Trialist’s Group (2008) Effect of anastrozole and tamoxifen as adjuvant treatment for early-stage breast cancer: 100 month analysis of the ATAC trial. The Lancet Oncology 9, 45–53.


Table 1. Published studies of adherence to oral adjuvant therapies in post-menopausal women with early/advanced-stage breast cancer

<table>
<thead>
<tr>
<th>Author</th>
<th>Sample Size</th>
<th>Age Group</th>
<th>Design</th>
<th>Approach</th>
<th>Adherence rate/tamoxifen/anastrozole</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lash et al. 2006</td>
<td>462</td>
<td>65-79</td>
<td>Survey</td>
<td>Questionnaire + interview</td>
<td>31% at 2-year follow-up tamoxifen</td>
</tr>
<tr>
<td>Demissie et al. 2001</td>
<td>303</td>
<td>55-74</td>
<td>Survey</td>
<td>Medical records</td>
<td>15% at 3-year follow-up tamoxifen</td>
</tr>
<tr>
<td>Grunfeld et al. 2005</td>
<td>110</td>
<td>38-65</td>
<td>Survey</td>
<td>Questionnaire</td>
<td>46% at 2-year follow-up tamoxifen</td>
</tr>
<tr>
<td>Owusu et al. 2008</td>
<td>961</td>
<td>65-80</td>
<td>Survey</td>
<td>Questionnaire</td>
<td>49% before tamoxifen 5 years</td>
</tr>
<tr>
<td>Guth et al. 2008</td>
<td>325</td>
<td>60-75</td>
<td>Survey</td>
<td>Medical records</td>
<td>31% from 1 to 5 years tamoxifen</td>
</tr>
<tr>
<td>Ell et al. 2009</td>
<td>487</td>
<td>50-63</td>
<td>RCT</td>
<td>Interviews, QoL assessment + questionnaire</td>
<td>32% at 1-year follow-up tamoxifen</td>
</tr>
<tr>
<td>Atkins and Fallowfield 2006</td>
<td>131</td>
<td>32-88</td>
<td>Mixed method</td>
<td>Interviews + questionnaire</td>
<td>55% tamoxifen follow-up, 61% anastrozole at 1 year</td>
</tr>
<tr>
<td>Fink et al. 2004</td>
<td>597</td>
<td>65-80</td>
<td>Cohort study</td>
<td>Medical records + telephone interviews</td>
<td>17% at 1-year tamoxifen</td>
</tr>
<tr>
<td>Partridge et al. 2003</td>
<td>2,378</td>
<td>66-84</td>
<td>Cohort study</td>
<td>Prescription refill records</td>
<td>23% at 1-year follow-up tamoxifen</td>
</tr>
<tr>
<td>Partridge et al. 2008</td>
<td>12,391</td>
<td>35-65</td>
<td>Longitudinal study</td>
<td>Prescription refill records</td>
<td>50% at year 4 follow-up tamoxifen</td>
</tr>
<tr>
<td>Ziller et al. 2009</td>
<td>100</td>
<td>65-72</td>
<td>Survey</td>
<td>Self-report prescription refill record</td>
<td>23% &amp; 50% at years 1 &amp; 4 tamoxifen, 31% for anastrozole</td>
</tr>
<tr>
<td>Sodjo &amp; Devinc 2011</td>
<td>13,593</td>
<td>45-63</td>
<td>Cohort study</td>
<td>Prescription refill records</td>
<td>73% at 1-year AI</td>
</tr>
<tr>
<td>Hershman et al. 2011</td>
<td>8,769</td>
<td>50-65</td>
<td>Survey</td>
<td>Automated pharmacy records</td>
<td>49% at 4.5 years for tamoxifen, 72% AI</td>
</tr>
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AI, third-generation aromatase inhibitors (anastrozole, letrozole, exemestane); QoL, quality of life; RCT, randomised controlled trial.
Table 2: Checklist of information to include when reporting randomised trials and surveys

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