

# Breast cancer patients' experiences of adherence and persistence to oral endocrine therapy: A qualitative evidence synthesis

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## ABSTRACT

**Purpose:** Adjuvant endocrine therapy (AET) significantly reduces the risk of breast cancer recurrence and mortality in women with hormone receptor (HR+) breast cancer. Despite the documented survival benefits with AET, non-adherence and non-persistence remains a significant problem. This systematic review of qualitative research aimed to synthesise breast cancer patients' experiences of adherence and persistence to oral endocrine therapy.

**Methods:** The ENTREQ guidelines were followed. A systematic search strategy was performed across eleven electronic databases (Embase, Cinahl, Pubmed, Psycinfo, Proquest, Lenus, Scopus, Web of Science, Rian.ie, ETHOS e-theses online, DART Europe). Thomas and Harden's three-stage approach to thematic analysis was undertaken on the findings of all included studies. Confidence in the findings were reviewed using GRADE-CERQual.

**Results:** Twenty-four qualitative studies were included in the synthesis. Three analytic themes were identified (We don't have an option; the side effects are worse than the disease; help us with information and support). Adherence was often driven by women feeling they had no option and a fear of cancer recurrence. Persistence was helped with support and information. Non-adherence and non-persistence were associated with debilitating side effects, inadequate information and lack of support.

**Conclusions:** Adherence and persistence to AET was often suboptimal among breast cancer patients. Women commonly felt isolated and neglected as a result of insufficient information and support from healthcare professionals. If women are to persist with AET, primary care providers should be aware of the facilitators and barriers to adherence, and they should be knowledgeable in symptom management strategies.

## 1. Introduction

Breast cancer is the most common cancer in women worldwide and is the main cause of death among women living in under developed regions (Globocan, 2012). However, improvements in the screening process and advances in treatment, including the use of adjuvant endocrine therapy (AET) has resulted in reduced mortality (Berry et al., 2005). AET is used to prevent possible recurrence in women with hormone receptor-positive breast cancer (Lambert et al., 2018a). Standard therapies for hormone receptor-positive breast cancers include selective estrogen receptor modulators (SERMs) (tamoxifen) or aromatase inhibitors (AIs) (anastrozole, letrozole and exemestane) which inhibit estrogen synthesis (Ekinci et al., 2018). Clinical

guidelines stipulate that this therapy be taken daily for a treatment period of at least five, and up to ten years, depending on risk, to achieve optimal benefit (Early Breast Cancer Trialists' Collaborative Group, 2005, 2011). There is an increased risk of breast cancer recurrence and mortality among women with reduced hormonal exposure, which can be caused by non-persistence or non-adherence of AETs (Hershman et al., 2011). Despite the documented clinical efficacy of AETs, non-persistence and non-adherence are common practices among women receiving hormonal therapy (Cahir et al., 2015; Paranjpe et al., 2019).

The terms adherence and persistence have varying definitions. Adherence can be defined as a degree of conformity to the prescribed treatment/medication in terms of timing, dosage and frequency, and persistence can be referred to as the continuation of treatment from

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initiation to discontinuation (Wassermann and Rosenberg, 2017). Non-adherence and non-persistence to endocrine therapy is influenced by a number of factors (Paranjpe et al., 2019). It can be related to the side effects of these drugs which can have a negative impact on the patient's quality of life (Barlow et al., 2013). Tamoxifen is associated with a variety of menopausal side effects, such as night sweats, hot flushes, vaginal dryness, weight gain, loss of libido and fatigue (Moon et al., 2017). Tamoxifen is often prescribed to young, pre-menopausal women who experience premature menopause and infertility which are contributing factors to non-adherence and non-persistence among these women (Pellegrini et al., 2010). Side effects of tamoxifen therapy is reported as the primary reason for non-adherence (Grunfeld et al., 2005). Other factors which can contribute to intentional non-adherence to AETs are beliefs about cancer, social support and lack of information (Cluze et al., 2012). Aromatase inhibitors (AIs) are often prescribed to post-menopausal women with hormone receptor positive breast cancer (Mao et al., 2013). AI associated arthralgia (joint pain) can result in sub-optimal adherence and early discontinuation among this patient group (Dowling et al., 2017).

A scoping search was initially undertaken to help guide the focus of this review and to determine the amount and type of evidence already published, as recommended by Flemming et al. (2019). Extensive research on this topic have focused on measuring non-adherence and non-persistence in terms of the number of pills taken and its impact on recurrence of breast cancer and mortality (Murphy et al., 2012). However, these types of studies fail to provide an in-depth understanding into the process of non-adherence and non-persistence (Verbrugghe et al., 2017). A scoping search revealed a number of recently published qualitative studies on women's adherence, suggesting increasing interest on this topic. Qualitative research provides an insight into the lived experiences and beliefs of the women prescribed AETs, identifies reasons for non-adherence and non-persistence and what motivates these women to adhere and persist with the therapy (Moon et al., 2017). Moreover, qualitative research provides a better understanding of adherence practices among breast cancer patients prescribed AETs and provides health care professionals with a deeper understanding and contribute to the development of interventions to increase adherence and persistence rates and improve patients' quality of life (Moon et al., 2017).

## 2. Aim

The aim of this qualitative evidence synthesis (QES) was to identify and synthesise all the available qualitative research relating to breast cancer patients' experiences of adherence and persistence to oral endocrine therapy. The individual qualitative studies in QES expose a human depth and richness of experience. The subsequent evidence synthesis presents themes across time and geographical distance which serve to inform oncology nursing practice and education. Moreover, comprehensive synthesis of qualitative research can also be useful to identify research gaps (Sandelowski and Barroso, 2010; Tong et al., 2016) thus providing direction for future research.

## 3. Methods

This qualitative evidence synthesis adopted Thomas and Harden's (2008) method of thematic synthesis. The ENTREQ statement was followed in reporting this review (Tong et al., 2012).

### 3.1. Search strategy

The PICO framework (Population, Interest, Context) was used to guide the search strategy, informed by all possible terms of the study's key words which included "breast cancer", "adjuvant endocrine/hormonal therapy", "adherence and persistence" and "qualitative" and developed by the third author, a medical librarian (Table 1). Eleven

databases were searched (CINAHL, Embase, Psych Info, Pubmed, Lenus, SCOPUS, Web of Science, Rian.ie, Dart Europe, Ethos and Proquest). To avoid publication bias, unpublished theses were included in the search. Mixed method studies were included in this review if the qualitative data supported that of the inclusion criteria. No year limit was set but language was limited to English. The initial search retrieved 465 references. A subsequent quality control check of Google scholar identified 3 additional studies which were all exported into the reference management software, Endnote X9.

### 3.2. Screening and study selection

Following removal of duplicates in Endnote, 354 studies were imported into Covidence (Covidence, 2018), an online blind screening and data extraction tool. Title and abstract screening was undertaken independently by the first and second authors. Papers were included if they met the following inclusion criteria:

- 1 Studies in the English language only.
- 2 Qualitative and/or mixed method studies with primary data to include personal experiences or perceptions, interviews, direct observation, focus groups, participating action research, grounded theory, phenomenology, ethnography, content analysis, thematic analysis, narrative analysis, generic qualitative studies.
- 3 Studies involving adult patients  $\geq 18$  years.
- 4 Studies to include breast cancer survivors who have been prescribed and commenced on adjuvant endocrine/hormonal therapy after completing primary treatment for breast cancer.
- 5 Studies including both selective estrogen-receptor modulators (Tamoxifen) and aromatase inhibitors (Anastrozole, Letrozole, Exemestane).
- 6 Studies addressing the adherence and non-adherence practices of adult patients undergoing oral adjuvant endocrine/hormonal therapy.
- 7 Studies addressing patients' experiences/perceptions of adherence and persistence to oral adjuvant endocrine/hormonal therapy.

Forty seven studies meeting the inclusion criteria were subjected to full text screening by the first and last authors. Disagreements were resolved through discussion, and 23 studies were excluded from the review (Fig. 1 and Table 2).

### 3.3. Appraisal process, data extraction and data analysis

Data analysis was undertaken by the first and last authors guided by Thomas and Harden's (2008) method of thematic analysis. Thematic synthesis combines approaches from both grounded theory and meta-ethnography (Barnett-Page and Thomas, 2009). Line-by-line coding of each study's findings (i.e. study participants' verbatim accounts and researchers' interpretations) was initially undertaken by the first author following which the generated codes were re-examined and compared against codes across all the studies. The second stage of the process involved the first and last author grouping the correlated codes into logical descriptive themes. In the third stage of data synthesis, the agreed descriptive themes were used by the first and final authors to answer the review question and the development of three analytical themes.

Quality appraisal of each study was undertaken by the first and last authors using the Critical Appraisal Skills Programme, 2017 (CASP) (Table 3). The GRADE-CERQual assessment was also undertaken to illustrate the level of confidence in the review findings (Table 4). This process involved the first and last author assessing each of the four CERQual components (methodological limitations, relevance, coherence and adequacy) and agreeing on their confidence on each review finding in terms of high, moderate, low or very low (Lewin et al., 2015).

**Table 1**

Terms used for search strategy across databases using elements of review question. PICO (Population, Phenomenon of Interest, Context).

Patient Population	Interest	Context
Breast cancer patients on adjuvant endocrine/hormonal therapy	Adherence and persistence	Experiences Qualitative
Breast Cancer	Adherence	Experience
Breast Malignancy	Compliance	Behaviors
Breast Neoplasm	Conformance	Behaviours
Breast Carcinoma	Patient compliance	Perceptions
Adjuvant breast cancer	Medication adherence	Views
Breast cancer survivor	Medication compliance	
Breast cancer survivorship	Compliance with medication regimen	
Survivor	Compliance with therapeutic regimen	
Survivorship	Non-adherence	
Breast cancer stage I Breast cancer stage II	Non-compliance	
Breast cancer stage III Primary breast cancer	Non-conformance	
Adjuvant endocrine therapy	Persistence	
AET	Non-persistence	
Adjuvant therapy		
Endocrine therapy		
Adjuvant hormonal therapy		
Hormonal therapy		
Adjuvant anti-hormonal therapy		
Adjuvant anti-hormone therapy		
Anti-hormone therapy		
Anti-hormonal therapy		
Aromatase inhibitors		
AI		
Anastrozole		
Arimidex		
Exemestane		
Aromasin		
Letrozole		
Femara		
Hormone-receptor positive		
HR+		
Estrogen receptor positive		
ER positive		
ER+		
Oestrogen receptor positive		
Tamoxifen		
Progesterone receptor positive		
PR positive		
PR+		
Selective estrogen receptor modulators		
SERMs		
Selective oestrogen receptor modulators		

## 4. Synthesis of findings

### 4.1. Included studies

Twenty four studies were included for the final synthesis (Table 2). The studies were published between 2010 and 2018 from eight different countries across three continents, with most originating from the USA. Sample sizes within the individual studies ranged from 11 to 43, with a total sample of 577 women interviewed, excluding the sample of women who posted messages on websites in one study (Mao et al., 2013).

Three analytical themes were identified, as follows: 'We don't have an option'; 'the side effects are worse than the disease' and 'help us with information and support'.

### 4.2. We don't have any option

Women initially accepted AET and viewed this phase as the next necessary step to avoid cancer recurrence and death. Although the decision was ultimately theirs, they felt they had no choice based on the recommendations from health care professionals and their own personal fear of recurrence.

Women embarked on this new treatment phase with feelings of

belief and trust in their physicians, and some women's trust and confidence in their oncologists influenced their decision to take AET (Bluethmann et al., 2017; Brett et al., 2018; Farias et al., 2017; Harrow et al., 2014). Women also felt obligated to take AET and were given no choice by their physicians (Bluethmann et al., 2017; Humphries et al., 2018; Iacorossi et al., 2018; Moon et al., 2017; Verbrugge et al., 2017; Wickersham et al., 2012). Moreover, encouragement from physicians regarding AET persistence was identified by some women as important in their decision to discontinue AET or not (Lambert et al., 2018b, p. 7). In addition, women's perceived risk was also based on the information provided to them by health care professionals (Harrow et al., 2014; Humphries et al., 2018; Lambert et al., 2018b). Based on this information, women who perceived themselves as low risk were more inclined to discontinue AET early (Lambert et al., 2018b, p.6).

Women's views on their necessity to take AET were also strongly influenced by their fear of cancer recurrence (Bourmaud et al., 2016; Brauer et al., 2016; Cahir et al., 2015; Cheng et al., 2017; Harrow et al., 2014; Humphries et al., 2018; Hurtado-de-Mendoza et al., 2018; Iacorossi et al., 2018; Lambert et al., 2018b; Moon et al., 2017; Van Londen et al., 2014). AET was described as "a life line" (Cahir et al., 2015, p. 3120) and would "keep the boogie man [cancer] away" (Wickersham et al., 2012, p.3). Weighing-up the benefits of taking AET against the risks and associated side effects was an approach taken by

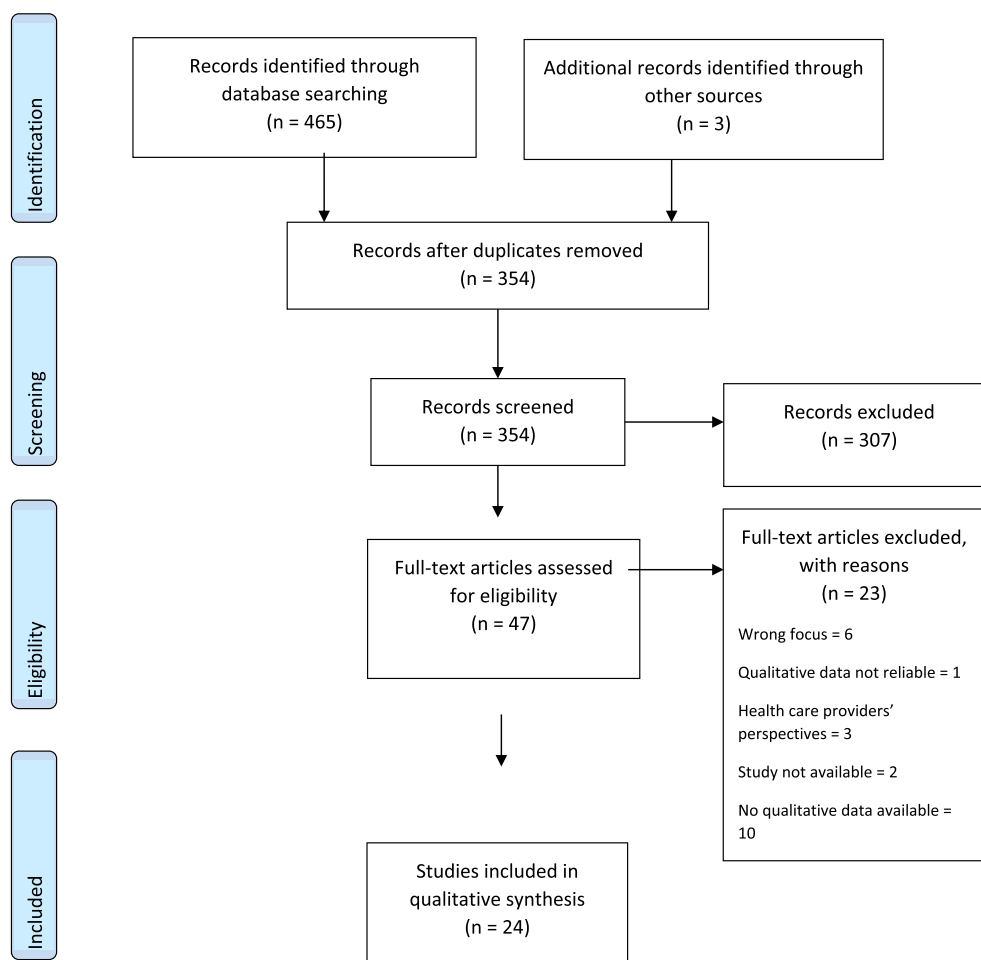


Fig. 1. Prisma flow diagram.

some women (Bluethmann et al., 2017; Cahir et al., 2015; Moon et al., 2017; Wen et al., 2017). Other women were influenced by guilt and anticipated regret, questioning themselves if their cancer returned had they refused AET (Cahir et al., 2015; Humphries et al., 2018). However, some women believed that taking AET meant they were being active in preventing cancer recurrence (Moon et al., 2017), and “in control by doing everything in my power to fight this.” (Lambert et al., 2018b, p. 6).

Self-management strategies for persistence included routines such as visual cues, external aids (alarms) and medication organiser (pillbox), as reminders to take their AET as part of their daily routine (Cahir et al., 2015; Harrow et al., 2014; Humphries et al., 2018; Iacorossi et al., 2018; Wells et al., 2016; Wen et al., 2017; Wickersham et al., 2012).

#### 4.3. The side effects are worse than the disease

The side effects women experienced were often unexpected and had a profound impact on their quality of life (Cahir et al., 2015; Harrow et al., 2014; Lambert et al., 2018b; Verbrugghe et al., 2017; Wells et al., 2016; Wickersham et al., 2012; Wen et al., 2017) forcing many women to question whether the potential of a cancer free survival was worth persisting with a reduced quality of life. Poor symptom management influenced decisions on persistence with AET (Brett et al., 2018; Lambert et al., 2018b; Moon et al., 2017).

For some women, the “attack on femininity” (Pellegrini et al., 2010, p. 476) as a result of AET caused them to question persistence. Younger pre-menopausal women were immediately “thrown into the menopause” (Brett et al., 2018, p. 294), a process which should have otherwise taken years to occur, and one which they were not fully expecting (Brett

et al., 2018; Iacorossi et al., 2018; Wen et al., 2017). Among younger women without children and those who were planning a family at the time of diagnosis, fertility was an important issue and of greater necessity than AET to prevent recurrence (Cahir et al., 2015; Pellegrini et al., 2010; Wen et al., 2017).

The symptoms of menopause brought on by AET such as hot flushes, weight gain, vaginal dryness and loss of libido (Brett et al., 2018; Iacorossi et al., 2018; Pellegrini et al., 2010; Wen et al., 2017), in addition to the loss of sexual desire and vaginal dryness, affected relationships with partners (Brett et al., 2018; Brier, 2017; Iacorossi et al., 2018; Pellegrini et al., 2010; Verbrugghe et al., 2017). Also, many women felt aged as a result of stiffness associated with arthralgia (Flanagan et al., 2012; Lambert et al., 2018b).

Side effects associated with AET also affected women's social lives (Barlow et al., 2013; Brett et al., 2018; Lambert et al., 2018b) and mood (Brett et al., 2018; Moon et al., 2017; Wells et al., 2016; Wen et al., 2017). The side effects also compromised women's ability to function within their family and occupational roles which caused feelings of loneliness and worthlessness (Bourmaud et al., 2016; Brauer et al., 2016; Brett et al., 2018; Brier, 2017; Harrow et al., 2014; Lambert et al., 2018b; Mao et al., 2013; Van Londen et al., 2014; Verbrugghe et al., 2017; Wells et al., 2016; Wen et al., 2017). A ‘tipping point’ was reached for women where the prospect of a cancer free future was not worth the reduced quality of life (Beryl et al., 2017; Bluethmann et al., 2017; Brett et al., 2018; Cahir et al., 2015; Mao et al., 2013; Moon et al., 2017; Van Londen et al., 2014).

**Table 2**  
Characteristics of included studies.

Study No	Author(s)	Year	Country	Design/Method	Sample	Analysis	Study Focus	Methodological Quality CASP (10)
1	Barlow et al.	2013	United Kingdom	Qualitative Unitary Appreciative Inquiry (UAI)	12 women with breast cancer undergoing long term hormone treatment who described their side effects as being onerous.	Thematic synthesis	This study focused on investigating if spiritual healing could support patients undergoing hormonal therapy and reduce their side effects, thus preventing drug holidays from the treatment.	6
2	Beryl et al.	2017	USA	A longitudinal, qualitative study	35 newly diagnosed breast cancer patients eligible for adjuvant endocrine therapy.	Constant comparative method of analysis	The focus of this study was to map the decision-making process for women considering and commencing adjuvant endocrine therapy.	9
3	Bluethmann et al.	2017	USA	Mixed-methods explanatory sequence design with a qualitative emphasis. Grounded theory.	30 women who had been recommended AET (tamoxifen and aromatase inhibitors) by their physician. Purposively sampling survivors who were adherent and non-adherent	Open coding to reduce data into themes	The focus of this study was to explore the range of survivors' experiences with prescribed AET.	9
4	Bournaud et al.	2016	France	A mixed-methods study consisting of a qualitative study to identify educational needs and a feasibility study assessing the efficacy of the program.	11 women with breast cancer being treated with AET (tamoxifen or AI's)	Qualitative content analysis	The focus of this study was to develop and test the feasibility of a tailored educational program, with the aim of improving adherence to AET.	7
5	Brauer et al.	2016	USA	Qualitative grounded theory	27 women with breast cancer over the age of 65, being treated with Aromatase Inhibitors	Constructivist grounded theory	The focus of this study was to understand how older breast cancer patients make decisions about persisting with aromatase inhibitors and manage treatment related side effects.	10
6	Brett et al.	2018	United Kingdom	Qualitative with semi-structured interviews	32 women prescribed AET, 2–4 years following their diagnosis of breast cancer Both adherers (n = 19) and non-adherers (n = 13)	Framework analysis	The focus of this study was to explore factors that influence adherence and non-adherence to AET.	9
7	Brier	2018	USA	A mixed methods study consisting of a qualitative analysis using interviews	The sample was purposively selected which consisted of 13 adherent women and 9 of their partners, and 12 non-adherent women and 6 of their partners	A grounded theory approach using a constant comparison method of analysis	The focus of this study (Chapter 4) was to explore the role of partners in breast cancer patients' adherence to aromatase inhibitors.	10
8	Cahir et al.	2015	Ireland	Qualitative study using semi-structured interviews	31 women purposively sampled with stage 1–3 breast cancer, prescribed AET greater than 3 months	Thematic analysis based on the framework approach	The focus of this study was to qualitatively investigate influences on AET medication taking behaviour in women with stage 1–3 breast cancer.	10
9	Cheng et al.	2017	China	A Secondary analysis of the qualitative data derived from a mixed-method study	Archived interview transcripts from 19 breast cancer survivors (< 5 years since diagnosis)	Secondary analysis of each transcript through qualitative content analysis	The focus of this study was to reveal Chinese breast cancer survivors' views and experiences of self-management in extended survivorship.	6
10	Farias et al.	2017	USA	A qualitative study	22 women with breast cancer who filled a prescription for AET (tamoxifen, exemestane, anastrozole or letrozole) in the previous 12 months	Inductive constant comparison approach	The focus of this study was to explore, from the patients' perspective, how physicians communicated with them about all aspects of AET.	9
11	Flanagan et al.	2012	USA	A non-experimental qualitative descriptive study	21 women with breast cancer undergoing AET – focus groups	Content analysis	The focus of this study was to understand the experiences of women undergoing AET.	10
12	Harrow et al.	2014	United Kingdom	Qualitative study using semi-structured interviews	30 women with breast cancer prescribed tamoxifen or AI (anastrozole or letrozole) for 1–5 years	Constant comparative method was applied within the framework approach	The focus of this study was to explore women's experiences of taking AET, and how their beliefs about the purpose of the medication, side-effects experienced and communication with health care professionals might influence adherence.	10

(continued on next page)

Table 2 (continued)

Study No	Author(s)	Year	Country	Design/Method	Sample	Analysis	Study Focus	Methodological Quality CASP (10)
13	Humphries et al.	2018	Canada	A qualitative study guided by the Theory of Planned Behaviour (TPB)	43 breast cancer patients (34 in focus groups & 9 individual interviews) prescribed AET within the previous 2 years	Thematic analysis	The focus of this study was to explore breast cancer patients' beliefs related to early adherence to AET.	9
14	Hurtado-de-Mendoza et al.	2018	USA	Mixed-methods Design (telephone interviews)	30 women with breast cancer (White = 15) (black = 15) prescribed AET	Content analysis	The focus of this study was to explore the clarity and relevance of the Beliefs about Medicine Questionnaire (BMQ) in the context of adherence behaviours to AET both black and white breast cancer survivors.	6
15	Iacorossi et al.	2018	Italy	Qualitative exploratory design	27 women with breast cancer who were being treated with AET, mainly tamoxifen	Framework analysis approach	The aim of this study was to explore the experiences of adherence to AET in women with breast cancer.	10
16	Lambert et al.	2018	Canada	Interpretive descriptive methodology and relational autonomy theory	22 women diagnosed with early stage breast cancer prescribed AET. Purposive sampling was performed to include persistent (n = 15) and non-persistent (n = 6) women (non-initiation n = 1)	Inductive thematic analysis was used to analyse the interviews and descriptive statistics was used to summarize the quantitative data	The focus of this study was to explore breast cancer patients' experiences and perspectives of AET use and to describe how personal, social and structural factors influence AET persistence.	9
17	Mao et al.	2013	USA	A mixed-methods study including quantitative and qualitative analysis	1000 randomly selected messages related to arthralgia posted on 12 message boards online	Analysis of the qualitative data was performed using content analysis	The focus of this study was to understand the frequency and content of side effects and associated adherence behaviours discussed by breast cancer patients related to aromatase inhibitors (AI), with particular emphasis on arthralgia.	9
18	Moon et al.	2017	United Kingdom	Qualitative grounded theory	32 breast cancer patients who had been prescribed tamoxifen therapy	Inductive thematic analysis	The focus of this study was on the women's lived experiences of tamoxifen, their motivation to adhere and their reasons for non-adherence and non-persistence.	10
19	Pellegrini et al.	2010	France	Qualitative, grounded theory	34 women with breast cancer prescribed tamoxifen therapy	Constant comparative method of analysis	The focus of this study was on the women's underlying beliefs and experiences of tamoxifen therapy.	10
20	Van Londen et al.	2014	USA	A qualitative design using 4 focus groups	4 groups with a total of 14 breast cancer patients, aged > 50 years with AET related symptoms	Thematic synthesis	The focus of this study was to investigate the women's experiences related to taking AET and managing the associated symptoms.	10
21	Verbrugge et al.	2017	Belgium	Qualitative grounded theory	31 women with breast cancer receiving AET (both tamoxifen and aromatase inhibitors)	Constant comparative method of analysis	The focus of this study was to gain an insight on the process of non-adherence and non-persistence by researching influencing factors and their inter-relatedness in breast cancer patients taking AET (both tamoxifen and aromatase inhibitors).	10
22	Wells et al.	2016	USA	A cross sectional qualitative study	25 historically or medically underserved breast cancer patients prescribed AET	Content analysis	The focus of this study was to evaluate the barriers and facilitators to taking AET among medically and historically underserved breast cancer patients within the first 5 years after primary treatment for breast cancer.	10
23	Wen et al.	2017	USA	A qualitative design using semi-structured interviews	6 white and 6 African American women prescribed tamoxifen or aromatase inhibitors	Thematic synthesis	The focus of this study was to explore women's barriers and facilitators to their adherence to AET and experiences with AET related symptoms. This study also explored any racial differences between	9

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Table 2 (continued)

Study No	Author(s)	Year	Country	Design/Method	Sample	Analysis	Study Focus	Methodological Quality CASP (10)
24	Wickersham et al.	2012	USA	A qualitative descriptive study	12 women aged 58–67 years with early stage breast cancer who were prescribed anastrozole	Qualitative content analysis	Caucasian and African American women in their experiences and requirements. The focus of this study was to describe the medication taking experiences of post-menopausal women with early stage breast cancer receiving anastrozole therapy.	10

#### 4.4. Help us with information and support

Women believed that more information on side effects and management strategies would help them adhere and persist with AET. Women often felt unprepared for the side effects of AET due to the lack of information provided by health care professionals (Bluethmann et al., 2017; Brett et al., 2018; Cahir et al., 2015; Humphries et al., 2018; Moon et al., 2017; Van Londen et al., 2014) and they believed that more information on perceived risk, potential side effects and management strategies would help them with adherence and persistence with AET (Moon et al., 2017; Verbrugge et al., 2017).

The level of information and education provided by health care professionals at initiation and at follow-up appointments was considered insufficient (Brett et al., 2018; Iacorossi et al., 2018; Moon et al., 2017; Wen et al., 2017). Women also felt isolated and abandoned by health care professionals, reporting less structure and lack of continuity of care during the transitional period into primary care, where follow-up appointments were less frequent (Bourmaud et al., 2016; Brauer et al., 2016; Brett et al., 2018; Cahir et al., 2015; Flanagan et al., 2012; Harrow et al., 2014; Iacorossi et al., 2018; Lambert et al., 2018b). However, when support from health care professionals was effective, it promoted adherence (Brett et al., 2018). In addition, partner support in terms of being ‘very patient and understanding around sexual issues’ also promoted adherence (Brier, 2017, p.86).

Women sought information and support from non-professional sources including the internet, online forums and from other breast cancer survivors. This informal support helped women self-manage side effects and persist with adherence (Bourmaud et al., 2016; Brauer et al., 2016; Brett et al., 2018; Iacorossi et al., 2018; Van Londen et al., 2014; Wells et al., 2016), and other breast cancer survivors were an important source for sharing knowledge and practical coping strategies (Brauer et al., 2016; Cahir et al., 2015; Flanagan et al., 2012; Humphries et al., 2018; Mao et al., 2013; Van Londen et al., 2014; Wen et al., 2017).

#### 5. Discussion

This qualitative evidence synthesis has identified that contributing factors to women’s adherence and persistence with AET included women’s own personal beliefs of having no option, fear of recurrence, informational support from healthcare professionals on managing symptoms and social support. These findings are consistent with results from a recent systematic literature review which analysed the psychosocial issues associated with AET adherence (Van Liew et al., 2014). Women’s personal beliefs regarding AET adherence and persistence were identified as contributing factors from initiation and throughout the treatment phase, which led to processes of weighing-up the risks and benefits of AET. Identification of psychosocial factors that influence adherence with AET is central in developing interventions with a potential to improve adherence practices. (Humphries et al., 2018). A recent integrated review suggests that non-adherence to AET is complex and is often influenced by many psychosocial factors, such as side effect experience, lack of routine, negative attitudes towards medication, and inadequate health care professional relationships (Lambert et al., 2018a).

This review has found that women’s adherence and persistence was often driven by fear of the drug, fear of the side effects and the fear of possible cancer recurrence and death (Bourmaud et al., 2016; Cheng et al., 2017; Harrow et al., 2014; Iacorossi et al., 2018; Van Londen et al., 2014). This fear is often generated from missing information and inadequate knowledge, therefore the provision of knowledge in relation to AET side effects and benefits could help women become more involved in their treatment, allowing for the development of behavioural strategies to support adherence (Iacorossi et al., 2018).

A consistent finding in this review was that the presence and severity of the treatment side effects contributed to adherence and persistence (Bluethmann et al., 2017; Brett et al., 2018; Cahir et al., 2015; Mao et al., 2013; Moon et al., 2017; Van Londen et al., 2014). These

**Table 3**  
CASP quality assessment table.

	1. Was there a clear statement of the aims of the research?	2. Is a qualitative methodology appropriate?	3. Was the research design appropriate to address the aims of the research?	4. Was the recruitment strategy appropriate to the aims of the research?	5. Was the data collected in a way that addressed the research issue?	6. Has the relationship between researcher and participants been adequately considered?	7. Have ethical issues been taken into consideration?	8. Was the data analysis sufficiently rigorous?	9. Is there a clear statement of findings?	10. How valuable is the research?
1	Barlow et al. (2013)	✓	✓	✓	✓	✓	✓	✓	✓	✓
2	Beryl et al. (2017)	✓	✓	✓	✓	✓	✓	✓	✓	✓
3	Bluethmann et al. (2017)	✓	✓	✓	✓	✓	✓	✓	✓	✓
4	Bournaud et al. (2016)	✓	✓	✓	✓	✓	✓	✓	✓	✓
5	Brauer et al. (2016)	✓	✓	✓	✓	✓	✓	✓	✓	✓
6	Brett et al. (2018)	✓	✓	✓	✓	✓	✓	✓	✓	✓
7	Brier 2017 (2018)	✓	✓	✓	✓	✓	✓	✓	✓	✓
8	Cahir et al. (2015)	✓	✓	✓	✓	✓	✓	✓	✓	✓
9	Cheng et al. (2017)	✓	✓	✓	✓	✓	✓	✓	✓	✓
10	Farias et al. (2017)	✓	✓	✓	✓	✓	✓	✓	✓	✓
11	Flanagan et al. (2012)	✓	✓	✓	✓	✓	✓	✓	✓	✓
12	Harrow et al. (2014)	✓	✓	✓	✓	✓	✓	✓	✓	✓
13	Humphries et al. (2018)	✓	✓	✓	✓	✓	✓	✓	✓	✓
14	Hurtado-de-Mendoza et al. (2018)	✓	✓	✓	✓	✓	✓	✓	✓	✓
15	Iacorossi et al. (2018)	✓	✓	✓	✓	✓	✓	✓	✓	✓
16	Lambert et al., 2018a,b	✓	✓	✓	✓	✓	✓	✓	✓	✓
17	Mao et al. (2013)	✓	✓	✓	✓	✓	✓	✓	✓	✓
18	Moon et al. (2017)	✓	✓	✓	✓	✓	✓	✓	✓	✓
19	Pellegrini et al. (2010)	✓	✓	✓	✓	✓	✓	✓	✓	✓
20	Van Londen et al. (2014)	✓	✓	✓	✓	✓	✓	✓	✓	✓
21	Verbrugge et al. (2017)	✓	✓	✓	✓	✓	✓	✓	✓	✓
22	Wells et al. (2016)	✓	✓	✓	✓	✓	✓	✓	✓	✓
23	Wen et al. (2017)	✓	✓	✓	✓	✓	✓	✓	✓	✓
24	Wickersham et al. (2012)	✓	✓	✓	✓	✓	✓	✓	✓	✓



**Table 4**  
GRADE CERQual, confidence in individual review findings.

Review Finding	Supporting quotes	Studies contributing to review findings	Confidence in evidence and explanation of CERQual judgement
<p><b>We don't have an option</b></p> <p>Initially women felt they had no option but to commence AET. This was influenced by their oncologist's advice and a personal fear of recurrence. Adherence was helped by women using simple strategies to remind them take their treatment.</p>	<p><i>I believe in my doctors, so if they tell me [taking AET] is the right thing to do, that's what I've got to do. (3; p.5)</i></p> <p><i>I'm not enjoying it... I'll put up with that to try to prevent a reoccurrence. (so when weighing things up) Arimidex wins hopefully, that it's inhibiting my cancer from coming back. It's a bad disease but there are many, many, many more survivors than ever before and I want to be a survivor... If there are rules that you have to follow to survive, then I'm going to follow the rules... (5; p. E995)</i></p> <p><i>I must admit I take it if they [doctors] say it's a good idea I'm very much...I think because of my experience has been so positive with them [doctors] I've not come away doubting anything (6; p.293).</i></p> <p><i>Why am I continuing with it? I think a lot of it has to do with kind of the confidence in my doctor...she is the doctor and she knows what the clinical trials are showing (10; p.7).</i></p> <p><i>It was based on the doctor having said that the risk was, you know, the benefits were minimal and that if I didn't take it, it would... really, I understand that it wouldn't really matter... and I think I remember reading somewhere or hearing somewhere that they were kind of overprescribing. Would that be right? (12; p.6)</i></p> <p><i>... basically because I trust the clinical advice I'm being given (12; p.4).</i></p> <p><i>... you must trust him [doctor]. It's like chemo treatment. It's preferable to not have it but you are told that you must (13; p.7)</i></p> <p><i>It [AET] was strongly recommended because I was in a risky age group. And then, because my cancer was hormone sensitive and very reactive (13; p.9)</i></p> <p><i>I was just told that I had to take it (15; p. E59).</i></p> <p><i>It wasn't a choice at all. I mean they're professionals so I just listened to what they said (18; p. 985).</i></p> <p><i>The physician told me I had to take the AHT medication and that I didn't have any other choice than taking the AHT (21; p.6).</i></p> <p><i>He [doctor] told me that I'd have to take it, and so I took it (24; p.4).</i></p> <p><i>"Mine was so small and stage 1, so it wasn't like a huge, life-threatening fact. So, I think not taking the pills would be better for me at the four year mark" (16, p.6)</i></p> <p><i>He [oncologist] said you wouldn't complain if you were on chemotherapy, given intravenously. You wouldn't complain about the side effects. And I said, no. And he said, well, look at it this way. You are taking a little bit of chemo every day, and so you just have to learn to deal with it (16; p.7)</i></p> <p><i>I'm still alive but there's huge consequences that I live with every day and the knock-on effect... makes it really difficult and, you know, if you were to ask me, would I still... going back, would I still go on tamoxifen? Absolutely because I wouldn't risk cancer coming back (12; p.5)</i></p> <p><i>I have to take this treatment if I want to live. If I didn't take it, I would be six feet under (4; p. E98)</i></p> <p><i>It's my life rope. I feel that's what is preventing the cancer coming back (8; p. 3120)</i></p> <p><i>I would be afraid if I stopped and it came back it would be like why didn't I stay on it, I'm after causing all this trouble again (8; p.3120)</i></p> <p><i>I take the medication regularly because recurrence means death (9; p.1046)</i></p> <p><i>If I don't take it I feel a bit guilty. I mean to say that if my cancer comes back, I'll say well there, you didn't follow it. (13; p.9)</i></p> <p><i>I don't have strong feeling [sic] about my meds, I feel that the cancer is gone, the meds help ensure that the cancer won't come back (14; p.437)</i></p> <p><i>It's as if it acts as a protection cover now I take it and I hope it works it protects me (15; p.E60)</i></p> <p><i>It was a way to fight the disease and to make sure I didn't get it back. I read about the side effects, but to me, it was all about winning the battle. I felt I was in control by doing everything in my power to fight this. (16; p.6)</i></p> <p><i>I feel like I am doing something to prevent the cancer returning (18; p.986)</i></p> <p><i>It shocks me because I felt the fear of God in me. I had to take this. I didn't ask the questions which is so unusual for me (20; p.4)</i></p> <p><i>I guess the benefits, in my opinion, outweigh the risk and the side effects (23; p.106)</i></p> <p><i>I fill my pill box up on a Monday and I put all my tablets in and then just in case, you take it in the morning and then you say to yourself, did I take my tablets, I go back and look at today and say I did (8; p. 3122)</i></p> <p><i>Got the routine, I take the dog out, come back, have all the, have a wee drop breakfast and have the rest of the pills (12; p.5)</i></p> <p><i>At breakfast, my jar of peanut butter...every morning it is there (13; p.7)</i></p> <p><i>I have learned to keep it near the cup of coffee... I remind myself by keeping it in view then, as soon I have taken it I put it away to avoid taking it twice (15; p. E61)</i></p> <p><i>In the morning my routine is I'm going to go to the kitchen, I'm going to get my coffee ready, I'm going to get out the pills and then I'm going to drink them with water and then I'm going to have my breakfast and my coffee (22; p.4126)</i></p> <p><i>I have an app on my phone. At the time, the app sends you a reminder and if you don't click I took my medication in like 15 min, it plays a tune (23; p.109)</i></p> <p><i>When I started it, that's when I put into my day (pill minder)... I've had no trouble</i></p>	<p>3- 6, 8-10, 12-16, 18, 20-24</p>	<p><b>High Confidence.</b></p> <p>Sixteen studies with no concerns about coherence, relevance, adequacy and methodological limitations. One study (study 9) with minor concerns about methodology and adequacy. One study (study 14) with moderate concerns about methodology, relevance and adequacy.</p>

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Table 4 (continued)

Review Finding	Supporting quotes	Studies contributing to review findings	Confidence in evidence and explanation of CERQual judgement
<p><b>The side effects are worse than the disease</b></p> <p>Women experienced a myriad of debilitating side effects and some reached a 'tipping point' where quality of life won over quantity of life.</p>	<p><i>remembering to take it, and that seems to be a good time (after super) since its after my work day, except when I have a meeting, I don't forget (24; p.6)</i></p> <p><i>I have friends, but (they are) friends who don't understand a thing about endocrine therapy. For one of them, my treatment goes right over her head, she can't understand I'm tired. It's upsetting, so I don't talk about it anymore. Even my mother doesn't understand (4; E98)</i></p> <p><i>And I have two, three grandchildren. I love children... so, when I see them, I want to play with them... but physically I can't do it. So, that makes me – really upsets me. I think that's the thing (5; p. E995)</i></p> <p><i>I got thrown into early menopause... One of the things that upset me most at the time was that I lost all interest in sex overnight. It didn't help my husband as you can imagine (6; p.294)</i></p> <p><i>I felt almost suicidal with it (6, p. 294).</i></p> <p><i>I feel so unattractive on, I mean that's just part of who I am anyway, but this whole experience I just feel so unattractive ...I have this big S for survivor hanging over my head and that's all I am. (7; p.88)</i></p> <p><i>My husband said last night I have been useless for three years pretty much (7; p.86)</i></p> <p><i>It breaks my heart that I will never be a mother. It's a hard thing to give up your womb, to give up five years of your fertility but my way of looking at things is I'd rather be childless than leave my child motherless (8; p3121)</i></p> <p><i>Well the surgery and initial treatments took away some of my feeling about being a woman, and just as that was getting better this just zaps that away. I have no and I mean no libido (11; p.73)</i></p> <p><i>"I feel like an old man" (11; p.73).</i></p> <p><i>I had quite a busy job... so I stopped that so you know I really could pretty much say I'm doing hardly anything and yet I'm still exhausted all the time (12; p.5)</i></p> <p><i>The only thing that bothers me is forced menopause, hot flushes... and the loss of sexual desire (15; p. E60)</i></p> <p><i>It affected me in my working environment and it affected me in my free time, and my family (16; p.5)</i></p> <p><i>I cannot live this way with the pain. I can barely function at my job and I need to work (17; p.260)</i></p> <p><i>I felt so low, was having suicidal thoughts, really didn't feel like myself at all. I was in so much pain and that I'd made the decision that I was going to come off tamoxifen (18; p.987)</i></p> <p><i>As for the libido, there was nothing left at all. I'm young, my husband too, it was not easy (19; p.476).</i></p> <p><i>To kill off the female hormones that I produce is unacceptable to me. It is an additional mutilation after the mastectomy, a loss of my female image. I was born a woman and I want to remain a woman. With this treatment, we have to make up our minds to take it every single day for five years. Five years is a long time, and these five years are important when you are not far from the menopause like me, because there's no turning back. We are pushed into the menopause without being able to go back. It also means that we will not have access to alternative treatments for menopause. So we will age more quickly (19; p.476).</i></p> <p><i>I am more forgetful. I work harder at work to do the same job that I used to just do. It's harder for me to stay focused, to concentrate, to think clearly, to remember everything (20; p.5)</i></p> <p><i>In the beginning, it was very difficult for me that my husband had to clean the house and I could only look on. I sat there crying because I like to clean the house and I could do nothing (21; p.5)</i></p> <p><i>I do not feel normal anymore. I do not feel like a woman anymore (21; p.5).</i></p> <p><i>You can't cook, you can't clean, you can't bathe because... the pain is in all your body (22; p.4127)</i></p> <p><i>There are days that I feel very tired, I don't want to get out of bed, there are days that I feel a lot of pain in my muscles, all my body hurts, very depressed, depression, I feel like crying (22; p.4127)</i></p> <p><i>I was psychologically unprepared to the extent of the side effects because I have been an extremely busy, active person... but the medication did something to me emotionally where I couldn't do it... So not being able to function in the capacity that I am used to doing really affected me psychologically (23; p.108)</i></p> <p><i>I am going through so much with this new medication that I am taking, that I have not worked a full week since this year (23; p.108)</i></p> <p><i>It affected my skin, became dry, my hair became brittle... everything is dropping and sagging. The emotional effects of going through menopause for me was the most challenging, when the physical effects not so much for me (23; p.108)</i></p> <p><i>Overall it feels like a torch... the chest area and face and forehead, my foreheads like soaking wet now (24; p.5)</i></p> <p><i>After the disease [cancer], my husband and I had to go ahead. We thought: 'If that is the case, there's no point in taking tamoxifen and wasting five years. Tamoxifen did not seem vital to me, nor very reliable. Our wish to have a child was very strong, we did not agree with waiting (19; p.476)</i></p>	2-8, 11, 12, 15-24	<p><b>High Confidence.</b></p> <p>Seventeen studies with no concerns about coherence, relevance, adequacy and methodological limitations. One study (study 11 with minor concerns on coherence and adequacy) with minor concerns about methodology and adequacy.</p>

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Table 4 (continued)

Review Finding	Supporting quotes	Studies contributing to review findings	Confidence in evidence and explanation of CERQual judgement	
<b>Help us with information and support</b> Women often felt invisible and unhappy with the information on side-effects and support provided by health care professionals and sought support from non-professional sources. Being better prepared and supported helped adherence and persistence.	<i>Me and my husband discussed he wants another baby, and with me being on the tamoxifen, they told me I couldn't have children. So that's the only thing that is a big problem in my personal life (23; p.109)</i>			
	<i>I was aching and I was tired and I was lethargic and it got to the point in 5 weeks I could hardly bend over... I said, I'm not going to do this (2, p.83)</i>			
	<i>I'm not taking it...I can't deal with it...it's too hard (2,p. 85)</i>			
	<i>I've had tamoxifen, and I've had breast cancer. I would rather have breast cancer (3; p.7)</i>			
	<i>And I didn't want to go out and I became quite withdrawn really, so no, it wasn't acceptable (6; p. 294)</i>			
	<i>I called my doctor and told her I was going to stop taking Femara, that it was affecting me adversely, and that my quality of life was more important (3; p.6)</i>			
	<i>It just stops you getting on with your life. You have been through surgery, then chemotherapy, then you take the hormone drugs. You get to a stage when you want to get back to normal, but these drugs stop you doing that (6, p. 296).</i>			
	<i>I think you need to take life by the horns. You make that decision and take the consequences. I took the decision not to continue because I wanted my normal life again. It is about weighing up what is important to you, not the doctor (6; p.296)</i>			
	<i>I chose a lesser time left. I said at my age, does it matter if the cancer comes back one way or another but if I have these few years of, I don't go gallivanting or that, I like my home and I like being involved in the community, going to the club and that. Coming off the tablet has given me back that quality of life (8; p. 3126)</i>			
	<i>The side effects are potentially worse than the disease. It's like, why am I doing this? It's bizarre (16; p.5)</i>			
	<i>I had joint and bone pain with Arimidex and decided no more drugs even though I have one more year to go. I figured the small survival advantage was not worth all the side effects. I feel great... hope I made the right decision (17; p.260)</i>			
	<i>I thought actually I would rather be myself for however long that is, rather than be miserable for a longer period, and depending on what... whether the recurrence might occur or not I just thought well I'll take that chance (18; p.988)</i>			
	<i>You do get to a point where it just isn't worth it to fight it (20; p.7)</i>			
	<i>[My doctor] told me that I would probably have night sweats and hot flashes but that's all I really expected. I didn't expect the [severe side effects] I had....(3; p. 5)</i>	3-6, 8, 11, 12	<b>High Confidence</b> Thirteen studies with no concerns about coherence, relevance, adequacy and methodological limitations. Study 11- minor concerns about coherence and adequacy	
	<i>One [doctor] told you 'take this' and that is it, no-one explains ...anything [to you] (4; p.E98)</i>	13, 15, 17, 18, 20, 21, 23.		
<i>The doctors, they are not listening, they are always in a hurry (4; p.E98)</i>				
<i>You feel like you don't have all the structures we talked about before, so now you're winging it, and that's scary (5; p. E995)</i>				
<i>I would have liked more information to prepare for the side effects. I was given lots of information about the side effects of chemotherapy and how to manage them, but I wasn't expecting the side effects of AET. So perhaps that made it worse. (6; p.293)</i>				
<i>I had a long conversation with him [Doctor] about it- he really cared. He swapped me onto this one- I know he is doing what he can. If you feel someone cares, it kind of encourages you to keep going... (6; p.293)</i>				
<i>These out patients' appointments, you see a different doctor all the time and they spend more time, looking through my file trying to read up what's happened to me. They're so busy you barely get time to talk to them at all about how you're feeling. You get your treatment and then you toddle off on your merry way and you're left to deal with the rest of it on your own. (8; p. 3127)</i>				
<i>No one's ever asked if I'm still taking it (12; p.5)</i>				
<i>Education is necessary in order to understand the importance of it all (15; p. E61)</i>				
<i>I would have preferred to see always the same oncologist, I had difficulties because when doctors changed I found myself thinking I had to start again, to find problems, misunderstandings (15; p. E61)</i>				
<i>This is the one thing that I do find a lot of women struggling most with, that they feel so... they're just not listened to. They're not being validated in what they're experiencing (18; p.990)</i>				
<i>I didn't know anything about it. Really no one's sort of explained what it is. They just said tamoxifen will help stopping recurrence (18; p.989)</i>				
<i>I don't think it was really explained to me, all the things that might happen I don't remember. I'll be honest with you, I really don't remember (20; p.4)</i>				
<i>They (providers) just go by what they read in a book... I learn more from people who have been through it (20; p.6)</i>				
<i>I would like to say to physicians who work by appointment, to take a little more time and to listen a little better. I had the feeling that I could not be outside fast enough. I was not dressed yet and he was already writing a prescription. That hurts (21; p.7)</i>				
<i>When I mentioned side effects I got the reaction: You have to accept you are getting older. At that point I disconnected myself from the conversation, there was no longer any point in talking to this person. I was furious, but you can't do anything with that furiousness, and I didn't want to do anything with it anymore... At that moment you collapse and you think: It doesn't make sense anymore to say anything (21; p.7)</i>				
<i>I do not have much information on the medication, like the side effects and like the</i>				

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Table 4 (continued)

Review Finding	Supporting quotes	Studies contributing to review findings	Confidence in evidence and explanation of CERQual judgement
	<p><i>outcome...when you take an antibiotic and you take it for 5 days, and you start feeling better... It's like I am hoping that it will repress the cancer cells, but do I have or don't I have cancer cells? I am just taking it in the dark (23; p.107)</i></p> <p><i>On the internet, a patient said that you should take the pills in the middle of lunch, so I tried to do the same (4; p.E98).</i></p> <p><i>Don't get me wrong. My GP is lovely. But they don't know much about treatments for breast cancer. I'd rather talk to someone at the hospital (6; p.295)</i></p> <p><i>I went to a really good support centre. It is lovely for people who are in a time in their life, when it is like the rug has been taken from underneath you. I feel that if you go to the things that are in place to help you, then you have a better chance of coming along the road and coming out the other end and thinking yeah, I'm good now (8; p.3121)</i></p> <p><i>needed to talk this through in a group like this (11; p.75)</i></p> <p><i>We were twelve and twice a day, morning group and evening [discussion] group, I received all the information from them because they had gone through it before me (13; p.7)</i></p> <p><i>I look for information on my own... they just told me to take that drug because there was a 45% possibilities not to face other problems and nothing more. Then one compares and discusses with friends, on the internet, and evaluates the effects that can be attributed to the drug (15; p.E61)</i></p> <p><i>Last night at this site I found 13 other ladies with the same problem. I was so happy to read I wasn't the only one and that my intuition was right. It was the meds. Now my oncologist wants me to start aromasin. When I see her Wednesday I'm telling her no way (17; p.260)</i></p> <p><i>I googled Arimidex and started to read about it... I mean I have a folder that's probably this thick about it (22; p.4127)</i></p> <p><i>I found that the Facebook group that I belong to is really helpful for me, you post things or I see other women posting things, and everybody kind of chimes in and that's helpful (23; p.110)</i></p>		

findings were also documented in a recent systematic review of 29 studies (Murphy et al., 2012). It is known that arthralgia associated with AET can be helped with vitamin D supplementation (Dowling et al., 2017) and exercise (Baglia et al., 2019). Emerging evidence on the use of homeopathic medicine to reduce hot flushes associated with AET also offers hope for women (Heudel et al., 2019). However, evidence-based strategies for managing most AET related symptoms can prove to be challenging (Cella and Fallowfield, 2008). The development of patient specific self-management programmes are needed to address the physical and psychological challenges associated with AET (Murphy et al., 2012). Although symptom specific interventions are being developed (Niravath, 2013; Walker et al., 2010), guidelines are required to provide health professionals with standardised protocols that can be adapted to individual women's needs (Lambert et al., 2018a).

Inadequate information and support from health care professionals led women to seek information from other sources including the internet, online forums and other breast cancer survivors (Bourmaud et al., 2016; Brauer et al., 2016; Brett et al., 2018; Iacorossi et al., 2018; Van Londen et al., 2014; Wells et al., 2016). A health service initiative involving advanced practice nurses and/or specialised nurses could provide the necessary information and follow-up support required by these women to optimise adherence and persistence with AET (Albert et al., 2011). The current lack of appropriate interventions represents a missed opportunity for health promotion (Murphy et al., 2012). Early menopause and the possibility of infertility was found to be of great importance among younger women for whom preserving their femininity and fertility was vital, in terms of reproduction, but also as a symbolic barrier against this life-threatening disease (Pellegrini et al., 2010). The review showed that some younger women were willing to trade off some survival benefits of AET for the preservation of their fertility (Cahir et al., 2015; Pellegrini et al., 2010; Wen et al., 2017). Physicians need to have a greater understanding of fertility values among younger women, so they can assist them to make informed decisions and thereby improve adherence with AET (Wen et al., 2017).

Due to the longevity of treatment, follow up care tends to occur within primary care settings to reduce the burden on the Oncology services (Lambert et al., 2018a). The review identified that women often reported feelings of isolation and neglect as a result of insufficient support and poor communication between healthcare professionals (Bourmaud et al., 2016; Brauer et al., 2016; Brett et al., 2018; Cahir et al., 2015; Flanagan et al., 2012; Harrow et al., 2014; Iacorossi et al., 2018; Lambert et al., 2018b). The structure and delivery of follow-up care has been found to influence adherence and persistence of AET (Kahn et al., 2007). If women are to persist with AET, primary care providers should be aware of the facilitators and barriers to adherence, and they should be knowledgeable in symptom management strategies (Lambert et al., 2018a). Indeed, recent findings reported in the American Cancer Society's study of long term cancer survivors (including 870 with breast cancer) focused on women's need for information on long-term treatment side effects (Playdon et al., 2016). However, a one-way approach of information provision does not promote adherence and patients' sense of a meaningful connection with their health care professional may enhance adherence (Finitis et al., 2019).

Finally, due to the recommended clinical extension of AET from 5 to 10 years, there is a need for further advanced nursing roles and clinical nurse specialist posts to meet the needs of women attending nurse-led review clinics. Women want to see the same named HC professional at each review visit and to know what side effects they should expect from AET (Meade et al., 2017). Specialist oncology nurses are ideally placed to co-ordinate survivorship care plans focused on improving women's knowledge of side AET side effects.

## 6. Study limitations

The search strategy aimed to include all relevant literature, however, it was limited to English language publications only. In addition, many of the included studies within the review failed to distinguish between aromatase inhibitors and tamoxifen.

## 7. Conclusion

This is the first known qualitative evidence synthesis of studies exploring breast cancer patients' experiences of adherence and persistence to oral endocrine therapy. Quality assessment using the CASP tool showed that most were of high quality. Confidence in the Evidence from Reviews of Qualitative (GRADE-CERQual) identified high confidence in all three analytic themes.

The potential cost of non-adherence to AET for these women is high in terms of reduced treatment efficacy and increased risk of death. The findings in this review will provide healthcare professionals with guidance on addressing women's unmet information and symptom management needs to improve their adherence to AET and ultimately improve their survivorship.

## Declaration of competing interest

None declared.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ejon.2019.101706>.

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