

**UNDERSTANDING ADHERENCE TO ADJUVANT ENDOCRINE THERAPY IN  
BREAST CANCER SURVIVORS**

by

Leah Kimberley Lambert

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The following individuals certify that they have read, and recommend to the Faculty of Graduate and Postdoctoral Studies for acceptance, the dissertation entitled:

**UNDERSTANDING ADHERENCE TO ADJUVANT ENDOCRINE THERAPY IN  
BREAST CANCER SURVIVORS**

Submitted by **Leah K. Lambert** in partial fulfillment of the requirements for the degree of  
**Doctor of Philosophy in Nursing**

**Examining Committee:**

Dr. Lynda G. Balneaves

---

Co-supervisor

Dr. A. Fuchsia Howard

---

Co-supervisor

Dr. Carolyn C. Gotay

---

Supervisory Committee Member

Dr. Alison Phinney

---

University Examiner

Dr. Mary A. De Vera

---

University Examiner

**Additional Supervisory Committee Members:**

Dr. Stephen L. K. Chia

---

Supervisory Committee Member

## **Abstract**

**Background:** Adjuvant endocrine therapy (AET) is highly efficacious, significantly reducing breast cancer recurrence and mortality for women with hormone receptor-positive breast cancer. Yet, many women do not adhere to prescribed AET. The purpose of this study was to explore breast cancer survivors' and healthcare providers' (HCPs) experiences and perspectives related to AET and adherence.

**Methods:** This study explored personal, social, and structural factors influencing breast cancer survivors' AET adherence, including an integrative review of patient-reported factors associated with AET adherence and two interpretive description studies with breast cancer survivors prescribed AET and with HCPs who care for women undergoing AET.

**Findings:** The integrative review summarized patient-reported factors associated with AET adherence, including side effects, necessity beliefs, self-efficacy, the patient-HCP relationship, social support, and continuity of follow-up care. Interviews with 22 breast cancer survivors revealed that they struggled with persistence with AET, which they described as a balancing act between quantity and quality of life that was influenced by several different, yet connected, factors. Interviews with 14 HCPs highlighted unique experiences and challenges they faced in providing care to women undergoing AET. They described the nature of AET discussions, challenges in transitioning women to primary care, the difficulty addressing AET-related side effects, and dealing with AET discontinuation. HCPs made key recommendations for improving AET adherence, including developing sustainable models of care for delivering high-quality, cost-effective care to breast cancer survivors.

**Conclusion:** The study findings highlight the multifaceted nature of AET adherence from the perspectives of breast cancer survivors and HCPs. Improving understanding of real-world factors

influencing AET adherence is an important step in developing effective patient- and HCP-informed interventions. The development and evaluation of supportive care strategies that address the AET-related challenges experienced by breast cancer survivors and HCPs are needed to potentially increase the quality of women's lives, improve AET adherence, and ultimately, disease-free survival.

## **Lay Summary**

The purpose of this study was to explore why many breast cancer survivors do not take adjuvant endocrine therapy (AET) as prescribed by their doctor. The research objectives were to:

1. Examine past research on the personal (e.g., side effects, beliefs), social (e.g., patient-healthcare provider relationship), and structural (e.g., access to health care) factors associated with breast cancer survivors' AET use;
2. Explore breast cancer survivors' experiences and views of AET and describe how personal, social, and structural factors influenced their AET use; and
3. Explore healthcare providers' experiences and views on providing care to breast cancer survivors prescribed AET, including how social and structural factors influenced AET-related care. Healthcare providers' recommendations for how care and AET adherence could be improved were also obtained.

This research offered recommendations for how to improve the resources and services available to breast cancer survivors who are prescribed AET and areas requiring further research.

## Preface

This dissertation is the original work of Leah K. Lambert, the author. This study was approved by the University of British Columbia Behavioural Research Ethics Board under the project title “Understanding Adherence to Adjuvant Endocrine Therapy in Breast Cancer Survivors” (certificate H13-00207). Co-authors of the manuscripts included in this dissertation were my supervisory committee members Drs. Lynda G. Balneaves, A. Fuchsia Howard, Stephen L.K. Chia, and Carolyn C. Gotay. A version of Chapter 2 was published. Lambert, L.K., Balneaves, L.G., Howard, A.F., & Gotay, C. (2018). Patient-reported factors associated with adherence to adjuvant endocrine therapy after breast cancer: An integrative review. *Breast Cancer Research and Treatment*. 167(3), 615-633. doi: 10.1007/s10549-017-4561-5. The final publication is available at [link.springer.com](http://link.springer.com): <https://link.springer.com/article/10.1007/s10549-017-4561-5>. This article was included in my dissertation with permission from Springer Nature and reformatted using the American Psychological Association (APA) style for inclusion in this dissertation. A version of Chapter 3 was published. Lambert, L.K., Balneaves, L.G., Howard, A.F., Chia, L.K., & Gotay, C. (2018). Understanding adjuvant endocrine therapy persistence in breast cancer survivors. *BMC Cancer*. 18(1), 732-745. doi: 10.1186/s12885-018-4644-7. Inclusion of this manuscript published in *BMC Cancer* was included in this dissertation under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>) and reformatted using APA style for this dissertation.

I, Leah K. Lambert, was responsible for all aspects of this study including participant recruitment, data collection, analysis, and initial drafts of all chapters and manuscripts. My supervisory committee members Drs. Lynda Balneaves and Stephen Chia contributed to the

research questions and study design. Dr. Lynda Balneaves provided guidance on all components of this study including the initial design, data collection and analysis, and writing. Drs. Lynda Balneaves and A. Fuchsia Howard assisted with data analysis and made substantial contributions to draft revisions. All respective manuscript authors discussed the study findings, contributed to manuscript revisions, and read and approved the final manuscripts. Chapter 4 will be further developed for publication in a peer-reviewed journal with the following authors in order: Leah K. Lambert, Lynda G. Balneaves, A. Fuchsia Howard, Stephen L.K. Chia, and Carolyn C. Gotay.

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## **List of Abbreviations**

AET – Adjuvant endocrine therapy

AFH – A. Fuchsia Howard

AI – Aromatase inhibitors

ASCO – American Society of Clinical Oncology

BC – British Columbia

BC Cancer – British Columbia Cancer (known as the BC Cancer Agency until 2018)

BCOU – Breast Cancer Outcomes Unit

eCASE – Electronic Consultative Access to Specialist Expertise

HCP – Healthcare provider

HR+ – Hormone receptor-positive

LGB – Lynda G. Balneaves

LKL – Leah K. Lambert

QOL – Quality of life

RACE – Rapid Access to Consultative Expertise

RCT – Randomized controlled trial

UBC – University of British Columbia

U.S. – United States of America

WHO – World Health Organization

## Acknowledgements

I would like to express my sincere gratitude to the women who graciously shared their personal stories in the hopes of helping other women undergoing AET to receive the best survivorship care possible. Thank you to the healthcare providers for sharing your experiences and perspectives related to this significant clinical issue. Your expertise and insights were invaluable in better understanding the issues you face as clinicians in providing care to women diagnosed with breast cancer.

Dr. Lynda Balneaves, thank you for believing in me. You are always very thoughtful and thorough in your review of my work and ideas, which reflects how much you invest in and care for your students. Your years of guidance, expertise, and encouragement have been instrumental in my success as a graduate student. I am truly grateful to have had your generous support throughout my doctoral training. Dr. A. Fuchsia Howard, thank you for your endless encouragement to stay motivated and keep progressing. I appreciated your pragmatic approach and for posing challenging questions to improve my work. Dr. Stephen Chia, thank you for identifying AET adherence as an important clinical issue that required further attention, and for facilitating in-kind support from BC Cancer. Your expertise and clinical wisdom throughout the research process was integral to the success of this dissertation. Dr. Carolyn Gotay, I am grateful for your guidance, contributions, and encouragement. You always made time to connect with me and posed insightful and practical queries that strengthened this research. Dr. Sally Thorne, thank you for taking me under your ‘wing’ and welcoming me into your inner circle of esteemed oncology nurses. Thank you to BC Cancer for supporting this study and providing access to the British Columbia Outcomes Unit database for recruitment purposes.

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## **Dedication**

I dedicate this work to my brother Adam and my kids – Chloe, Adam, and Emma.

Adam, your courage, determination, and strength inspired me to give back to the oncology community by engaging in work aimed at improving the lives of others diagnosed with cancer. I continue to be in awe of how you embrace life and prioritize the things that bring you joy. Chloe, Adam, and Emma, while this work took time away from you, it was meaningful and demonstrated that hard work and persistence pays off. I hope throughout your lives you will continue to be curious, empathetic, and passionately pursue your dreams.

# CHAPTER 1: INTRODUCTION

## 1.1 Structure of the Dissertation

The overarching aim of my dissertation was to explore why a significant proportion of breast cancer survivors do not take adjuvant endocrine therapy (AET) as prescribed. I have presented my dissertation in a manuscript-based format, which consists of five chapters including this *Introduction*. Chapter 1 begins with an introduction to the structure of the dissertation and research problem. I then provide background information on AET adherence in the context of breast cancer; outline the theoretical and methodological influences that informed this research; and detail the overarching study approach, including the three research objectives. In Chapter 2, I present the results of the integrative review of the literature examining the patient-reported factors found to influence adherence to AET among breast cancer survivors. In Chapter 3, I discuss the findings of the interpretive description study that explored the personal, social, and structural factors influencing breast cancer survivors' experiences and perspectives related to AET and how these factors affected their AET use. In Chapter 4, I review the results of the interpretive description study with healthcare providers (HCPs) regarding their experiences and perspectives in providing care to breast cancer survivors prescribed AET, including their recommendations for improving AET-related care and adherence. In Chapter 5, I provide an overview of findings from the integrative review and interpretive description studies with breast cancer survivors and HCPs. In this final chapter I also include *Recommendations for Research and Practice* and outline study limitations.

I conducted Chapters 2 through 4 as separate research studies; therefore, each of the findings chapters includes an introduction, methods, results, discussion, and conclusion section. As a result, some concepts are repeated in each chapter, particularly in the introduction sections,

as I explored AET adherence in the context of breast cancer in all three studies. In each study, however, I approached the issue of AET non-adherence from a different perspective and while there is some overlap, the findings from each study provide a unique contribution to better understanding why many women are non-adherent to AET after breast cancer.

## **1.2 Timeline and Evolution of the Study Approach**

To provide some context to the timeline and structure of my dissertation, I conducted this work over an extended period of time from 2011 to 2019 for two main reasons. First, the research timeline included three, one-year parental leaves. Second, data collection included two lengthy sampling periods due to the difficulty I experienced in recruiting participants to the interpretive description studies in Chapters 3 and 4. The following is an overview of the study timeline and description of how the study approach evolved over the course of this dissertation.

By November 2011, I had satisfied all University of British Columbia (UBC) Doctorate in Nursing course requirements and successfully defended my dissertation research proposal, and thus advanced to candidacy. From January to December 2012, I took parental leave from my doctoral program with my first child. After returning to my program in January 2013, we received ethical approval from the UBC Behavioural Research Ethics Board to conduct this dissertation research. In July 2013, I began recruiting breast cancer survivors to the interpretive description study in Chapter 3; however, recruiting non-adherent women to this study was difficult. The British Columbia Cancer (BC Cancer) database used to recruit breast cancer survivors, which had originally been developed to assess AET adherence in British Columbia (BC), was limited to women 50 years or older at diagnosis and referred to BC Cancer between 2005 and 2008. To facilitate recruitment, we then filed an amendment to our ethics application to expand the eligibility criteria of potential participants and broaden our sampling methodology to

include snowball and convenience sampling methods. In September 2013, we received UBC ethics approval for these amendments and expanded the eligibility criteria of potential participants to include women in the study who were 18 to 79 years of age at diagnosis and referred to BC Cancer between January 2005 and August 2012. Recruitment of breast cancer survivors continued until July 2014 after implementing several sampling strategies to invite additional non-adherent women to the study.

After preliminary analysis of my interviews with breast cancer survivors, my supervisory committee and I re-evaluated the feasibility of our initial study approach and determined the data did not support proceeding with the Delphi study we had initially proposed to undertake. This was due to the complex nature of AET non-adherence revealed in interviews and the resulting lack of recommendations from women on how to improve adherence. We also determined that two of the study questionnaires women completed prior to participating in the interviews were not applicable in many cases. The first survey was the Reported Adherence to Medication questionnaire that assesses the tendency to forget to take medication or to alter the prescribed dose (Horne, Weinman, & Hankins, 1999). The second survey was the Functional Assessment of Cancer Therapy Endocrine Subscale (FACT-ES), which measures symptoms and side effects related to AET in breast cancer (Fallowfield, Leaity, Howell, Benson, & Cella, 1999). Initially, the objective of my research was to explore breast cancer survivors' adherence to AET. However, when I interviewed breast cancer survivors, it became apparent that AET persistence, defined as continuously taking AET for the prescribed treatment duration (Hadji, Ziller, et al., 2013), was the more predominant issue in this sample. Women were not forgetting to take their medication or arbitrarily changing their dose of AET; they experienced challenges in persisting with AET for the recommended five-year treatment period. Considering that these questionnaires

were not applicable to many women who had already discontinued AET, the minimal amount of data I collected with these surveys was not reported in this dissertation.

From September 2014 to August 2015 I took parental leave with my second child. Upon my return in September 2015, I determined the body of literature on the factors associated with AET adherence had evolved in the time between the study inception and completion of data collection. In October 2015 I decided, in consultation with my supervisory committee, to pause further analysis of the breast cancer survivor interview data and conduct an updated, thorough integrative review of the literature on patient-reported personal, social, and structural factors associated with breast cancer survivors' AET adherence. Reevaluating the literature was important for me to assess how the evidence on AET adherence had changed so as to understand new developments and identify remaining gaps in knowledge about AET adherence. I chose to specifically review patient-reported factors to gain greater insight into the factors associated with AET non-adherence that were derived directly from breast cancer survivors to better understand the elements that impacted their lives and adherence.

In January 2016, I completed the first draft of the integrative review, resumed analysis of the breast cancer survivor data, and began planning recruitment of HCPs to the interpretive description study in Chapter 4. The integrative review manuscript underwent several revisions and an updated literature search was conducted prior to its submission in May 2017. In August 2016, I began recruiting HCPs to the interpretive description study in Chapter 4. Recruitment of HCPs to this study was also challenging and after using several sampling strategies recruitment was closed in April 2017. Of particular note, is the absence of family physicians in the sample of HCPs in Chapter 4. We used various recruitment strategies facilitated through the BC Cancer

Family Practice Oncology Network and convenience and snowball sampling, but were unsuccessful in recruiting family physicians to our study.

In May 2017, we submitted the integrative review manuscript to *Breast Cancer Research and Treatment*, which was accepted for publication in November 2017. In August 2017, we submitted the breast cancer survivor interpretive description manuscript in Chapter 3 for publication in the *Journal of Cancer Survivorship*, which was rejected by the editor due to a need to vary the topics and methodologies reported in the journal. We subsequently submitted this Chapter 3 manuscript to *BMC Cancer* in January 2018, which was accepted for publication in July 2018. From September 2017 to August 2018, I took parental leave with my third child. Upon my return in September 2018, I resumed analysis of my interviews with HCPs and completed this dissertation in May 2019.

As a result of these delays, the information in the following *Background* section is a reflection of the literature at the time I conceptualized the study in 2011. While this introductory section provides pertinent information to situate the research problem and provide justification for the study, an updated, thorough review of the literature as of January 2017 is presented in Chapter 2. Furthermore, I compare and contrast the findings of this dissertation to the broader literature on AET adherence, and specifically more recent research published since the integrative review was conducted in 2017 (Chapter 2). I reflect on this recent research in the *Discussion* section of Chapters 3 and 4 as well as the final Chapter (Chapter 5) to situate my dissertation findings in the broader context of AET adherence and cancer survivorship care.

### **1.3 Research Introduction**

Breast cancer is the most common cancer in pre-and post-menopausal women worldwide, with an estimated 23,000 new women diagnosed each year in Canada (Canadian Cancer

Society's Steering Committee, 2010). Breast cancer is a major cause of premature mortality in Canadian women and is the leading cause of death in women under the age of 50 (Canadian Cancer Society's Steering Committee, 2010). In Canada, an upward trend in the number of women diagnosed with breast cancer was seen from 1980 through the early 1990s due to improved early detection of breast malignancies using mammography screening (Canadian Cancer Society's Steering Committee, 2010). Breast cancer mortality rates, however, have substantially declined since the late 1980s due, in part, to more effective treatments, including the use of AET (Berry et al., 2005; Canadian Cancer Society's Steering Committee, 2010). AET is a treatment for breast cancer that significantly reduces the risk of recurrence and mortality for women with early-stage, hormone receptor-positive (HR+) breast cancer, if taken as prescribed for the recommended five-year treatment period (Burststein et al., 2010; Hershman et al., 2011). Unfortunately, adherence to AET is suboptimal and less than half (49%) of breast cancer survivors take the recommended dose of AET for the full duration of therapy (Hershman et al., 2010).

A growing body of research has focused on identifying the reasons for AET non-adherence. However, much of this literature has focused on assessing the relationship between demographic and clinical factors and AET non-adherence, which does not account for the range of personal (e.g., medication beliefs) and contextual influences (e.g., access to follow-up care) that might shape and determine women's AET adherence. As a result, a significant gap exists in understanding other reasons why an alarming number of women diagnosed with breast cancer do not adhere to AET over the recommended five-year treatment period. If effective strategies for targeting suboptimal adherence are to be developed, it is essential that we look beyond the demographic and clinical predictors of adherence. Qualitative research is needed to explore in

greater depth the real-world experiences of breast cancer survivors and HCPs related to AET and to identify additional factors that are particularly influential. In using qualitative methods to explore reasons for AET non-adherence, it is important to focus specifically on the broader social and structural contexts of women's lives to understand how these influence women's experiences with AET. We need to delve into women's and HCPs' stories to uncover how complex psychosocial issues, including beliefs, values, relationship issues, work challenges, and attributes of the healthcare system and service delivery influence AET adherence. Knowledge about breast cancer survivors' experiences and preferences related to AET, and their motivations associated with adherence to therapy, is needed to inform the development of patient-centred care initiatives and adherence interventions.

Within the literature, researchers have used the terms adherence and persistence interchangeably when referring to women's AET use (Cahir, Guinan, Dombrowski, Sharp, & Bennett, 2015; Gotay & Dunn, 2011; Van Liew, Christensen, & de Moor, 2014). For the purposes of this dissertation, I defined adherence using the World Health Organization's (WHO) definition:

the extent to which a person's behaviour – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider (2003, p. 3).

This definition effectively encompasses the concepts of adherence and persistence. In Chapter 3, the language will shift to specifically focus on AET persistence. Apart from Chapter 3, the terms "adherence" and "non-adherence", or variations (e.g., "adherent"), will be used to encompass both concepts of adherence and persistence as these two terms are so often conflated in the literature.

## 1.4 Background

### 1.4.1 Adjuvant Endocrine Therapy

Adjuvant endocrine therapy, including tamoxifen and aromatase inhibitors (AI), is a standard of care treatment for women with HR+ breast cancer. For decades, tamoxifen was the gold standard adjuvant treatment for HR+, early breast cancer (Early Breast Cancer Trialists' Collaborative Group (EBCTCG), 2005). More recently, AIs were approved for use in the management of HR+ breast cancer as a primary, sequential, or extended adjuvant treatment (Burstein et al., 2019, 2010). A demonstrated survival benefit has been shown for women with advanced disease, and consequently, AIs are now being used routinely to treat metastatic breast cancer (Gibson, Dawson, Lawrence, & Bliss, 2007).

The most common type of AETs used to treat HR+ breast cancer are tamoxifen and AIs, such as anastrozole and letrozole (Burstein et al., 2010), which work by inhibiting estrogen from stimulating the growth of breast cancer cells. Tamoxifen and AIs have differing mechanisms of action. Tamoxifen is a selective estrogen-receptor modulator and blocks the action of estrogen in breast and other tissues by binding to estrogen receptors in cells. AIs suppress estrogen levels by inhibiting the aromatase enzyme that peripherally converts androgens to estrogens. While AETs differ in how they work in women's bodies, the objective is the same – to inhibit the growth of breast cancer cells.

For the two-thirds of women with HR+ breast cancer, AET reduces the risk of recurrence and mortality. For example, tamoxifen reduces the risk of recurrence by almost half throughout the first 10 years ( $RR\ 0.53$  [ $SE\ 0.03$ ] during years 0–4 and  $RR\ 0.68$  [ $0.06$ ] during years 5–9 [both  $2p < 0.00001$ ]) and improves disease-free survival by approximately a third throughout the first 15 years ( $RR\ 0.71$  [ $SE\ 0.05$ ] during years 0–4,  $RR\ 0.66$  [ $SE\ 0.05$ ] during years 5–9, and  $RR\ 0.68$

[0.08] during years 10–14;  $p < 0.0001$  for “extra mortality reduction for each separate time period”) in women with early-stage breast cancer (Early Breast Cancer Trialists’ Collaborative Group (EBCTCG), 2011, p. 771). Until recently, AET was prescribed for five years after initial treatment for women diagnosed with HR+ breast cancer. In 2010, the American Society of Clinical Oncology (ASCO) published clinical practice guidelines recommending AET for up to 10 years in eligible women (Burstein et al., 2010). The benefit of AET demonstrated in randomized controlled trials (RCT), and the prevalence of AET use in breast cancer care, highlights the importance of supporting adherence to this potentially life-conserving treatment.

Evidence suggests that the benefits of AET are greatest when women adhere to therapy for the prescribed treatment period. Women who adhere to AET for less than five years have a significantly higher rate of breast cancer recurrence and mortality (Burstein et al., 2010; Hershman et al., 2011). AET non-adherence and early discontinuation are associated with an increased risk of mortality (49% and 26%, respectively) (Hershman et al., 2011). Results of a meta-analysis found that five years of tamoxifen significantly reduced breast cancer recurrence and mortality versus only one or two years of tamoxifen (Early Breast Cancer Trialists’ Collaborative Group (EBCTCG), 2005). The association between AET adherence and survival outcomes underscores the importance of full adherence. Unfortunately, adherence to AET is suboptimal in real-world settings, and over the recommended five-year course of AET, rates of adherence decrease. A study conducted in Ireland found that within 12 months after initiating therapy, 22% of breast cancer patients were reportedly non-adherent to AET (Barron, Connolly, Bennett, Feely, & Kennedy, 2007). In the United States of America (U.S.), approximately 50% of women discontinued treatment before the recommended five-year period (Hershman et al., 2010; Owusu et al., 2008; van Herk-Sukel et al., 2010).

In BC, where this research was conducted, BC Cancer has the mandate for cancer control for the entire province. As such, more than 80% of breast cancer patients in BC are referred to BC Cancer for treatment and care, with the BC Cancer pharmacy responsible for the dispensing of all BC Cancer-approved drug therapies, including AET. For over 20 years, BC Cancer has maintained a prospective database in the Breast Cancer Outcomes Unit (BCOU), which contains baseline demographic, pathology, treatment, and outcomes data. Through linkages between the BCOU database and BC Cancer pharmacy data repository, the rates of AET adherence were previously examined within the BC population of women with HR+ early stage breast cancer (Chan, Speers, O'Reilly, Pickering, & Chia, 2009). A total of 2,414 women were identified who were either post-menopausal or over 50 years of age with pathologically newly diagnosed Stage I-III, HR+ breast cancer between 2005 to 2008. Overall, the non-adherence rate was 40% in this population of women. This statistic supported the critical need for research that explores non-adherence to AET to inform the development and evaluation of strategies that will address barriers to adherence experienced by breast cancer survivors.

At the time of this study design, aside from demographic and clinical predictors of AET non-adherence (Hershman et al., 2010), little was known about the factors that influenced breast cancer survivors' adherence to AET. It was well documented in the literature that one of the primary reasons for non-adherence was the AET-associated adverse effects that can negatively affect women's quality of life (QOL) (Cella & Fallowfield, 2008; Gotay & Dunn, 2011). Although AETs differ in their side effect profiles, no single agent is considered better or worse in terms of adverse effects (Burstein et al., 2010). Hot flashes are the most common vasomotor symptom experienced by women taking AET, regardless of the type of endocrine agent received (Cella & Fallowfield, 2008). In general, AIs are associated with joint and muscle pain, decreased

bone density, a higher risk of osteoporosis, bone fractures, and ischemic heart disease (Burstein et al., 2010). Tamoxifen is associated with an increased risk of deep vein thrombosis; pulmonary embolism; uterine cancer; and other gynecological health issues, including an increased risk of hysterectomy (due to abnormal uterine pathology), vaginal discharge, and benign uterine pathology (e.g., hyperplasia, vaginal bleeding) (Burstein et al., 2010; Duffy, 2005). Side effects can have a profound impact on women's QOL and are one of the reasons breast cancer survivors do not adhere to AET in clinical trials and in clinical practice (Atkins & Fallowfield, 2006; Cella & Fallowfield, 2008; Chlebowski & Geller, 2007; Gotay & Dunn, 2011).

I provide a more detailed discussion in *Section 1.4.3* below of the factors found to influence AET adherence, and specifically in Chapter 2, I include a thorough review of the patient-reported factors influencing AET adherence. First, I will present an overview of adherence to other long-term therapies.

## **1.4.2 Adherence to Long-Term Therapies**

The WHO describes that access to medication is a necessary but insufficient condition for the successful prevention and treatment of disease (WHO, 2003). A requirement for the effectiveness of any medication regime is optimal adherence. Non-adherence to medication is a well-known, long-standing problem in chronic disease populations and has been well documented in the literature over the past several decades (DiMatteo, 2004b). Poor adherence is the main reason for suboptimal clinical benefit of pharmaceutical agents and can result in medical and psychosocial complications of disease, reduced QOL, and wasted healthcare resources (Dunear-Jacob et al., 2000). Many patients with chronic illnesses, including asthma, hypertension, diabetes, and HIV/AIDS, require long-term treatment and experience difficulty adhering to their recommended medication regimen regardless of their medical condition,

disease severity, and access to health care (WHO, 2003). Non-adherence often begins in the first few weeks of treatment and increases over time, with approximately 50% of all patients being reportedly non-adherent to prescribed medication regimes (Nieuwlaat et al., 2014).

Adherence has been described as a multidimensional phenomenon determined by the interplay of patient-, therapy-, HCP-, and system-related factors (WHO, 2003). Research has identified correlates and predictors of non-adherence, including patient-related factors, characteristics of the disease and its treatment, social factors, and attributes of the healthcare system and service delivery (WHO, 2003). In a review of adherence to oral cancer treatments, Ruddy and colleagues (2009) summarized several factors found to affect medication adherence in oncology populations, including personal (e.g., health beliefs, emotional state), treatment-related (e.g., adverse effects, costs), and health system factors (e.g., inadequate follow-up care). However, research on the factors associated with medication non-adherence has mostly focused on demographic factors, clinical characteristics, or individual-level factors that are within patients' control and negatively affect their medication-taking behaviours (e.g., forgetfulness, reducing doses) (Osterberg & Blaschke, 2005).

In terms of individual-level factors, increasingly more attention has been paid to investigating the effects of health beliefs on medication adherence. Patients' personal beliefs about their disease and treatment have been found to influence adherence among individuals diagnosed with chronic health conditions. For instance, patients' perceived need to take their medication (i.e., necessity beliefs), as well as concerns about therapy (e.g., adverse effects) have been associated with medication non-adherence (Horne & Weinman, 1999; Mann, Ponieman, Leventhal, & Halm, 2009). In a study of 324 participants from four chronic illness groups, including oncology patients, Horne and Weinman (1999) found that individuals with higher

necessity beliefs were more likely to be adherent to prescribed medication and those who expressed concerns about the need to take the therapy were less likely to adhere. Patients' beliefs about medication were more powerful predictors of adherence than demographic and clinical characteristics (Horne & Weinman, 1999). In a meta-analysis that investigated the relationship between disease severity and adherence in a number of medical conditions, DiMatteo and colleagues (2007) found that individuals' perceived disease severity predicted adherence. Specifically, patients who perceived the severity of their medical condition as a threat, were more likely to adhere (DiMatteo, Haskard, & Williams, 2007).

Much less is known about the influence of social (e.g., social support) and health system factors (e.g., healthcare services and delivery) on medication adherence. Some evidence indicates that social factors, including the quality of patient-HCP relationships (Schneider, Kaplan, Greenfield, Li, & Wilson, 2004) and social support from family members (Mayberry & Osborn, 2012), can influence patients' adherence to medication. Specifically, social support has shown to have a substantial effect on patient adherence to medical regimens in chronically ill populations (DiMatteo, 2004a). A meta-analysis summarizing research on social support and patient adherence to medical treatment showed a significant correlation between structural (e.g., marital status, living arrangements) and/or functional social support (e.g., practical and emotional support, family cohesiveness) and patient adherence (DiMatteo, 2004a). Practical support demonstrated the highest correlation with treatment adherence, and adherence was found to be 1.74 times higher in patients from cohesive families and 1.53 times lower in patients from families in conflict (DiMatteo, 2004a). In addition to social relationships, factors related to individuals' connections and interactions with their HCPs have been found to influence medication adherence. Among patients taking antiretroviral therapies for the treatment of HIV,

several characteristics of the patient-physician relationship, including the quality of the relationship and communication with physicians, were associated with higher medication adherence (Schneider et al., 2004).

Not surprisingly, structural features of the healthcare system can also influence patients' adherence to medication. Continuity of care and medication costs are two commonly reported structural factors. A longitudinal study that followed individuals newly diagnosed with Type 2 diabetes over seven years found that continuity of care was positively associated with medication adherence (Chen, Tseng, & Cheng, 2013). In terms of medication costs, in an analysis of 5,732 survey responses, Law and colleagues (2012) found that approximately one in ten Canadians who received a medication prescription reported cost-related non-adherence. Other structural factors reported in the literature to be associated with medication non-adherence relate to health-system barriers, such as limited access to healthcare (Osterberg & Blaschke, 2005). Understanding the factors that influence medication adherence in chronic disease populations provides some insight into factors that might also influence AET adherence due to similarities in the long-term management of chronic illnesses that also require taking daily medication.

### **1.4.3 Factors Influencing Adherence to AET**

The AET adherence literature has mainly focused on identifying demographic and clinical predictors of non-adherence. Several administrative database studies, clinical trials, and surveys of adherence have identified disease severity (i.e., lymph node involvement) (Fink, Gurwitz, Rakowski, Guadagnoli, & Silliman, 2004), comorbidities (e.g., depression, heart conditions) (Sedjo & Devine, 2011; van Herk-Sukel et al., 2010), severity of side effects (Kahn, Schneider, Malin, Adams, & Epstein, 2007), and type of breast surgery (i.e., lumpectomy versus mastectomy) (Hershman et al., 2011) to be predictive of AET adherence. Data also indicate that

age is associated with breast cancer survivors' adherence to AET, with younger (<45 years) (Atkins & Fallowfield, 2006; Hershman et al., 2011; Sedjo & Devine, 2011) and older (>70 years) women (Owusu et al., 2008; van Herk-Sukel et al., 2010) being at higher risk for non-adherence.

A significant gap in the AET literature exists concerning the personal (e.g., beliefs and values), social (e.g., social support, patient-HCP relationships), and structural factors in the healthcare system (e.g., continuity of care) that may be influential in women's decisions and behaviours related to AET adherence. Some evidence indicates that the role of patients' beliefs and expectations about health can influence adherence behaviour (Partridge, Avorn, Wang, & Winer, 2002). When I began this dissertation research, only a few studies had assessed the ways in which women perceive the risks and benefits of AET to be critical to adherence, with those who perceived AET to be beneficial being more likely to adhere to treatment (Fink et al., 2004; Grunfeld, Hunter, Sikka, & Mittal, 2005; Lash, Fox, Westrup, Fink, & Silliman, 2006). Breast cancer survivors who believed there was no benefit from taking tamoxifen (Grunfeld et al., 2005), or who had negative or neutral beliefs about the value of tamoxifen (Fink et al., 2004) were more likely to be non-adherent to therapy. In contrast, women with positive views about tamoxifen at baseline, or improving views over time, were less likely to discontinue tamoxifen (Lash et al., 2006). An association has also been found between adherence and perceived health locus of control (Atkins & Fallowfield, 2006). Women who viewed themselves as having less influence over their own health and believed powerful others (e.g., HCPs, family members, friends) could improve their health were less likely to adhere to AET (Atkins & Fallowfield, 2006).

Even less was known about the social and structural factors influencing AET adherence. Comparatively little research had been conducted on HCPs' perspectives related to AET adherence and the effects of the healthcare team on patients' adherence (WHO, 2003). An observational, linguistics study of oncologist-patient discussions related to AET revealed that physicians experienced difficulty communicating risk and sharing information with women about managing the negative effects of therapy (Davidson, Vogel, & Wickerham, 2007). The level of decision-making support received and having insufficient communication with their prescribing physician about potential side effects also influenced breast cancer survivors' adherence to AET (Kahn et al., 2007). In a study of 881 breast cancer survivors, women satisfied with the amount of provider support, involvement in decision making, and information about potential side effects were proportionally more likely to continue with tamoxifen use four years after diagnosis (Kahn et al., 2007). The larger body of literature on treatment adherence suggests that a meaningful patient-provider relationship can help to overcome significant barriers to adherence; however, few HCPs routinely ask about adherence or offer the decision support required by patients (WHO, 2003).

From a structural perspective, there is some evidence to suggest the type of care can influence AET adherence. Research conducted in the U.S. found that women with one physician who was responsible for follow-up care were more likely to persist with tamoxifen than women without a physician responsible for their care (Kahn et al., 2007). In addition, breast cancer survivors in the U.S. who received follow-up care from a medical oncologist were more likely to continue with AET than women receiving care from other types of physicians (Pini, Griggs, Hamilton, & Katz, 2011). Research suggests that other HCPs also have an influence on adherence. One study conducted in Germany found greater AET adherence rates among women

who were in contact with a breast cancer care nurse compared to those who did not have contact with a nurse (Albert et al., 2011). Another structural factor found to influence AET adherence is medication costs. Women in the U.S. who had less insurance coverage for prescriptions were more likely to discontinue AET, even when controlling for age, education, and income (Pini et al., 2011).

When I conceptualized this dissertation study, very little was known about the other personal, social, and structural factors that might be impacting the high rate of non-adherence to AET. A growing interest by other researchers in investigating the reasons for non-adherence has resulted in several new studies being published on the subject since my study began. Consequently, I decided to revisit the literature to conduct an integrative review of the patient-reported factors influencing AET adherence, which is presented in Chapter 2.

#### **1.4.4 Adherence Interventions**

Interventions that support adherence to medication may help close the gap between the efficacy of therapies demonstrated in clinical trials and their effectiveness in clinical practice. In addition to the positive impact on the health status of patients, higher rates of adherence can result in economic benefits at a societal level (WHO, 2003), including savings generated by reducing the need for healthcare services in instances of disease relapse. Indirect savings may be realized from increased QOL, which may lead to the preservation of the social and occupational aspects of patients' lives (WHO, 2003). Interventions to improve medication adherence in chronic disease populations are often multifaceted and complex (Haynes, Ackloo, Sahota, McDonald, & Yao, 2008). Effective interventions routinely involve the use of several methods to improve medication adherence and almost always include a combination of:

more convenient care, information, reminders, self-monitoring, reinforcement, counseling, family therapy, psychological therapy, crisis intervention, manual telephone follow-up, and supportive care (Haynes et al., 2008, p. 1).

In a Cochrane review of medication-adherence interventions, the authors were unable to identify any common characteristics among intervention studies; therefore, the most effective method to improve medication adherence remains unclear (Haynes et al., 2008). However, there is some evidence to support the effectiveness of a number of strategies, including education, behavioural, medication monitoring, and supportive care approaches.

Intervention studies involving the delivery of multiple education and counseling sessions by a physician, nurse, health educator, or pharmacist have shown a significant improvement in medication adherence in chronic illness populations (Kripalani, Yao, & Haynes, 2007). Meta-analyses of RCTs focused on adherence to antiretroviral medication for HIV revealed that most effective interventions either provided participants with treatment information or involved a discussion of their understanding, motivations, and expectations about taking antiretroviral therapy (Simoni, Pearson, Pantalone, Marks, & Crepaz, 2006). One study that evaluated the effectiveness of a couples-based intervention at increasing adherence to antiretroviral therapy demonstrated some success (Remien et al., 2005). The intervention was delivered by a nurse practitioner through four sessions and over a five-week period to foster support from patients' partners, and to help couples address sex and intimacy issues. Session content included education about antiretroviral therapy and the importance of adherence to health outcomes, as well as strategies to overcome barriers to adherence and enhance partner support. The intervention showed significant improvements in medication adherence. Over time, however, these effects

diminished and there were no significant differences between the two groups at the six-month follow-up (Remien et al., 2005).

Behavioural interventions that use education and motivation strategies to increase patients' understanding of their medical condition and its treatment have been shown to positively affect medication adherence (Kripalani et al., 2007). These interventions commonly include strategies to help patients simplify dosage regimes, or involve repeat assessments of patients' medication use (Kripalani et al., 2007). Increasingly, researchers have also used technology to deliver medication adherence interventions. For instance, one study used automated telephone technology to deliver an intervention to monitor anti-hypertensive use and counsel patients on adherence (Friedman et al., 1996). Participants in the intervention arm were required to call a telephone-linked computer system twice a week to report their blood pressure; name, dose, and frequency of medication; medication adherence; and presence of any side effects associated with the anti-hypertensive. In exchange, the automated system, which spoke to participants using computer-controlled speech, provided medication education and motivational counseling to promote adherence. The information obtained was regularly sent to a participant's physician. The intervention resulted in significant improvements in adherence and blood pressure for those who received the intervention compared to controls (Friedman et al., 1996). Another example is a RCT that harnessed wireless communication technology (e.g., text messages) to assess if mobile phone communication between HCPs and patients starting antiretroviral therapy improved medication adherence and suppression of viral load (Lester et al., 2010). Patients in the intervention arm received weekly text messages from a clinic nurse to ask about their status using a simple "How are you?" message and to remind patients that telephone support was available. Patients then had to reply by text within 48 hours if they were doing well or were

experiencing issues. A clinician called patients who expressed difficulties or had not replied within 48 hours. Patients who received the text message intervention had significantly better adherence and viral suppression compared to controls (Lester et al., 2010). Overall, interventions that use technology show some promise in promoting medication adherence and supplementing standard care, particularly in limited-resource settings.

Some researchers have made recommendations on how to improve AET adherence (Doggrell, 2011; Hadji, 2010; Partridge et al., 2008; Verma, Madarnas, Sehdev, Martin, & Bajcar, 2011). Yet, in a review of the literature, Doggrell (2011) found that despite the numerous suggestions made, few approaches have been scientifically tested and none had proven effective at increasing AET adherence rates (Hadji, 2010). Perhaps the difficulty with many of the recommendations was that they only offered general, fairly non-descript, approaches for improving adherence (e.g., improved communication, symptom management) (Doggrell, 2011; Hadji, 2010), rather than providing clinicians with evidence-based and clearly articulated intervention strategies to implement into clinical practice. There has also been limited testing of AET adherence interventions, with the exception of a large-scale ( $n = 4,924$ ) RCT that was initiated to examine adherence to the AI, anastrozole, in postmenopausal women (Luck et al., 2011). This trial did not show a difference in AET adherence in the intervention arm (i.e., standardized information and reminder service throughout year one of AI use) and was terminated due to a high dropout rate.

Interventions commonly used in chronically ill populations include multiple strategies that target patients, HCPs, and the healthcare system (WHO, 2003). In order to address AET non-adherence in breast cancer populations, research must then focus on identifying patient- and HCP-informed strategies for optimizing adherence that address not only the personal factors, but

also the social and structural factors influencing women's adherence to AET. Perhaps the interventions tested to date have not been effective because we do not have a thorough understanding of the issues underlying AET non-adherence. Most notably missing from the literature underpinning much of the thinking on how to improve AET adherence is breast cancer survivors' experiences and perspectives related to AET. Identification of what women perceive to be the underlying issues influencing treatment decisions and adherence behaviours needs to be a central consideration in designing adherence strategies if they are to be patient-centred and effective in real-world settings. Equally important to informing future intervention strategies are the perspectives of HCPs that deliver AET-related care to determine how features related to the clinical context shape the provision of care and AET adherence.

## **1.5 Methodological and Theoretical Orientations**

In this section, I discuss the methodological and theoretical orientations underpinning this dissertation research. First, I outline the methodology used to guide this research followed by a discussion of the relational autonomy lens that informed data collection and analysis for all three studies and the presentation of results for the integrative review (Chapter 2) and interpretive description study with breast cancer survivors (Chapter 3).

### **1.5.1 Interpretive Description**

The purpose of conducting research within an applied discipline, such as nursing, is to generate knowledge that can be used to ultimately improve patient outcomes. As such, nursing research is concerned with examining clinically relevant and meaningful problems in a way that has the potential to positively influence individual and societal health. It was well documented in the broader literature on adherence to long-term therapies that medication adherence was a complex and multifaceted problem, with many determinants (WHO, 2003). Yet, the literature on

AET non-adherence, at the time of this study design, provided limited explanation of the reasons for non-adherence because it mainly focused on identifying clinical and demographic characteristics of non-adherence. While this body of work provided important information about identifiable risk factors, it did not account for the potentially modifiable patient-, HCP- and health system-related determinants known to influence adherence to other long-term therapies (WHO, 2003). My aim was to understand this significant clinical issue in more depth by uncovering breast cancer survivors' and HCPs' experiences and perspective related to AET and adherence and the factors that influenced women's AET use. As such, I chose to use the qualitative approach of interpretive description to guide this line of inquiry.

Interpretive description is an established qualitative research approach to knowledge generation within applied clinical disciplines (Thorne, 2008, 2016; Thorne, Kirkham, MacDonald-Emes, & Macdonald-emes, 1997). A common feature of this type of inquiry is the explicit attending "to the value of subjective and experiential knowledge as one of the fundamental sources of applied practice insight" (Thorne, 2016, p. 82). I used interpretive description to inform the design logic of the qualitative studies in Chapters 3 and 4. The overarching purpose of these studies was to conduct exploratory research into breast cancer survivors' and HCPs' experiences and perspectives on AET adherence to generate new insights that could inform clinical practice and future research.

My nursing disciplinary orientation initially informed how I approached the overall study design in terms of including not only breast cancer survivors, but also HCPs in an effort to explore factors related to the broader context surrounding AET adherence. This was due to my understanding that health decisions and behaviours are shaped by, and inextricably linked to, the broader context in which they are enacted. For instance, an assumption central to nursing

conceptualizations of human health issues is the notion that patients are unique and complex individuals whose health is determined by much more than physical and physiological aspects (Thorne, 2001). As such, I knew that understanding the multidimensional nature of AET adherence would necessitate an exploration of the contextual factors influencing breast cancer survivors' AET experiences. Interpretive description allowed me to identify and interpret common elements of this clinical issue in a way that also acknowledged its inherent complexity (Thorne, 2016). Interpretive description also provided a way to explore relationships among influencing factors, and to consider how these factors interacted to shape AET adherence. Comparing similarities and differences among data helped to illuminate the inherent differences within women's and HCPs' experiences and the variances across their perspectives (Thorne, 2016).

The methodological approach of interpretive description suggests that investigators conducting applied research enter a study with the assumption that a priori theory cannot encompass the multiple realities of human experience (Thorne, 2008). In framing the theoretical orientation of this dissertation, I considered the relevance and potential application of several theories to inform this research, including decisional, social cognitive, and relational autonomy theories, which I discuss in the next section.

## **1.5.2 Study Scaffolding**

### **1.5.2.1 Initial Considerations**

Prior to undertaking this study, it was unclear what was happening with respect to breast cancer survivors' AET adherence behaviour and if women were engaging in overt decision-making processes related to their medication-taking behaviours. Initially, I looked to two theoretical perspectives that provided some background to health decisions and behaviours (e.g.,

medication adherence): social cognition and decisional theories. Social cognition theories, including the Health Belief Model, Theory of Planned Behaviour, and Protection Motivation Theory, had previously been used to describe and explain variance in health behaviours (Horne, Weinman, Myers, Midence, & Horne, 1998; Munro, Lewin, Swart, & Volmink, 2007). Social cognition models primarily focus on identifying the factors underlying health behaviours that are thought to have an effect on an individual's health and are somewhat within their control, including an individual's attitudes, beliefs, and expectations regarding potential outcomes (Abraham & Sheeran, 2005; Munro et al., 2007). Patient decision-making research has largely originated from normative theory (e.g. expected utility theory) or descriptive theory (e.g. information processing theory) (Pierce & Hicks, 2001). More recently, naturalistic decision-making frameworks have emerged as an alternative approach to studying how decisions are made in 'real-world' situations (Broadstock & Michie, 2000; Klein, 2008). Briefly, normative approaches to decision making attempt to explain behaviour as a result of a rational analysis based on logical and known conclusions that are supported by probable evidence (Bell, Raiffa, & Tversky, 1998). Descriptive theory is concerned with understanding how individuals think and act and, hence, how they make decisions (Baron, 2008). In contrast to classical decision theories, which assume a more analytical approach to decision making, naturalistic frameworks are concerned with "more automatic, intuitive processing such as the use of heuristic short-cuts" that are employed in decision making (Broadstock & Michie, 2000, p. 191).

While many decisional and social cognition theories, models, and frameworks exist, there is no one comprehensive, gold standard approach available to guide health-related, decision-making investigations (Broadstock & Michie, 2000; Pierce & Hicks, 2001). The issue with using decisional and/or social-cognition theory to guide adherence investigations is that these theories

do not adequately capture the social and structural context of individuals' lives and the impact these factors can have on adherence decisions and behaviours. Another major limitation is that these theories do not consider non-cognitive factors, such as emotions, and it is well-established that most health decisions are not solely rational. The concepts outlined in these models may be useful for understanding how certain aspects, such as perception of risk and self-efficacy, influence medication decisions for one decision point (e.g., the decision to initiate AET) or over a short period of time (e.g., adhering to a one-week course of antibiotics). Explaining the variance in adherence to long-term therapies, however, is more complex due to a myriad of factors, and particularly factors outside of an individual's control, that can change over time. Such may be the case in AET protocols that last for five years or more. Adopting a theoretical model that would be useful for exploring only certain aspects of AET adherence would limit investigation of other dimensions that might hold significant relevance in understanding this clinical issue.

#### **1.5.2.2 Relational Autonomy**

Through my training and professional experience as a nurse, I was familiar with an individual's right to make autonomous decisions about their health care. Based on findings from the literature and my disciplinary knowledge, I also recognized that understanding the larger context of women's lives would be essential to understanding their AET adherence decisions and behaviours. This line of thinking led me to the feminist conceptualization of relational autonomy.

Autonomy is generally understood as an individual's capacity for self-determination and self-governance to make decisions about their own life (Mackenzie & Stoljar, 2000). In reaction to the more traditional and individualistic understanding of patient autonomy, which has viewed patients as free and independent individuals, feminist scholars have proposed a relational

understanding of autonomy that takes multiple contexts and relationships into account and the impact of social, political, and economic conditions on the lives of individuals (Donchin, 1995; Sherwin, 1998). Susan Sherwin has conceptualized a relational view of autonomy as:

a capacity or skill that is developed (and constrained) by social circumstances. It is exercised within relationships and social structures that jointly help to shape the individual while also affecting others' responses to her efforts at autonomy (Sherwin, 1998, p. 36).

Sherwin suggests that the individualistic nature of healthcare decisions emphasizes the importance of HCPs ensuring patients have the requisite information needed to make a rational decision with little, if any, attention paid to the circumstances in which those decisions are made (1998). Sherwin's account of relational autonomy highlights the importance of attending to the ways social and structural forces affect women's lives in exploring health decisions and behaviours (1998). Building on Sherwin's notion of relational autonomy, Macdonald (2002) suggests an understanding of relational autonomy requires:

more than mere freedom from interference; it requires that one's relationships with particular individuals and institutions be constituted in such a way as to give one genuine opportunities for choice (p. 197).

In particular, a relational autonomy lens highlights the need to examine aspects of the clinical context that are central to patient autonomy, including the nature of patient and HCP interactions and the delivery of healthcare. People engage in health decisions and behaviours not only based on their own personal values, beliefs, and attitudes, but also because of external factors, such as their relationship with HCPs and access to healthcare resources (Ells, Hunt, & Chambers-Evans, 2011; Mackenzie & Stoljar, 2000; Sherwin, 1998).

Ells and colleagues (2011) argue that relational autonomy is an essential component of patient-centred care as it “draws attention to contextual features – such as the structures and policies of clinical settings – that support or limit autonomy” (p. 96). Specifically, a relational understanding of autonomy has been used to examine decision making within healthcare contexts to consider positive and negative implications of social relationship (e.g., family and patient-HCP relationships) to patient autonomy (Entwistle, Carter, Cribb, & McCaffery, 2010; Ho, 2008). These authors highlight the importance of social structures, interactions, and relationships in enabling or constraining patient autonomy and encourage consideration of how and why social influences either support or undermine an individual’s agency related to their health decisions and behaviours (Ells et al., 2011; Entwistle et al., 2010; Ho, 2008). Specifically in the context of breast cancer, relational autonomy has been used in qualitative research exploring women’s decision making about cancer screening and risk-reducing surgery among women who carry BRCA1 or BRCA2 gene mutations to illuminate their personal experiences as well as the wider social and structural contexts within which they make decisions (Howard, Balneaves, Bottorff, & Rodney, 2011). Howard and colleagues found that women’s decision-making process was not only shaped by personal factors, but also by contextual conditions including characteristics of healthcare services and the nature of consultations with HCPs.

The social and structural factors that shape the context of women’s lives and the healthcare environment in which patients receive care can have a considerable effect on adherence (WHO, 2003). As noted previously, however, the bulk of the research examining AET adherence has focused primarily on patient-related factors (e.g., demographic and clinical characteristics and health beliefs), to the relative neglect of social and structural factors. With respect to health behaviours, such as medication adherence, it remains important to maintain some focus on the

individual (Sherwin, 1998). While a relational interpretation of autonomy demands attention be paid to how social and structural factors affect women's lives, it does not deny that autonomy ultimately resides within the individual. Hence, consideration of the personal circumstances of women's lives is imperative to better understanding the reasons why women are non-adherent to AET (Sherwin, 1998).

I chose to approach each phase of this dissertation using the theoretical lens of relational autonomy to consider individual-level factors and to specifically draw attention to the wider context of women's lives and the healthcare system. Using Sherwin's relational interpretation of autonomy as a theoretical lens allowed for the personal nature of AET-related decisions, as well as the social and structural influences on breast cancer survivors' AET experiences, decisions, and behaviours to be made visible. Relational autonomy theory provided a useful lens to guide how I collected and analyzed the data by balancing the personal nature of AET adherence decisions and behaviours with the influence of the larger context in which adherence is enacted. Specifically, the interview questions and data analysis were guided by relational autonomy theory to explore how factors such as beliefs, attitudes, qualities of the patient-HCP relationship, healthcare resources, and follow-up care influenced breast cancer survivors' and HCPs' perspectives and experiences related to AET. I also used relational autonomy to guide the organization of the study findings of the integrative review (Chapter 2) and interpretive description study with breast cancer survivors (Chapter 3) into personal, social, and structural categories. The results of this dissertation extend understanding of AET non-adherence and previous work that was focused primarily at the individual level by providing insight into the ways in which contextual influences affect AET adherence.

## **1.6 Research Purpose and Objectives**

The overarching purpose of my dissertation was to explore why breast cancer survivors have suboptimal levels of adherence to prescribed AET. I developed three specific research objectives from this overall purpose that I address in three corresponding manuscripts presented in Chapters 2 through 4. These research objectives were:

1. To examine previous research on the patient-reported personal, social, and structural factors influencing breast cancer survivors' adherence to AET;
2. To explore breast cancer survivors' experiences and perspectives related to AET and describe how personal, social, and structural factors influence AET persistence; and
3. To explore HCPs' experiences and perspectives in providing care to breast cancer survivors prescribed AET and identify how social and structural factors influence the provision of AET-related care and adherence.

### **1.6.1 Research Objective 1**

The first research objective was to conduct an integrative review of the quantitative and qualitative literature on the patient-reported factors found to influence breast cancer survivors' adherence to AET. The aim was to identify, appraise, and synthesize the existing evidence on patient-reported factors associated with AET adherence within the quantitative and qualitative literature. Specifically, I wanted to understand what was known about the personal and contextual determinants of AET adherence from the perspective of breast cancer survivors, and identify any gaps in the literature that warranted further exploration.

### **1.6.2 Research Objective 2**

The second research objective was to qualitatively explore breast cancer survivors' experiences and perspectives related to AET to better understand why women are non-persistent

with AET. I sought to explore the underlying personal, social, and structural factors shaping breast cancer survivors' experiences with AET and their resulting persistence to inform future research and practice recommendations to improve support for women undergoing AET and optimize persistence. The findings provided important insights that underscored the importance of also gaining the perspectives of HCPs to further understand how features of the healthcare system and delivery shape AET-related care and persistence.

### **1.6.3 Research Objective 3**

The third research objective was to qualitatively explore HCPs' experiences and perspectives of providing care to breast cancer survivors' prescribed AET. I wanted to better understand, from the perspective of HCPs, the larger context in which care is provided to women undergoing AET, including how personal, social, and structural factors shape the structure and delivery of AET-related healthcare services. I also wanted to identify HCPs' perceptions of strategies that would be most effective for optimizing AET adherence.

## **1.7 Ethical Considerations**

All participants were provided information about the study, assured their participation was voluntary, and asked to sign a consent form prior to participating in the interviews. Confidentiality was assured by assigning participants a numerical identification number and stripping all data of personal identifiers. A master sheet matching names to identification numbers was kept separate from the data in a locked drawer in Dr. Howard's (co-investigator) research office at UBC. Only research team members directly involved in the data collection and analysis had access to participant information. Investigators worked within the ethical principles of the *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* (Canadian Institutes of Health Research Natural Sciences and Engineering Research Council of Canada,

2010). Ethical approval ensuring patient safety and data security was obtained from the UBC Research Ethics Board and amendments to this application were sought as warranted. Women were encouraged to share their AET decisions with their oncology care team. We anticipated there would be minimal risks associated with participating in the interview components of the study; however, we recognized that some women may experience distress as a consequence of reflecting on their cancer experience. In the event women expressed high distress or difficulties coping with the post-treatment period we would refer them to the Patient and Family Counseling Program at BC Cancer, which is provided to all patients free of charge. None of the participants we interviewed required referral to this counseling program. A standard script (Appendix A.5) was used to guide conversations with breast cancer survivors regarding the importance of discussing with their HCPs any decisions they had made about AET or any difficulties they had experienced related to therapy, including adhering to their prescribed AET regimes, refusing AET, or considering withdrawing from treatment.

## **1.8 Rigor**

The credibility of qualitative research within the methodological orientation of interpretive description can be evaluated using the concepts of epistemological integrity, representative credibility, analytic logic, and interpretive authority (Thorne, 2016). First, the interpretive description studies in Chapters 3 and 4 demonstrate *epistemological integrity* through a defensible line of reasoning, which begins with research questions that attend to disciplinary assumptions about the “value of subjective and experiential knowledge as one of the fundamental sources of applied practice insight,” (p. 82) and continues through the research process to interpretation of the study findings. Second, *representative credibility* was fostered by using varied data sources and multiple perspectives (i.e. breast cancer survivor and HCP

interview data, field notes, and comparison to existing literature) and triangulating these sources during analysis to better understand AET adherence in the context of breast cancer. Sampling breast cancer survivors who were adherent and non-adherent to AET, as well as HCPs from multiple disciplines allowed us to explore, describe, and interpret individual variations across commonalities (Thorne, 2016). The *analytic logic* in the research process was enhanced through reflexivity of the researchers and by establishing an audit trail. Prior to conducting the interviews, I developed reflective memos regarding my assumptions about the factors influencing study participants' decisions and behaviours related to AET and adherence. Field notes on the content and interactions during individual interviews comprised part of the audit trail (Koch, 2006). Throughout the research process, I developed memos to track methodological and analytical decisions, including the creation and refinement of codes, themes, and interpretations made by the research team. I also kept a reflective journal to document and further explore critical reflections, relationships among data, and questions that arose throughout the research process. Two members of the investigative team reviewed several transcripts and confirmed the coding before finalizing the coding scheme. As well, I kept complete records of research team meetings as memos and used these as part of the audit trail. Lastly, *interpretive authority* refers to the credibility and trustworthiness that the study findings represent some truth about the phenomenon under study that is separate from researcher bias or experience (Thorne, 2016). I used methods such as conceptual mapping, analytic memos, and continual reflective note taking throughout the analysis and interpretation phases to account for potential personal biases and assumptions and to ensure the study findings were embedded in the data and trustworthy. I also continued to engage with the raw data throughout the research process by confirming conceptualizations and interpretations accurately reflected the data from interview

audio files, transcripts, and field notes. Lastly, I used rich quotes to support the study interpretations and demonstrate legitimacy of the study findings. Together these steps helped enhance the rigor of the interpretive description studies.

## **1.9 Summary**

AET has made a significant contribution to the treatment of breast cancer; however, many women experience difficulty in adhering to AET over the recommended five-year period. The association between adherence and survival outcomes underscores the critical need to identify the reasons why women do not adhere to AET. This presents both a significant challenge and also an important opportunity. Increasing adherence to AET has the potential to improve the effectiveness of treatment and, thus, patient outcomes. While progress has been made in understanding some aspects of the personal, social, and structural factors associated with adherence to AET, there remains much to be learned. An in-depth exploration of breast cancer survivors' and HCPs' experiences and perspectives related to AET is an important step in informing the future development of strategies to support women in remaining motivated and committed to these long-term therapies and also to ensure their QOL is supported.

This dissertation research represents a significant step in identifying why breast cancer survivors have suboptimal levels of adherence to AET and translating these findings into patient- and HCP-informed support strategies to improve patient outcomes. The findings of this dissertation informed several recommendations for research and clinical practice that I outline in Chapter 5.

## **CHAPTER 2: PATIENT-REPORTED FACTORS ASSOCIATED WITH ADHERENCE TO ADJUVANT ENDOCRINE THERAPY AFTER BREAST CANCER: AN INTEGRATIVE REVIEW**

A version of this chapter was previously published in *Breast Cancer Research and Treatment* (Lambert, Balneaves, Howard, & Gotay, 2018).

### **2.1 Introduction**

Breast cancer is the most common cancer in women worldwide, with an estimated 1.67 million new diagnoses in 2012 (International Agency for Research on Cancer, 2012). Breast cancer is the leading cause of death in women residing in less developed regions and the second cause of cancer deaths in women from more developed countries. Mortality, however, is declining due in part to screening and treatment advances, including the use of AET (Berry et al., 2005). AET is a treatment that significantly reduces recurrence and mortality in women with HR+ breast cancer (Burstein et al., 2010). The most commonly prescribed AETs are tamoxifen and AIs. Women who are non-adherent or non-persistent with AET have a dramatic increase (49% and 26% respectively) in their risk of mortality (Hershman et al., 2011). Updated clinical practice guidelines recommend extending AET use from five years to ten years (Burstein et al., 2014), with research suggesting extended tamoxifen can reduce the risk of breast cancer-related mortality by one third during the first 10 years of therapy and by half during the second decade following diagnosis (Davies et al., 2013). Despite the radical difference made by AET in breast cancer outcomes, up to 50% of women do not adhere to prescribed regimens (Hershman et al., 2010; Owusu et al., 2008; van Herk-Sukel et al., 2010) and 31–73% of women are non-persistent with AET (Murphy, Bartholomew, Carpentier, Bluethmann, & Vernon, 2012).

The high rate of AET non-adherence (Banning, 2012; Chlebowski & Geller, 2007; Gotay & Dunn, 2011) and non-persistence (Murphy et al., 2012) has been well documented with numerous demographic and clinical correlates and predictors (e.g., age, disease severity, comorbidities, toxicity) identified. Attention, however, must be paid to the personal, social, and structural factors that influence women's AET decisions. Recently, researchers have sought to address this gap by asking breast cancer survivors about their experiences and reasons for non-adherence and non-persistence with AET. To my knowledge, this is the first review to examine and summarize these patient-reported factors that influence AET adherence and persistence. The purpose of this manuscript is to review the personal, social, and structural factors influencing AET adherence and persistence in breast cancer populations to inform future research and clinical strategies.

## **2.2 Methods**

An integrative review methodology (Whittemore & Knafl, 2005) was used to explore and summarize studies investigating patient-reported factors that influence AET adherence and persistence. Integrative reviews allow for the inclusion of experimental and non-experimental research, whereas systematic reviews are typically limited to experimental studies (Whittemore & Knafl, 2005). We searched PubMed, Medline, CINAHL, Embase, and PsycINFO databases for studies published between January 1, 1998 (when the Early Breast Cancer Prevention Trialists' Collaborative Group published a review of trials showing the efficacy of tamoxifen (Early Breast Cancer Trialists' Collaborative Group (EBCTCG), 1998)) and January 18, 2017. Each database was systematically searched using keyword descriptors and database subject headings used to index and catalog biomedical information. Search terms included *adheren\**, *nonadheren\**, *non-adheren\**, *contin\**, *discontin\**, *complan\**, *non-complan\**, *persist\**, *non-*

persist\*, initiat\*, or non-initiat\*; tamoxifen, aromatase inhibitor\*, letrozole, anastrozole, or exemestane; adjuvant endocrine, adjuvant hormon\*, endocrine, or hormon\* combined with treat\* or therap\*; and breast cancer or breast neoplasm\*. Eligibility criteria included primary quantitative or qualitative research studies (i.e., not systematic reviews, meta-analyses, or commentaries) that: (1) were written in English; (2) were published in a peer-reviewed journal; (3) assessed AET adherence and/or persistence through objective measurement (e.g., medical record or pharmacy refill database abstraction) or self-report evaluations; (4) included statistically significant patient-reported factors associated with AET adherence and/or persistence in female breast cancer survivors in the quantitative literature or included factors women described as influencing their AET experience in the qualitative literature.

The concepts of AET adherence and persistence are often combined or used interchangeably within the literature when referring to AET use (Cahir, Guinan, et al., 2015; Gotay & Dunn, 2011; Van Liew et al., 2014; Wuensch et al., 2015). Consequently, the WHO's definition of adherence is used, which is defined as “the extent to which a person's behaviour – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider” (2003, p. 3). This definition effectively encompasses the concepts of non-adherence and non-persistence.

Patient-reported factors refer to patient-reported outcome and experience measures and are defined as “any aspect of a patient's health status that comes directly from the patient” (U.S. Departments of Health and Human Services FDA Center for Drug Evaluation and Research, U.S. Department of Health and Human Services FDA Center for Biologics Evaluation and Research, & U.S. Department of Health and Human Services FDA Center for Devices and Radiological Health, 2006). Patient-reported factors include, but are not limited to, patients' perspectives on

physical health (e.g., symptoms), emotional health (e.g., anxiety, depression), social health (e.g., social support), QOL (Howell et al., 2013), and the delivery of healthcare services (e.g., continuity of follow-up care). Patient-reported factors capture patients' perceptions, experiences, and beliefs on cancer and treatment and is an area of research that has gained much attention in recent years due to its potential to improve patient outcomes (Howell et al., 2015).

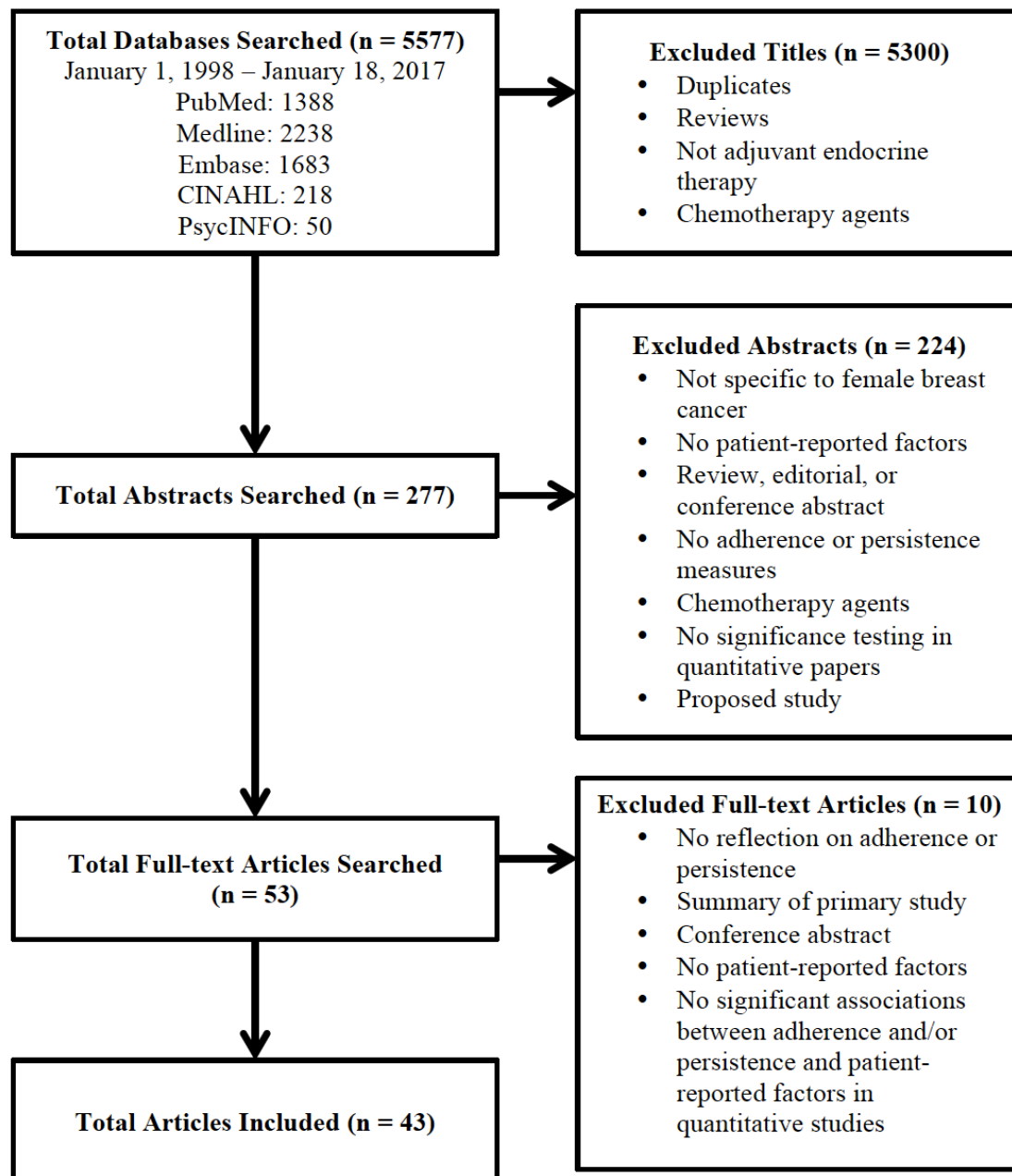
The quality of eligible studies was evaluated using a two-point scale (high or low) to assess methodological rigor and data relevance (Whittemore & Knafl, 2005). Generic methodological criteria outlined by Whittemore (2005) for quantitative studies and Burns (1989) for qualitative studies were utilized to assess key methodological constructs (i.e., sampling, data collection protocol, data analysis, threats to validity). No studies were subsequently excluded based on a low-quality ranking. The lead author scanned title citations and abstracts to determine relevance based on the eligibility criteria. Reference lists of relevant primary sources were hand searched to identify additional studies. Data was extracted from eligible studies and entered into a matrix to categorize, display, and compare and contrast data (Whittemore & Knafl, 2005). Three authors (LKL, LGB, and AFH) independently reviewed the matrix. The matrix was divided into two subgroups (quantitative and qualitative studies) and each subgroup was iteratively analysed to identify patterns, themes, and relationships. Conceptual mapping was used to display and compare data. Categories extracted to the matrix included author, country, study design, data collection method and timing, sample characteristics (e.g., mean age, breast cancer disease status, type of AET used by participants) and size, factors explored, level and measurement of non-adherence/non-persistence, statistically significant patient-reported factors associated AET adherence/persistence in the quantitative literature, and factors women described as influencing their AET experience in the qualitative literature.

To expand understanding of the broader context of women's lives, the theoretical lens of relational autonomy (Sherwin, 1998) was used to identify the personal, social, and structural factors found to influence adherence, persistence, and women's AET experience, and to organize study findings in a matrix using these three categories. Personal factors include QOL, side effects, current medication use, beliefs and attitudes, and self-efficacy. Social factors include the quality of the patient-HCP relationship and social support from friends and family. Structural factors in the healthcare system include the type and continuity of follow-up care and medication costs. This is not an inclusive list as other factors were identified during the analysis process.

### **2.3 Results**

Initially, 5,577 studies were identified (see Figure 2.1) and 43 articles that met inclusion criteria are included in this review.

**Figure 2.1 Diagram of Study Selection**



Studies were conducted in North America, Europe, and Australia, and sample characteristics varied widely across studies. There was marked variability in sample sizes, study methodologies, and the operationalization of adherence and persistence. A variety of terms (e.g., adherence, persistence, discontinuation), data sources (e.g., medical records, prescription refills, self-report

evaluations), and measurement methods (e.g., less than 80 days covered by a prescription, discontinuation before five years) were used to determine women's adherence and persistence. Due to this variability and in keeping with the WHO's definition of adherence, the term adherence will be used herein to collectively refer to adherence and persistence. Variability also existed in the type, reliability, and validity of instruments used to assess study outcomes. It is important to note that several studies did not distinguish between women taking tamoxifen and AIs. Although the two classes of AET have different mechanisms of action and adverse effect profiles, both have the same goal of reducing the risk of breast cancer recurrence. Due to similarities in daily regime, duration of therapy, and impact on women's QOL (Burstein et al., 2010), results of tamoxifen and AI use are combined in this review.

Several personal, social, and structural factors that influence AET adherence were identified. For ease of interpretation, quantitative and qualitative studies were summarized separately with statistically significant findings and major themes reported, respectively.

### **2.3.1 Quantitative Results**

A total of 34 quantitative manuscripts were examined: 29 studies used a survey design, three studies used a RCT, one study utilized an interventional single cohort design, and another was a prospective non-interventional study (see Table 2.1). Six pairs of these studies (Bradley, Dahman, Jagsi, Katz, & Hawley, 2015; Brier, Chambless, Gross, Chen, & Mao, 2017; Bright, Petrie, Partridge, & Stanton, 2016; Chim et al., 2013; Cluze et al., 2012; Fink et al., 2004; Friese et al., 2013; Huiart et al., 2012; Lash et al., 2006; Stanton, Petrie, & Partridge, 2014; Wouters, Maatman, et al., 2013; Wouters et al., 2014) and a set of three studies (Henry et al., 2012; Kadakia et al., 2016; Kidwell et al., 2014) analyzed data from the same patient sample using different measures or distinct time points.

**Table 2.1 Quantitative Studies Reviewed**

First author/year/country	Study design	Sample	Selected factors explored	Non-adherence/non-persistence	Significant patient-reported factors associated with non-adherence/non-persistence (-) or higher adherence/persistence (+)
Albert (2011) Germany	Cross sectional survey within 2-14 months post BrCa tx	$N = 149$ , $M = 60$ years, attending a BrCa centre, TAM/AI	Socio-demographics, QOL measures, receipt of information, consultation with a BrCa nurse	<i>Non-adherence</i> : 21% with contact to a BrCa nurse, 44% without contact to a BrCa nurse; self-report	<b>Structural</b> : contact with a BrCa nurse (+)
Arriola (2014) USA	Cross-sectional survey 6 months - 5 years post primary BrCa tx	$N = 200$ , $M = 58.5$ years, stages I-IV, seen by a medical oncologist or breast surgeon, TAM/AI	Socio-demographics, frequency of physician communication, medication beliefs	<i>Non-adherence</i> : measured, rate not reported; self-report	<b>Personal</b> : beliefs about AET necessity (+) <b>Social</b> : frequency of physician communication about AET importance and side effects (+)
Atkins (2006) UK	Cross-sectional semi-structured interviews $\geq 2$ years post dx	$N = 131$ , $M = 59.4$ years, TAM/AI	Socio-demographics, preferred route of administration, aspects of medication disliked, health locus of control	<i>Non-adherence</i> : 55% (83% non-intentional, non-adherence); self-report	<b>Personal</b> : disliked aspects of AET (e.g., side effects, difficulty swallowing, inconvenience) (-), belief that others (HCPs, family, friends) could improve their health (-), perceived themselves as having less influence over their health (-)
Bender (2014) USA	Prospective survey pre AET initiation and 6, 12, and 18 post initiation	$N = 91$ , $M = 56.7$ years, stages I-IIIa, TAM/AI	Socio-demographics, cognitive function, mood, anxiety, physical functioning, perceived tx efficacy, social support, side effects, financial hardship	<i>Non-adherence</i> : significantly increased during the first 18 months of AET (rate not reported); electronic medication monitoring	<b>Personal</b> : cognitive symptoms (-), musculoskeletal pain (-), weight concerns (-), gynecological symptoms (-), greater levels of depression and anxiety prior to initiating AET (-)
Aiello Bowles (2012) USA	Cross-sectional survey after receipt of AET Rx within 12 months post dx	$N = 538$ , $M = 64$ years, postmenopausal, stages I-IIb, TAM/AI	Socio-demographics, adverse effects	<i>Non-persistence</i> : 18.2% < 5 years, including 25% < 1 year; self-report and validated against pharmacy data	<b>Personal</b> : side effects (e.g., headaches; loss of appetite, upset stomach, or vomiting) (-)
Bradley (2015) USA <sup>a</sup>	Prospective survey 9 months post dx and 4	$N = 712$ , $M = 57.67$ years, stages 0-III,	Socio-demographics, insurance and prescription drug	<i>Non-persistence</i> : 20%; self-report	<b>Structural</b> : absence of prescription drug coverage (-)

First author/year/country	Study design	Sample	Selected factors explored	Non-adherence/non-persistence	Significant patient-reported factors associated with non-adherence/non-persistence (-) or higher adherence/persistence (+)
	years later	TAM/AI	coverage		
Brett (2016) UK	Cross-sectional survey 2-4 years post dx	$N = 211$ , $M = 63$ years, primary BrCa, TAM/AI	Socio-demographics, experiences and beliefs about AET	<i>Non-adherence</i> : 22% (14% intentional; 8% unintentional); self-report	<b>Personal</b> : side effects (-), greater concerns about taking AET (e.g., longevity of therapy, worry about long-term side effects) (-)
Brier (2017) USA <sup>b</sup>	Retrospective survey on average 26.7 months post initiation	$N = 437$ , $M = 62$ years, postmenopausal, stages I-III, AI	Socio-demographics, health beliefs	<i>Non-adherence</i> : 21.3%; medical chart	<b>Personal</b> : perceived greater barriers to AI tx (e.g., pain made taking AI more difficult and AI tx period too long) (-)
Bright (2016) USA <sup>c</sup>	Cross-sectional survey currently taking or taken AET in past 12 months	$N = 1,371$ , $M = 56$ years, stages 0-IV, TAM/AI	Socio-demographics, cancer-related symptoms, emotions regarding AET, AET barriers/facilitators	<i>Non-adherence</i> : 39% missed 1 or more AET doses in last month; self-report	<b>Personal</b> : any barrier to medication adherence (-), side effect-related barrier (-), behavioural barriers (-), cognitive facilitator regarding self-talk (+), behavioural barrier and no behavioural facilitator (-), lower perceived AET necessity (-), more negative emotions regarding AET (-)
Chim (2013) USA <sup>d</sup>	Retrospective survey on average 26.7 months post initiation	$N = 437$ , $M = 62$ years, postmenopausal, stages I-III, AI	Socio-demographics, joint pain	<i>Non-persistence</i> : 11% on average 29 months post initiation; medical chart	<b>Personal</b> : severity of joint pain (-) (i.e., score of 4 or greater on Brief Pain Inventory)
Cluze (2012) France <sup>e</sup>	Prospective survey at enrollment, 10, 16, and 28 months post dx	$N = 196$ , $M = 37$ years, stages I-III, TAM	Socio-demographics, side effects, patient-provider relationship, participation in AET decision, fear of recurrence, social support	<i>Non-adherence</i> : 42% interrupted (interruption = $\geq 2$ consecutive months without Rx refill) within 2 years; pharmacy refill database	<b>Personal</b> : lack of AET understanding (-), fluid retention (-), no longer fearing cancer relapse (-), taking $\leq 2$ tx modalities (-), $\geq 2$ menopausal symptoms <b>Social</b> : poor social support (-), no opportunity to ask question at dx (-)
Demissie (2001) USA	Prospective survey 5, 21, and 33 months post primary BrCa tx	$N = 189$ , $M = 67.7$ years, stages I-II, TAM	Socio-demographics, emotional health, physical function, tx decision-making process	<i>Non-persistence</i> : 15% within 3 years post dx; self-report	<b>Personal</b> : side effects (i.e., depression, nausea, visual complaints, vaginal bleeding) (-), higher self-efficacy related to communication with physicians (+), better physical functioning (-) <b>Structural</b> : greater number of BrCa physicians seen (+)
Fink (2004)	Prospective	$N = 516$ , $\geq 65$	Socio-demographics,	<i>Non-persistence</i> : 17%	<b>Personal</b> : neutral and negative beliefs about the

First author/year/country	Study design	Sample	Selected factors explored	Non-adherence/non-persistence	Significant patient-reported factors associated with non-adherence/non-persistence (-) or higher adherence/persistence (+)
USA <sup>f</sup>	survey at 3, 6, 15, and 27 months post BrCa surgery	years, stages I-IIIa, TAM	patients' beliefs about risk and benefits of TAM, medication use, side effects, QOL, HCP interaction and communication	during 2-years follow-up (68% adhered < 1 year); self-report validated against pharmacy data	value of TAM (-)
Friese (2013) USA <sup>g</sup>	Prospective survey 9 months and 4 years post dx	<i>N</i> = 743, <i>M</i> = 58.9 years, stages I-III or DCIS, non-Hispanic white, black or Latina, TAM/AI	Socio-demographics, follow-up care, adequacy of AET information, polypharmacy, medication beliefs, worry about recurrence	<i>Non-adherence</i> : 25.8% at 4 years, <i>non-persistence</i> : 15.1%; self-report	<b>Personal:</b> <i>Non-persistence</i> : polypharmacy (two or more medications weekly) (+)
Grunfeld (2005) UK	Cross sectional survey on average 2.75 years post initiation	<i>N</i> = 110, <i>M</i> = 56.3 years, primary BrCa, TAM	Socio-demographics, emotional and physical well-being, side effects, medication beliefs, regime	<i>Non-adherence</i> : 12%; self-report	<b>Personal:</b> lower perceived necessity (-), forgetting to take AET (-)
Hadji (2014) Germany	Prospective non-interventional survey at baseline, 3, 6, and 9 months after study start	<i>N</i> = 1916, <i>M</i> = 65 years, postmenopausal, early-stage BrCa, AI, and prior TAM permitted	Socio-demographics, arthralgia, side effects, presence of concomitant skeletal and muscular diseases	<i>Non-adherence</i> : 34% at 9 months post AI initiation; self-report	<b>Personal:</b> arthralgia (-)
Heisig (2015) Germany	Interventional single cohort - survey pre- and post intervention and 3 months later	<i>N</i> = 137, <i>M</i> = 56.03 years, stages 0-IV, TAM/AI	Socio-demographics, satisfaction with AET information, comprehension and recall of enhanced AET information	<i>Non-adherence</i> : 6.6% took ≤80% of AET, 26.5% missed at least one dose; self-report	<b>Personal:</b> satisfied with and able to comprehend AET information (+), satisfied with information on potential side effects (+)
Henry (2012) USA <sup>h</sup>	Prospective RCT - symptom surveys at baseline and 1, 3, 6, 12, and 24 months post	<i>N</i> = 500, <i>M</i> = 59 years, postmenopausal, stages 0-III, AI and prior TAM permitted	Socio-demographics, pain, side effects	<i>Non-persistence</i> : 32.4% within 2 years; medical record	<b>Personal:</b> preexisting pain (-)

First author/year/country	Study design	Sample	Selected factors explored	Non-adherence/non-persistence	Significant patient-reported factors associated with non-adherence/non-persistence (-) or higher adherence/persistence (+)
	initiation				
Hershman (2016) USA	Prospective telephone surveys at baseline and every 6 months for 2 years	$N = 523$ , > 20 years, stages I-III, TAM/AI	Socio-demographics, QOL, decision-making considerations, patient-HCP communication, social support, tx satisfaction, distress, side effects	<i>Non-persistence</i> : 18% within 2 years; pharmacy database	<b>Personal</b> : lower QOL (-), positive attitude toward AET (+), greater tx satisfaction (+), emotional distress (i.e., intrusive/avoidant thoughts about BrCa) (-), physical and concrete decision-making concerns (-)
Huiart (2012) France <sup>i</sup>	Prospective survey at baseline and 10 months post dx	$N = 246$ , $M = 36.9$ years, premenopausal, stages I-III, TAM	Socio-demographics, QOL, family life, use of social/medical services, depressive symptoms, social support	<i>Non-persistence</i> : 17% after 1 year, 29.7% after 2 years, 39.5% after 3 years; self-report	<b>Personal</b> : AET non-adherence behaviour at 10 months (-non-persistence) <b>Social</b> : low social support (-)
Huiart (2013) France	Prospective survey at baseline; interview at 10 months later	$N = 233$ , $M = 71.8$ years, stages I-III, AI	Socio-demographics, psychosocial characteristics, complementary medicine use, follow-up care, geriatric assessment	<i>Non-persistence</i> : 8.7% (year 1), 15.6% (year 2), 20.8% (year 3), 24.7% (year 4); pharmacy refill database	<b>Personal</b> : use of complementary medicine (-), polypharmacy (taking 4 or more medications) (+)
Kadakia (2016) USA <sup>j</sup>	Prospective RCT - symptom surveys at baseline and 1, 3, 6, 12, 24 months post initiation	$N = 490$ , $M = 59$ years, postmenopausal, stages 0-III, AI and prior TAM permitted	Socio-demographics, global HRQOL, depression, anxiety, symptom burden	<i>Non-persistence</i> : 32% within 2 years; medical record	<b>Personal</b> : worsening HRQOL and musculoskeletal symptom burden baseline to 1, 3, and 6 months (-), worsening depression, anxiety, cognitive, mood, and weight/body image clusters (-)
Kahn (2007) USA	Cross-sectional survey at 4 years post dx	$N = 881$ , 21-80 years, stages I-III, TAM	Socio-demographics, HCP support, role in AET decision, receipt of information about side effects, patient-HCP communication, health insurance status, side effects	<i>Non-persistence</i> : 21% at 4 years, 54% of those stopped within 3 years; self-report	<b>Personal</b> : severity of side effects (-), less than desired level of participation in decision making (-) <b>Social</b> : less than desired amount of support from HCP (-), decision to initiate AET without adequate HCP input (-), not informed about side effects in advance (-) <b>Structural</b> : one doctor responsible for follow-up care (+)
Kidwell	Prospective	$N = 449$ , $M = 59$	Socio-demographics,	<i>Non-persistence</i> :	<b>Personal</b> : greater number ( $\geq 3$ ) of symptoms

First author/year/country	Study design	Sample	Selected factors explored	Non-adherence/non-persistence	Significant patient-reported factors associated with non-adherence/non-persistence (-) or higher adherence/persistence (+)
(2014) USA <sup>k</sup>	RCT - symptom surveys at baseline and 1, 3, 6, 12, 24 months post initiation	years, postmenopausal, stages 0-III, AI and prior TAM permitted	sleep, fatigue, mood, pain	31.2% within 1 year; medical record	before AI initiation (-), baseline poor sleep quality (-), moderate-extreme difficulty concentrating (-)
Kimmick (2015) USA	Cross-sectional survey on average 35 months post initiation	$N = 112$ , $M = 63.7$ years, postmenopausal, stages I-III, TAM/AI	Socio-demographics, symptoms, self-efficacy re: taking medications & communication with HCPs, medication beliefs	<i>Non-adherence</i> : 33.9% intentional, 58.9% unintentional; self-report	<b>Personal</b> : higher self-efficacy for taking AET (+), lower self efficacy for physician communication (-), more symptoms (-)
Kyvernitis (2014) Germany	Prospective survey at 12 and 24 months post initiation	$N = 125$ , $M = 63.2$ years, postmenopausal, primary BrCa, AI	Socio-demographics, menopausal-like symptoms	<i>Non-adherence</i> : 32% non-adherence in year 2; self-report and medical chart review	<b>Personal</b> : anxiety at 12 months (-)
Lash (2006) USA <sup>l</sup>	Prospective survey 3, 6, 15, 27, 39, 51, and 63 months post BrCa surgery	$N = 462$ , $\geq 65$ years, stages I-III, TAM	Socio-demographics, beliefs about risk and benefits of TAM, medication use, side effects, QOL, medical interaction and communication	<i>Non-persistence</i> : 31% within 5 years; self-report validated against pharmacy data	<b>Personal</b> : polypharmacy at baseline (+), added a prescription during tx (-), initial or subsequent severe side effects (-), more positive views of TAM at baseline and positive change during follow-up (+)
Liu (2013) USA	Prospective survey at 6, 18 and 36 months post dx	$N = 303$ , $M = 51.2$ years, stages I-III, low-income, 54% Latina, TAM/AI	Socio-demographics, patient-centred communication, health insurance status	<i>Non-adherence</i> : 12%; self-report	<b>Personal</b> : greater self efficacy in patient-physician interactions (+), side effects (-) <b>Social</b> : patient-centred communication (+) <b>Structural</b> : absence of health insurance (-)
Quinn (2016) Ireland	Cross-sectional survey on average 3.03 years post dx	$N = 261$ , $M = 57.88$ years, early-stage BrCa, TAM/AI	Socio-demographics, social and emotional factors, side effects	<i>Non-adherence</i> : 32.2%, <i>non-persistence</i> : 10.9%; self-report	<b>Personal</b> : side effects (-) <b>Social</b> : low levels of emotional support (-)
Stanton (2014) USA <sup>m</sup>	Cross-sectional survey currently taking or taken AET in past 12 months	$N = 1465$ , $M = 56.03$ years, stages 0-IV, TAM/AI	Socio-demographics, anxiety, depression, patient-HCP relationship, recurrence worry, side effects, perceived AET necessity and concerns,	<i>Non-adherence</i> : 39% missed 1 or more AET doses in last month, <i>non-persistence</i> : 6.4%; self-report	<b>Personal</b> : <i>Non-adherence</i> : lower perceived AET necessity (-), more negative emotions regarding AET (-); <i>Non-persistence</i> : depressive symptoms (-), negative/lower positive emotions regarding AET (-) <b>Social</b> : <i>Non-adherence</i> : poorer relationship

First author/year/country	Study design	Sample	Selected factors explored	Non-adherence/non-persistence	Significant patient-reported factors associated with non-adherence/non-persistence (-) or higher adherence/persistence (+)
			emotions re: AET		with oncologist (-)
Wickersham (2013) USA	Prospective survey pre-tx and 6 months post initiation	$N = 198$ , $M = 59.1$ years, pre- and postmenopausal, $\geq 8$ years education, stages I-III or LCIS, TAM/AI	Socio-demographics, depressive symptoms, fatigue, anxiety, side effects	<i>Non-adherence</i> : 11.3%; electronic medication event monitoring	<b>Personal</b> : weight concerns (-)
Wouters (2013) Netherlands <sup>n</sup>	Cross sectional survey $\leq 3$ months - 4 years post initiation	$N = 241$ , $M = 57.2$ years, ER+ BrCa, TAM/AI	Socio-demographics, preferences for AET attributes	<i>Non-persistence</i> : 6.2%; self-report and validated against pharmacy data	<b>Personal</b> : lower benefit/drawback ratio (importance of efficacy versus other AET characteristics (e.g., side effects, regime duration)) (-)
Wouters (2014) Netherlands <sup>o</sup>	Cross-sectional survey $\leq 3$ months - 4 years post initiation	$N = 241$ , $M = 57.2$ years, ER+ BrCa, TAM/AI	Socio-demographics, side effects, AET knowledge and beliefs, worry about side effects, practical issues with AET, self-efficacy	<i>Non-persistence</i> : 6.2%; self-report and validated against pharmacy data	<b>Personal</b> : increased number of side effects (-), practical problems (e.g., refill problems, trouble with tablet intake) (-), lower perceived self-efficacy related to medication intake (-), lower levels of self-efficacy related to learning about AET (-)
Wuensch (2015) Germany	Cross sectional survey	$N = 281$ , $M = 51$ years, patient members of self-help and BrCa organizations	Socio-demographics, AET decision making, general support, information provided by physicians, side effects	<i>Non-adherence</i> : 14.6%; self-report	<b>Personal</b> : number of side effects (-), severity of side effects (-), recent depression (-) <b>Social</b> : someone in the family with BrCa (+), social support (+), received detailed answers to questions (+), received information on side effects (+)
<b>Table legend:</b> AI – aromatase inhibitor, AET – adjuvant endocrine therapy, BrCa – breast cancer, Dx – diagnosis, ER+ – estrogen receptor-positive, HCP – healthcare provider, HRQOL – health-related QOL, M – mean age, N – sample size, QOL – quality of life, RCT – randomized controlled trial, Rx – prescription, TAM – tamoxifen, Tx – treatment, UK – United Kingdom, USA – United States of America <b>Note:</b> a, g Data from the same sample; b, d Data from the same sample c, m Data from the same sample e, i Data from the same sample f, l Data from the same sample h, j, k Data from the same sample n, o Data from the same sample					

### 2.3.1.1 Personal Factors

It is well known that socio-demographic characteristics, including age, ethnicity, and income, are associated with AET adherence (Murphy et al., 2012). These factors are not discussed here. Patient-reported personal factors found to affect AET adherence included QOL, side effects, current medication use, beliefs and attitudes, and self-efficacy.

***QOL and side effects.*** The majority of studies found a significant correlation between side effects and AET non-adherence (Aiello Bowles et al., 2012; Atkins & Fallowfield, 2006; Bender et al., 2014; Brett et al., 2016; Bright et al., 2016; Chim et al., 2013; Cluze et al., 2012; Demissie et al., 2001; Hadji et al., 2014; Kadakia et al., 2016; Kahn et al., 2007; Kidwell et al., 2014; Kimmick et al., 2015; Kyvernitakis et al., 2014; Lash et al., 2006; Liu et al., 2013; Quinn et al., 2016; Stanton et al., 2014; Wouters et al., 2014; Wuensch et al., 2015). Women reporting lower overall QOL were more likely to discontinue AET early (Hershman et al., 2016; Kadakia et al., 2016). Specifically, non-adherence was significantly greater for women experiencing musculoskeletal pain (Chim et al., 2013; Hadji et al., 2014; Henry et al., 2012; Kadakia et al., 2016), headaches (Aiello Bowles et al., 2012), nausea or visual complaints (Demissie et al., 2001), gynecological symptoms (Bender et al., 2014; Demissie et al., 2001), menopausal symptoms (Atkins & Fallowfield, 2006; Cluze et al., 2012), cognitive symptoms (Bender et al., 2014; Kidwell et al., 2014), weight concerns (Bender et al., 2014; Kadakia et al., 2016; Wickersham et al., 2013), fluid retention (Cluze et al., 2012), poor sleep (Kidwell et al., 2014), and gastrointestinal symptoms (Aiello Bowles et al., 2012). Women with anxiety and depression prior to initiating AET (Bender et al., 2014) and experiencing depressive symptoms during therapy (Demissie et al., 2001; Kadakia et al., 2016; Kyvernitakis et al., 2014; Stanton et al., 2014) were more likely to be non-adherent. The number and severity of side effects also

influenced non-adherence, with a 20% increase in the likelihood of non-adherence for every additional side effect experienced (Wouters et al., 2014). Non-adherence was higher in women reporting a higher number (Kidwell et al., 2014; Kimmick et al., 2015; Wuensch et al., 2015) and intensity (Chim et al., 2013; Kahn et al., 2007; Lash et al., 2006; Wuensch et al., 2015) of side effects and who experienced worsening of symptoms during the first six months of AET (Kadakia et al., 2016).

***Current medication use.*** With regard to the relationship of poly-pharmacy and AET adherence, two studies found a positive association between poly-pharmacy (e.g., taking two or more medications weekly) and adherence (Frieze et al., 2013; Huiart, Bouhnik, et al., 2013), and two studies found women who took two or fewer medications were more likely to be non-adherent (Cluze et al., 2012; Lash et al., 2006). The use of complementary medicine was correlated with lower levels of adherence in one study (Huiart, Bouhnik, et al., 2013).

***Beliefs and attitudes.*** Women's beliefs and attitudes toward AET also influenced adherence. Negative or neutral beliefs about the necessity or value of AET (Arriola et al., 2014; Bright et al., 2016; Fink et al., 2004; Grunfeld et al., 2005; Hershman et al., 2016; Lash et al., 2006; Stanton et al., 2014) and intrusive or avoidant thoughts about breast cancer (Hershman et al., 2016) were associated with lower adherence. Women who considered AET efficacy less than or equally important to the drawbacks of therapy (Wouters, Maatman, et al., 2013), expressed a general dissatisfaction with AET (Atkins & Fallowfield, 2006; Hershman et al., 2016), or perceived barriers to treatment (e.g., treatment period was too long) (Brett et al., 2016; Brier et al., 2017; Bright et al., 2016) were less likely to adhere. No longer fearing a cancer relapse was also associated with lower adherence rates (Cluze et al., 2012). The use of cognitive facilitators,

including positive self-talk regarding the necessity of AET, however, was linked to greater adherence (Bright et al., 2016).

***Self-efficacy.*** Self-efficacy, the belief in one's ability or capacity to undertake certain behaviours, influenced AET adherence, with lower levels of perceived self-efficacy associated with decreased adherence rates (Atkins & Fallowfield, 2006; Demissie et al., 2001; Kimmick et al., 2015; Liu et al., 2013; Wouters et al., 2014). Women who perceived themselves as having less influence over their own health, or perceived others to be influential in their health decisions (e.g., HCPs, family), were more likely to be non-adherent (Atkins & Fallowfield, 2006). In contrast, women with greater self-efficacy in patient-HCP interactions were more likely to adhere (Demissie et al., 2001; Kimmick et al., 2015; Liu et al., 2013). Related to the concept of self-efficacy, women who were satisfied with their level of involvement in decision making were more likely to be adherent than women dissatisfied with their role in AET decisions (Kahn et al., 2007) or who had specific decision-making concerns (Hershman et al., 2016).

#### **2.3.1.2 Social Factors**

Social factors found to influence AET adherence included the quality of the patient-HCP relationship and social support from friends and family.

***Patient-HCP relationship.*** The quality of the patient-HCP relationship was identified as having a significant impact on AET adherence. Women who were not satisfied with the quality of the relationship with their HCP (Stanton et al., 2014) or the level of physician involvement in AET decisions were less likely to adhere (Kahn et al., 2007). Person-centered communication was consistently correlated with greater adherence (Arriola et al., 2014; Kahn et al., 2007; Liu et al., 2013; Wuensch et al., 2015). Specifically, women who were well-informed by their HCPs about the possibility of medication side effects were more likely to adhere to AET (Arriola et al.,

2014; Heisig et al., 2015; Kahn et al., 2007; Wuensch et al., 2015). Frequency of physician communication about the importance of AET was also associated with higher adherence (Arriola et al., 2014). In contrast, poor patient-physician communication with regards to the amount, type, and quality of information provided was inversely associated with adherence (Cluze et al., 2012; Kahn et al., 2007; Liu et al., 2013).

***Social support.*** Social support by family and friends was an important determinant of ongoing AET use. Women who reported higher levels of social support had greater adherence (Wuensch et al., 2015) compared to women with lower levels of support from significant others (Cluze et al., 2012; Huiart et al., 2012; Quinn et al., 2016).

### **2.3.1.3 Structural Factors**

Only a few studies identified significant associations between structural factors and AET adherence, including the type and continuity of breast cancer follow-up care and medication costs. Women who had a physician mainly responsible for their breast cancer-related follow-up care (Kahn et al., 2007), saw a greater number of breast cancer physicians (Demissie et al., 2001), or who were in contact with a breast cancer care nurse (Albert et al., 2011) were more likely to adhere. Two studies found the absence of insurance and prescription drug coverage was associated with non-adherence (Bradley et al., 2015; Liu et al., 2013).

### **2.3.2 Qualitative Results**

Of the nine qualitative studies included in this review representing 379 women, eight studies used semi-structured interviews and one utilized focus groups and interviews to explore women's AET experiences and perspectives (see Table 2.2). This research described how women struggled with several multifaceted issues related to AET. Many of the factors women

described as part of their AET experience are in keeping with the results reached about non-adherence in the quantitative literature.

### **2.3.2.1 Personal Factors**

Personal factors women reported as influencing women's AET experience included side effects, symptom management, beliefs and values, and personality characteristics.

**Side effects.** The literature highlights the significant impact AET-associated side effects can have on women's QOL. Women were surprised by the range and severity of symptoms they attributed to AET (Cahir, Dombrowski, et al., 2015; Wells et al., 2016; Wickersham, Happ, & Bender, 2012), including musculoskeletal pain and menopausal-like symptoms. For some women, menopausal-like symptoms threatened their body image and sense of femininity (Pellegrini et al., 2010). In particular, women had difficulty reconciling the idea of taking medication that increased survival, but had aging effects (Pellegrini et al., 2010). Women were conflicted by the trade-off between promoting survival and compromising their QOL (Cahir, Dombrowski, et al., 2015; Pellegrini et al., 2010; Wickersham et al., 2012). For other women, moving on from their breast cancer experience was important to their QOL and disruptive AET side effects prevented them from resuming a sense of normalcy (Brauer, Ganz, & Pieters, 2016; Cahir, Dombrowski, et al., 2015; Pellegrini et al., 2010).

**Symptom management.** In several cases, the burden of side effects lessened over time, making AET more tolerable (Brauer et al., 2016; Farias et al., 2017; Pellegrini et al., 2010). Some women felt a loss of control over their body and were dissatisfied with available options for managing side effects (Pellegrini et al., 2010; Wickersham et al., 2012). Other women deemed at low risk for a breast cancer recurrence, were given permission by their physician to stop AET early when side effects threatened their QOL (Harrow et al., 2014).

**Table 2.2 Qualitative Studies Reviewed**

First author/ year/ country	Study design	Sample	Selected factors explored	Non-adherence/non-persistence	Factors influencing women's AET experience. The (+/-) signs indicate women's perception of how these factors influenced their AET experience.
Brauer (2016) USA	Semi-structured, in-depth interviews	$N = 27$ , $M = 73.3$ years, stages I-III, AI	Socio-demographics, AI experience, management of AET-related challenges	<i>Non-adherence</i> : 3.7% missed doses; self-report	<b>Personal</b> : side effects (-), necessity beliefs (+), side effects improved over time (+), uncertain etiology of side effects (-), establishing routine (+), self-motivated to complete full duration of tx (+) <b>Social</b> : support from physicians and social networks (+)
Cahir (2015) Ireland	Semi-structured, in-depth interviews	$N = 31$ , $M = 51$ years, stages I-III, TAM/AI	Socio-demographics, AET barriers/facilitators	<i>Non-adherence</i> : 22.6%, <i>non-persistence</i> : 32.3%; self-report	<b>Personal</b> : regime (+), difficulty with regime (-), negative necessity beliefs (-), side effects (-), fear of recurrence (+), negative medication beliefs (-), too much negative AET information (-), lack of understandable AET information (-), privileged QOL (-), determination to complete tx (+), desire to finish tx (-), desire to take responsibility for own health (-) <b>Social</b> : lack of HCP support (-) <b>Structural</b> : lack of continuity of care (-), lack of HCP time (-)
Farias (2017) USA	Semi-structured, in-depth interviews	$N = 22$ , 53% < 55 years, 27% African American, TAM/AI	Socio-demographics, HCP communication, social, social factors, AET barriers/facilitators, perception of risk	<i>Non-persistence</i> : 0%; self-report	<b>Personal</b> : active management of side effects (+), side effects improved over time (+) <b>Social</b> : effective communication and support from physicians (+)
Harrow (2014) UK	Semi-structured, in-depth interviews	$N = 30$ , pre-and postmenopausal, TAM/AI	Socio-demographics, reasons for non-adherence, AET experience, social support	<i>Non-adherence</i> : 16.7% missed doses, 20% stopped temporarily, <i>non-persistence</i> : 10%; self-report	<b>Personal</b> : side effects (-), necessity beliefs (+), fear of recurrence (+), regime (+), forgetting (-) <b>Social</b> : trust in clinician advice (+)
Pellegrini (2010) France	Semi-structured, in-depth interviews	$N = 34$ , $M = 49$ years, early-stage BrCa dx in past 5 years, TAM	Socio-demographics, side effects, pt-HCP relationship, AET understanding and expectations, medication practices, views about health	<i>Non-persistence</i> : 6%, <i>non-initiation</i> : 12%; self-report	<b>Personal</b> : conflicting perceptions related to hormonal nature of TAM (-), side effects resulted in feeling a loss of control over body and threat to femininity and body image (-), perceived lack of tx option for managing side effects (-), uncertain etiology of side effects (-), difficulty reconciling taking a tx that has aging effects, but saves lives (-), fear of recurrence (+), acceptance of side effects over time (+); fertility concerns (-), regime (+)

First author/ year/ country	Study design	Sample	Selected factors explored	Non-adherence/non-persistence	Factors influencing women's AET experience. The (+/-) signs indicate women's perception of how these factors influenced their AET experience.
Simon (2014) Canada	Semi-structured interviews	$N = 161$ , $M = 56.6$ years, prescribed AET in the past 10 years	Socio-demographics, perceived AET benefits and risks, reasons for non-adherence	<i>Non-Adherence:</i> 19.3% <100% adherence, 6.8% <80% adherence; self-report	<b>Personal:</b> forgetting (-), side effects (-), negative necessity beliefs (-), fear of recurrence (+), perceived significance of cancer dx (+), 'meticulous' personality (+), reminder system (+), polypharmacy (+) <b>Social:</b> cancer history within family or peer group (+), influence of family or friends (+), parent to younger children (+) <b>Structural:</b> financial issues (-), regular follow-up care by HCP (+), works in medical-related profession (+), enrolled in research study (+)
Wells (2016) USA	Semi-structured, in-depth interviews	$N = 25$ , $M = 59.92$ years, historically or medically underserved, TAM/AI	Socio-demographics, AET barriers/facilitators, perception of risk	<i>Non-persistence:</i> 12%; self-report	<b>Personal:</b> side effects (-), routine (+), understanding importance of AET (+), forgetting (-), religious beliefs (-) <b>Social:</b> positive patient-physician relationship (+), social support (+), lack of information on side effects (-) <b>Structural:</b> insurance and cancer center subsidizing cost (+), medication costs (-)
Wickersham (2012) USA	Semi-structured, in-depth interviews	$N = 12$ , $M = 62.5$ years, postmenopausal, midway through AET	Socio-demographics, perceptions about AET, experience with side effects, AET regime	<i>Non-adherence:</i> 12.2% over 6-month period; self-report and electronic medication monitoring	<b>Personal:</b> fear of recurrence (+), necessity beliefs (+), side effects (-), belief that AET efficacy not affected by missing a dose (-), establishing routine (+), forgetting (-) <b>Social:</b> external motivation from family/friend/HCP (+), conflicting advice about side effects (-)
Wouters (2013) Netherlands	Online focus groups and individual interviews	$N = 37$ , $M = 57$ years, on average 28 months post dx, TAM/AI	Socio-demographics, patient-HCP relationship, social support, practical aspects of AET use, perceived efficacy, side effects, illness perception, coping styles, AET experience	<i>Non-adherence:</i> 8.1%, <i>non-persistence:</i> 8.1%; self-report	<b>Personal:</b> Experiences and belief clusters in order of relevance to adherence (most important to least): tenacity: (sense of doing everything to prevent BrCa); necessity beliefs; information: foreknowledge, misconceptions, AET duration; coping: appreciation, concerns, arduousness, support; efficacy: hesitation, commitment, dependence; side effects: avoidance, influence exertion, abiding; usage: memory, practicality
<b>Table legend:</b> AI – aromatase inhibitor, AET – adjuvant endocrine therapy, BrCa – breast cancer, Dx – diagnosis, HCP – healthcare provider, M – mean age, N – sample size, QOL – quality of life, TAM – tamoxifen, Tx – treatment, UK – United Kingdom, USA – United States of America					

***Beliefs and values.*** The motivation to adhere to AET, despite struggling with side effects, was linked to the higher priority women placed on survival over immediate QOL (Brauer et al., 2016; Cahir, Dombrowski, et al., 2015; Harrow et al., 2014; Pellegrini et al., 2010; Wickersham et al., 2012). Fear of recurrence had a powerful impact on women's beliefs about the necessity of AET (Cahir, Dombrowski, et al., 2015; Harrow et al., 2014; Pellegrini et al., 2010; Simon et al., 2014; Wells et al., 2016; Wickersham et al., 2012). Non-adherent women reported a lack of belief in the necessity of AET and a general distrust in medication (Cahir, Dombrowski, et al., 2015; Simon et al., 2014). For some women of child-bearing age, fertility preservation led women to forgo AET (Pellegrini et al., 2010).

***Personality characteristics.*** Women's adherence to AET was facilitated by certain personality characteristics, including tenacity (Wouters, van Geffen, et al., 2013), a meticulous personality (Simon et al., 2014), and the persistence to endure the difficult aspects of therapy (Brauer et al., 2016; Cahir, Dombrowski, et al., 2015; Wickersham et al., 2012). In addition, women who developed medication-taking routines and utilized reminder systems, visual cues, and storage strategies found these approaches helpful in remaining adherent (Brauer et al., 2016; Cahir, Dombrowski, et al., 2015; Harrow et al., 2014; Pellegrini et al., 2010; Simon et al., 2014; Wells et al., 2016; Wickersham et al., 2012). Other women, however, struggled with remembering to take AET and, in some cases, believed missing an occasional dose would not compromise the efficacy of therapy (Harrow et al., 2014; Simon et al., 2014; Wells et al., 2016; Wickersham et al., 2012).

#### **2.3.2.2 Social Factors**

***HCP relationship and information provision.*** A positive patient-HCP relationship, including trust in clinician advice (Harrow et al., 2014) and effective communication and support

from physicians (Brauer et al., 2016; Farias et al., 2017; Wells et al., 2016), helped women adhere to AET. Women identified information provision as an important factor influencing their AET experience, preferring to receive detailed information about AET prior to initiation (Wells et al., 2016; Wouters, van Geffen, et al., 2013). Many women, however, described receiving insufficient AET information from HCPs and conflicting advice about side effects (Cahir, Dombrowski, et al., 2015; Wells et al., 2016; Wickersham et al., 2012). As a result, women lacked an understanding of AET that led to misconceptions about therapy, including confusion about how AET works, the necessity and efficacy of therapy, and how to take prescribed regimes (Cahir, Dombrowski, et al., 2015; Pellegrini et al., 2010; Wouters, van Geffen, et al., 2013). Specifically, some women misunderstood the hormonal nature of AET, confusing it with other forms of hormone therapy perceived to have negative consequences, such as birth control or hormone replacement therapy (Pellegrini et al., 2010).

Other social factors that women reported as motivation to remain adherent to AET included support from social networks (Brauer et al., 2016; Simon et al., 2014; Wells et al., 2016; Wickersham et al., 2012; Wouters, van Geffen, et al., 2013), having a family member or knowing a peer with breast cancer, and having a young family (Simon et al., 2014).

### **2.3.2.3 Structural Factors**

Structural influences that women described as facilitating AET adherence included regular breast cancer follow-up care, working in a medical-related profession, and being enrolled in a research study (Simon et al., 2014). Structural barriers non-adherent women struggled with included lack of continuity of care and a perceived lack of time by HCPs to answer questions and address AET concerns (Cahir, Dombrowski, et al., 2015). Non-adherent women described a lack of clinical support, including inconsistencies in the provision of follow-up care (Cahir,

Dombrowski, et al., 2015). Finally, two studies found that financial issues (Simon et al., 2014) and medication costs were a barrier to AET adherence (Wells et al., 2016).

## **2.4 Discussion**

To our knowledge, this is the first integrative review to summarize the patient-reported factors found to influence AET adherence. These findings are consistent with the results of a recent systematic review, which analyzed the psychosocial factors associated with breast cancer survivors' AET adherence (Van Liew et al., 2014). Van Liew and colleagues also found social support, person-centered interactions with HCPs, and women's beliefs about the benefits of AET to be positively associated with adherence. A total of 10 out of the 14 studies in Van Liew et al.'s review overlapped with the 43 studies in this paper. In contrast to this review, Van Liew et al. focused exclusively on psychosocial variables associated with AET adherence in the quantitative literature. Using an integrative review methodology enabled an expanded search to consider a broader scope of personal, social, and structural factors found in both the quantitative and qualitative literature.

There was considerable overlap between the quantitative and qualitative literature among factors found to influence women's AET experience. Whereas the quantitative literature identified statistically significant factors associated with AET non-adherence, the qualitative literature offered some context to these relationships. For instance, quantitative results suggest that women who held negative beliefs about AET were more likely to be non-adherent. The qualitative literature supported these findings by offering a more in-depth understanding of how these negative beliefs were constructed and how they could possibly threaten adherence.

Strong evidence exists linking the presence and severity of side effects to non-adherence (Cahir, Guinan, et al., 2015; Murphy et al., 2012). Limited treatment options, however, are

available for managing AET-related side effects (Cella & Fallowfield, 2008), which challenges clinicians in providing support to women experiencing symptoms. Thus, an important step in addressing AET adherence is to develop more effective and patient-centred symptom management programs that comprehensively address the numerous physical and psychosocial challenges associated with AET. Although symptom-specific interventions are currently being developed and evaluated (Niravath, 2013; Walker et al., 2010), guidelines are needed to provide HCPs with standardized symptom management protocols that can be tailored to women's individual needs. Effective coping strategies (e.g., mindfulness, cognitive-behavioural therapy) are also needed for women experiencing symptoms secondary to AET that are not amenable to treatment.

In recent years, the literature has focused on identifying modifiable factors with the aim of finding practical ways to address AET non-adherence (Arriola et al., 2014; Cahir, Guinan, et al., 2015; Murphy et al., 2012). In particular, the patient-HCP relationship and the importance of high-quality communication have received increased attention. Women require sufficient information and communication about AET side effects to make informed treatment decisions, to engage in decision-making, and to remain adherent (Arriola et al., 2014; Heisig et al., 2015; Kahn et al., 2007; Liu et al., 2013; Wuensch et al., 2015). It is, therefore, imperative that breast cancer survivors receive adequate and understandable AET information about the importance, benefits, and risks of therapy before initiating treatment. In addition, person-centered communication that acknowledges women's values, beliefs, and the larger social and structural context in which treatment decisions are made will be important for adherence. The development and evaluation of tailored communication tools that support both patients and HCPs to have

more effective conversations about AET, side effects, and the related treatment decisions may be a critical focus of future research.

The structure and delivery of follow-up care was found to improve adherence (Albert et al., 2011; Demissie et al., 2001; Kahn et al., 2007). Given the longevity of AET, the increased burden placed on oncology health services will require follow-up care to occur within primary care settings. As a result, primary care providers may require an enhanced understanding of AET, including awareness of the barriers and facilitators influencing adherence, and knowledge of symptom management strategies for treating side effects. If women are to persist with AET, regular follow-up care with a knowledgeable HCP in the community will be essential.

To date, limited testing of AET adherence interventions has occurred. Three recent clinical trials investigated the effect of patient educational material (Hadji, Blettner, et al., 2013; Neven et al., 2014) and a patient information and reminder program (Ziller et al., 2013) on adherence in women receiving an AI, but were unable to demonstrate a significant improvement in adherence. Compliance interventions successfully implemented in chronically ill populations could provide insight into adherence to other long-term, self-administered oral medications and inform the development of AET-specific interventions.

Generalizability of the findings from this review to the broader breast cancer population is limited due to the variability of study sample sizes, methodologies, and differences in how adherence was operationalized and measured. Discrepancies in terminology, adherence measurements, and data sources may have affected the type of factors correlated with AET non-adherence. Research advances, such as ecological momentary assessment, may improve assessment of adherence by capturing women's actual medication ingestion over time and in real-world settings, thus minimizing recall bias (Kirchner & Shiffman, 2013). Many studies on

adherence have also failed to distinguish between tamoxifen and AIs. Future research is needed to examine how influencing factors differ across these two classes of AET, and how these factors interact with each other and intersect with demographic and clinical predictors of non-adherence.

All studies included in this review were based on AET being recommended for five years. A focus of future research will be to investigate if the factors identified in the current literature remain associated with adherence in the context of extended AET. Qualitative results from this review suggest there may be additional factors important to women, including concerns about premature aging and specific medication beliefs that were not assessed in larger quantitative studies and may play a role in adherence decisions.

## **2.5 Conclusion**

The potential cost of non-adherence to AET is high, including diminished treatment efficacy and an increased risk of mortality. This review highlights important personal, social, and structural factors that act as facilitators and barriers to AET adherence. To date, the majority of the literature has focused on the personal factors associated with adherence that were identified a priori. This body of research is somewhat acontextual and may provide an incomplete understanding of the social and structural factors that shape women's lives and, in turn, influence AET adherence. To strengthen our understanding, qualitative research is needed to explore personal, social, and structural factors, and determine how these factors interact to shape AET adherence.

Addressing women's unmet symptom management and information needs through person-centred care could improve breast cancer survivors' QOL and follow-up experience, and support them in persisting with long-term AET use. These factors, among others, have several clinical practice implications and are particularly salient given the recent expanded clinical care

guidelines recommending 10 years of AET. Going forward, it will be important to address the gaps in the literature to inform the development of effective intervention strategies aimed at optimizing adherence. Ultimately, the goal of reducing non-adherence to AET is to support women in becoming survivors who are able to live well beyond their breast cancer diagnosis.

## **CHAPTER 3: UNDERSTANDING ADJUVANT ENDOCRINE THERAPY PERSISTENCE IN BREAST CANCER SURVIVORS**

A version of this chapter was previously published in *BMC Cancer* (Lambert, Balneaves, Howard, Chia, & Gotay, 2018).

### **3.1 Introduction**

Breast cancer is the most common female cancer worldwide (International Agency for Research on Cancer, 2012), and it is the second leading cause of cancer deaths in Canadian women (Canadian Cancer Society's Advisory Committee on Cancer Statistics, 2015). Mortality, however, is declining due in part to effective treatments that include AET, such as tamoxifen and AIs (Berry et al., 2005). In women with HR+ breast cancer, AET reduces the risk of recurrence by up to 50% (Early Breast Cancer Trialists' Collaborative Group (EBCTCG), 2011). Until recently, five years of AET was standard treatment for women with HR+ breast cancer. In 2014, ASCO published guidelines that recommended AET be extended for up to 10 years in high risk women (Burstein et al., 2014).

Persistence, defined as continuously taking AET for the prescribed treatment duration (Hadji, Ziller, et al., 2013), has significant clinical relevance. Non-persistence has been associated with a reduced survival benefit for women who discontinue treatment early, and with a significant increase in mortality (26%) for women who stop AET before the recommended five-year period (Hershman et al., 2011). Meta-analyses have shown the positive effect of long-term AET use, with five years of tamoxifen being significantly more efficacious in reducing breast cancer recurrence (rate ratio 0.82) and mortality (rate ratio 0.91) than only one to two years of AET (Early Breast Cancer Trialists' Collaborative Group (EBCTCG), 2005). Despite

the demonstrated efficacy of AET, 31–73% of women with breast cancer are non-persistent in real-world settings (Murphy et al., 2012).

Studies have identified disease severity (Fink et al., 2004), comorbidities (Hershman et al., 2010; van Herk-Sukel et al., 2010), side effects (Kahn et al., 2007), and type of breast surgery (Hershman et al., 2010) as predictors of AET non-persistence. Younger (<40 years) (Hershman et al., 2010) and older (>70 years) women (Owusu et al., 2008; van Herk-Sukel et al., 2010) are also at higher risk for non-persistence. Relatively few studies have examined the influence of personal (e.g., beliefs, values), social (e.g., social support, patient-HCP relationship), and structural factors in the healthcare system (e.g., continuity of care, access issues) (Brett et al., 2018; Gotay & Dunn, 2011; Lambert, Balneaves, Howard, & Gotay, 2018; Moon, Moss-Morris, Hunter, & Hughes, 2017; Verbrugghe et al., 2017). Research suggests women with neutral or negative beliefs about the value of tamoxifen (Fink et al., 2004; Lash et al., 2006; Stanton et al., 2014), limited social support (Huiart et al., 2012), and dissatisfaction with their role in AET decisions (Kahn et al., 2007) were more likely to discontinue treatment prematurely. A higher quality patient-HCP relationship (Kahn et al., 2007), patient-centred communication (Liu et al., 2013), continuity of care (Kahn et al., 2007), prescription drug coverage (Bradley et al., 2015), and polypharmacy (Friese et al., 2013; Huiart, Bouhnik, et al., 2013; Lash et al., 2006) were also positively associated with AET persistence. More recently, researchers have used qualitative methodology to explore women's AET experiences and their resulting adherence and persistence decisions (Brett et al., 2018; Lambert, Balneaves, Howard, & Gotay, 2018; Moon, Moss-Morris, Hunter, & Hughes, 2017; Verbrugghe et al., 2017). What is unique about this study is the focus on the broader social and structural context and how these factors, along with personal factors, shape women's AET experiences and persistence.

Increasing AET persistence has the potential to improve the efficacy of treatment and ultimately patient outcomes. While some progress has been made in understanding the personal, social, and structural factors associated with AET persistence, breast cancer survivors' perspectives related to AET and persistence is notably missing from the literature. If effective, patient-centred strategies for targeting non-persistence are to be developed, it is essential we look beyond the identified demographic and clinical predictors, which provide an incomplete, and somewhat acontextual, understanding of AET non-persistence. Instead, qualitative inquiry that explores breast cancer survivors' experiences and perspectives is needed to better articulate the multifaceted nature of AET persistence.

The aim of this study was to explore breast cancer survivors' experiences and perspectives of AET use to describe how personal, social, and structural factors influence persistence.

### **3.2 Methods**

An interpretive description approach to inquiry (Thorne, 2016) and the theoretical lens of relational autonomy, was used to qualitatively explore women's experiences and perspectives related to AET persistence. Relational autonomy is an alternative interpretation of autonomy that considers the personal aspects of an individual's life, while also acknowledging that social, political, and economic conditions can influence one's decisions and behaviours (Sherwin, 1998). The bulk of the research on AET persistence has predominantly focused on individual aspects (e.g., demographic, clinical characteristics) in isolation from the social and structural context that shape persistence. A relational autonomy lens was used to explore how the personal nature of AET-related decisions and the broader social and structural contexts influence breast cancer survivors' AET experiences and persistence. Specifically, relational autonomy was used

to guide the interview questions and data analysis to explore factors such as beliefs, social support, relationships with HCPs, and access to and delivery of healthcare resources.

### **3.2.1 Participant Recruitment**

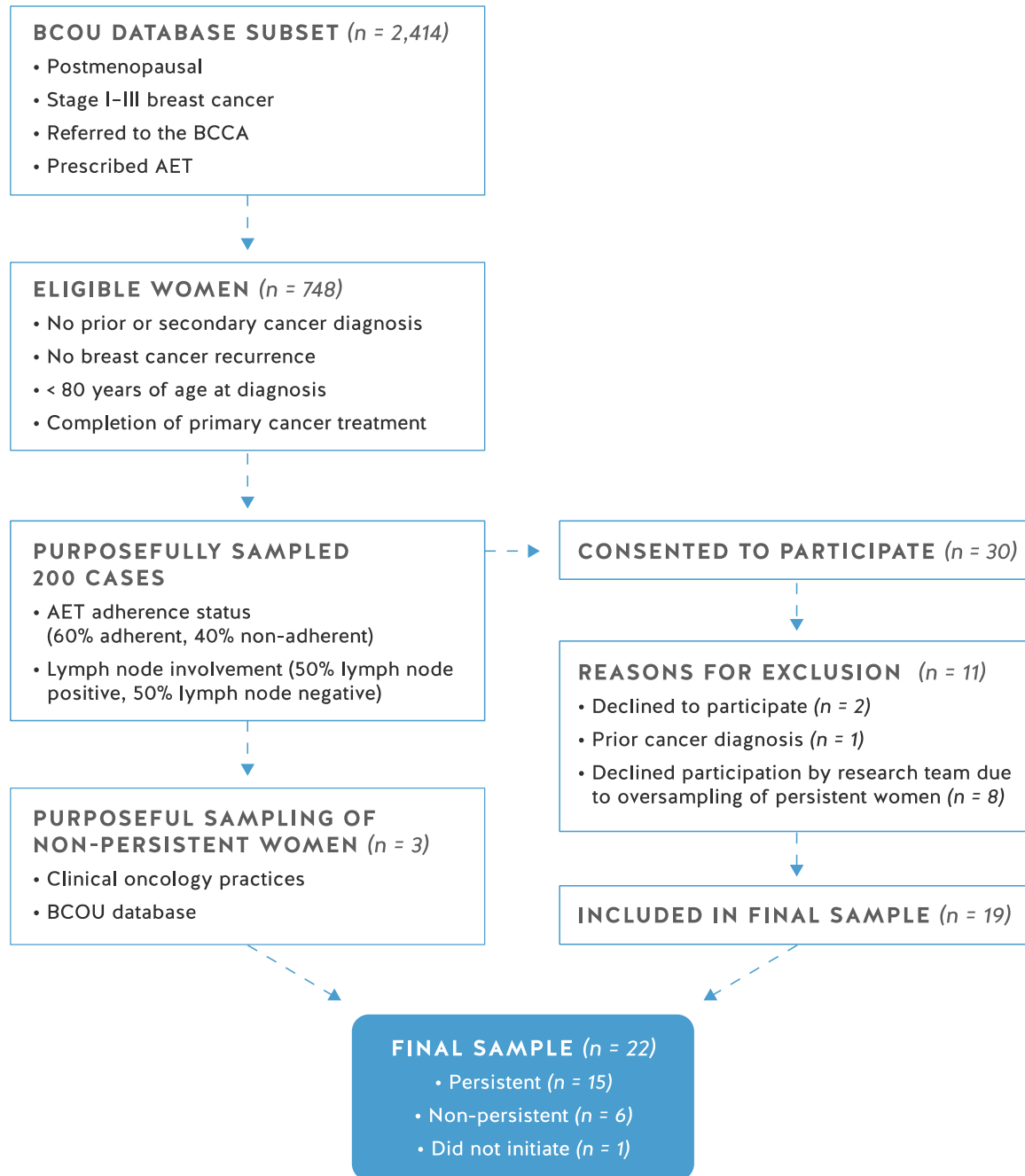
Eligibility criteria included women diagnosed with HR+ stage I to III breast cancer, referred to BC Cancer between January 2005 and August 2012, without a prior cancer diagnosis, recurrence of breast cancer, or secondary cancer diagnosis (excluding non-melanoma skin cancer), who had completed primary cancer treatment, were fluent in English, aged 18 to 79 years at diagnosis, and prescribed AET. The upper age limit of 79 years was chosen as an eligibility criterion to avoid contacting families of women who may have died since diagnosis. Upon approval from the UBC Behavioural Research Ethics Board, 748 women who met eligibility criteria were selected from BC Cancer's BCOU database subset ( $n = 2,414$ ), which had been generated for a previous study that found 40% of women with early-stage HR+ breast cancer were non-adherent to AET (Chan et al., 2009). From this sample, a letter of invitation was mailed to 200 women who were purposefully selected from four randomized lists that represented diversity across adherence behaviour (adherent versus non-adherent)<sup>1</sup> as well as disease severity (lymph node positive vs. lymph node negative). A total of 30 women provided consent (Appendix A.1) to participate, of which four (13.3%) were non-persistent with AET, resulting in a 15% response rate. Following initial consent, two women declined to participate without providing a reason and one woman with a prior cancer diagnosis was excluded from the study. In addition, eight women persistent with AET, who had been waitlisted, were respectfully declined participation by the research team due to oversampling of persistent women in order to

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<sup>1</sup> The BCOU database used prescription refill data to assess breast cancer survivors' AET adherence. After interviewing women, I found that AET persistence, not adherence, was the predominant issue in this sample and, therefore, women are referred to herein as persistent or non-persistent.

develop a sample that more closely represented the 40% non-adherence rate observed in the BCOU database (Chan et al., 2009). Due to the difficulty in recruiting non-persistent women to the study, additional purposeful sampling was conducted through the BCOU database and convenience sampling was used to invite non-persistent women through select oncology practices. After several months of recruitment efforts, three additional non-persistent women consented to participate and were included in the final sample of 22 women (see Figure 3.1).

**Figure 3.1 Breast Cancer Survivor Recruitment Strategy**



### 3.2.2 Data Collection and Analysis

The lead author (LKL) conducted semi-structured interviews with 22 women in person or by phone (see Appendix A.2 for interview guide) ranging from 26 to 80 minutes in duration (54 minutes on average), which were digitally recorded and transcribed verbatim. To address

possible biases held by the researchers, the investigative team developed reflective memos regarding assumptions they held about the factors influencing women's AET treatment decisions and behaviours prior to conducting the interviews. Field notes were kept to capture non-verbal behaviours occurring during the interviews and any related contextual information. The women completed a demographic form (Appendix A.3) and one item (Appendix A.4), previously used by Andersen et al. (1999), which assessed their perceived risk of breast cancer recurrence on a 0 to 100 percentage scale, with 0 meaning there is no chance they will get breast cancer again and 100 meaning they most definitely will get breast cancer again. Women received a \$15 honorarium at the conclusion of the interview. Data was organized using NVivo<sup>TM</sup> software. Data collection and analysis occurred concurrently, with the preliminary analysis informing the development of new interview questions and shaping existing ones (Thorne, 2000).

Inductive thematic analysis (Sandelowski, 2000) was used to analyze the interviews. Transcripts were read and re-read line-by-line, with key passages highlighted and memos created to reflect important themes. Two members of the research team (LKL and LGB) reviewed several transcripts to confirm the proposed coding before the coding scheme was finalized. The analytic strategy of constant comparative analysis was used to iteratively compare data and develop conceptualizations of the relationships among data (Thorne, 2000). The analysis drew on relational autonomy theory by examining the interrelationship among themes and the personal, social, and structural factors influencing AET persistence. Memos were kept to track methodological and analytical decisions (Koch, 2006) and were reviewed during the analysis, along with the field notes. Descriptive statistics were used to summarize the quantitative data.

### **3.2.3 Sample Characteristics**

Women classified as persistent ( $n = 15$ ) were either currently taking AET at the time of interview or had recently completed the recommended five-year treatment. Within this group were some women who reported occasionally missing a dose or taking short medication breaks of less than two weeks. Women classified as non-persistent ( $n = 6$ ) had discontinued AET before completing the recommended five-year treatment and one woman chose not to initiate AET.

Sample characteristics and survey data are shown in Table 3.1.

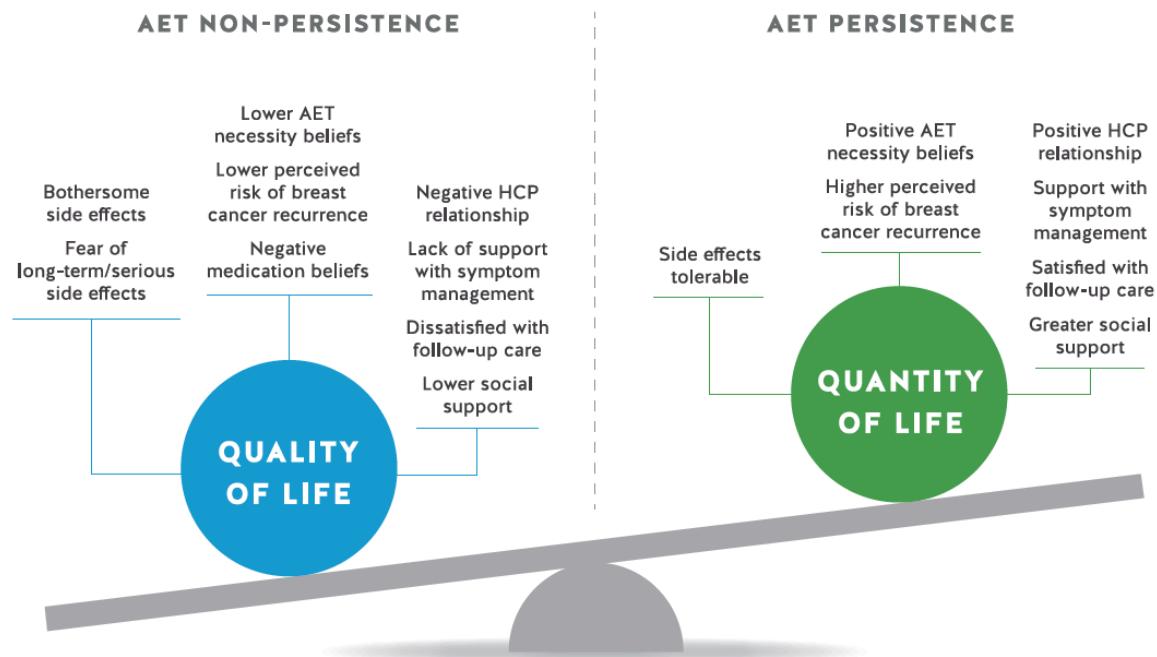
**Table 3.1 Breast Cancer Survivor Sample Characteristics**

<b>Sample Characteristics <i>n</i> = 22</b>	<b>Frequency (%)</b>
<b>Age at Diagnosis</b>	
18 - 44 years	-
45 - 59 years	11 (50)
60 - 79 years	11 (50)
<b>Lymph Node Status</b>	
Positive	10 (45)
Negative	12 (55)
<b>Hormone Status</b>	
ER+	22 (100)
PR+	16 (73)
Her2+	2 (9)
<b>Treatment History</b>	
Surgery	22 (100)
Chemotherapy	9 (41)
Radiation	18 (82)
<b>AET Use</b>	
Tamoxifen only	7 (32)
AI only	5 (23)
Both tamoxifen and AI	9 (41)
Did not initiate	1 (5)
<b>Persistence</b>	
Non-persistent	6 (27)
Did not initiate	1 (5)
Persistent	15 (68)
<b>Average Perceived Risk of Breast Cancer Recurrence (0–100%)</b>	
Non-persistent/did not initiate	33%
Persistent	29%

### 3.3 Results

For many breast cancer survivors, AET persistence became a balancing act between quality and quantity of life (see Figure 3.2) that was influenced by personal, social, and structural factors. These influencing factors and the interrelationships among them are described in detail below.

**Figure 3.2 Balancing Act Between QOL and Quantity of Life**



#### 3.3.1 Personal Factors

Personal factors included experience of AET-related side effects and beliefs regarding perceived risk of recurrence, medication, and necessity of AET.

##### 3.3.1.1 Side Effects

AET-related side effects (see Burstein et al. (2010) for a comprehensive list) had a profound impact on many women's QOL, and were the primary reason for non-persistence in the

sample. Many women did not frame their side effects as simply bothersome; rather, they used language such as “violent”, “excruciating”, and “intolerable” to describe their symptoms. They questioned whether the potential reduced risk of a breast cancer recurrence and increased survival benefit were worth persisting with AET given the severe negative physical and emotional impact on their daily lives.

I think the problem with breast cancer is that you're not sick, but it [AET] makes you feel worse than you ever felt. The side effects are potentially worse than the disease. It's like, ‘Why am I doing this?’ It's bizarre. (AET non-persistent)

My joints and the cramping were sometimes unbearable. I would cry. When it would hit me at night, I would be sound asleep and it would jolt me out of my deep sleep. In the beginning I did not know how to deal with it. It affected me in my working environment and it affected me in my free time, and my family. (AET persistent)

Some of the symptoms, including hot flashes, vaginal dryness, weight gain, hair loss, and joint pain, were associated with old age and altered women’s sense of identity. As one woman shared: “It feels like you’re an 80-year old person. It’s hard to move around, to stand up, to get up out of the chair and do certain things” (AET persistent). The women’s social lives were also affected by the severity and unpredictability of AET-related side effects:

I started to withdraw from social situations. I didn’t trust my body to co-operate. I missed out on quite a few things, because I was too afraid that [due to the diarrhea] I would have to run or, change my clothes or have a shower. And make a mess in public. Emotionally, it was devastating. (AET persistent after switching AET)

A couple of women took AET medication breaks to lessen their symptom severity and allow them to attend important social events, such as vacations and weddings.

AET-related side effects also compromised some women's ability to function in their occupational roles. These women missed work, were unable to maintain regular work schedules, or were prevented from returning to work. Several of these women chose not to disclose their struggle to employers or colleagues in an effort to avoid the stigma associated with breast cancer or appearing sick. Consequently, these women were not offered return to work programs or workplace accommodations (e.g., modified workloads) that might have helped them to cope with side effects. While not all women directly associated non-persistence with the negative impact of AET-related side effects on their careers, they did comment on how these work-related compromises had a substantial effect on their productivity, performance, and satisfaction with work.

Women's ability to tolerate and self-manage side effects varied considerably over time and across the sample. For some, AET-related side effects improved after an initial adjustment period. For others, a change in medication offered some relief from intolerable side effects. To enable them to cope with the side effects and persist with AET, several women reframed their symptom experience and implemented mantras, such as "suck it up buttercup". Other women made changes to their lifestyle to lessen the severity of side effects. There was a small group of women, however, who experienced intensified side effects as time went on, or found their symptoms became less tolerable, leading them to discontinue AET early.

### **3.3.1.2 Personal Beliefs About Recurrence and Medications**

How women perceived their risk of breast cancer recurrence differed across the sample and had a direct impact on their beliefs about the necessity of AET and tolerance of side effects,

which ultimately influenced their persistence with AET. In most cases, a higher perceived risk of recurrence motivated women to remain persistent with AET. In contrast, women who perceived their risk to be low were more inclined to consider ending AET early: “Mine was so small and Stage I [breast cancer], 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” (AET non-persistent). In the interviews, women described their perceived risk of recurrence as being influenced by several factors, including disease severity, fear of recurrence, family history of breast cancer, previous illness experiences, anecdotal stories of breast cancer outcomes, and risk estimates provided by HCPs.

During the first few months of AET use, when the impact of the side effects became apparent, several women questioned their ability to continue with AET. A heightened perception of risk related to recurrence and a strong belief in the necessity of AET encouraged persistence during this initial treatment period. Increased perception of risk also occurred after follow-up consultations with HCPs, when new health concerns developed, and after the death of a family member or friend from cancer.

Being on these pills you start to forget what it's for. It's just like taking another pill, but when you get some of the symptoms, when they start to flare up, then it reminds you of actually what you're doing. And then you kind of have to go back into the fight mode again and say, ‘Okay, this isn't going to kill me.’ (AET persistent)

For non-persistent women, their perception of risk related to breast cancer recurrence decreased in the later stages of therapy. After the third year of AET, four (18%) women in this sample discontinued therapy. The perceived risk-benefit ratio appeared to shift for these women; they wanted their lives and bodies back, and to feel normal again.

Beliefs about the necessity of AET were largely influenced by how it was positioned in discussions with HCPs as an essential and expected step in the treatment trajectory. Hence, most women, be they persistent or non-persistent, described AET as a treatment option they could not refuse.

I have to say that my very first reaction on discovering I had the sort of breast cancer that needed more than surgery was, 'I don't want to take tamoxifen'. I was prepared for everything else. But, I really, really was upset about the thought of taking tamoxifen. I was devastated. I didn't want to take something that was such a long-term thing. I knew I didn't want to take it, but I knew I had to take it. (AET non-persistent)

For women who were persistent with AET, they described holding positive beliefs about the medication, viewing it as essential to their health. AET was seen as a “security blanket”, an extra layer of protection in their fight against breast cancer and provided a sense of control over their disease: “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” (AET persistent).

Other women, however, feared overloading their body with “chemicals” and were concerned about the potentially serious and long-term adverse effects of AET. Furthermore, some women experienced difficulty reconciling the idea of taking a medication that had negative side effects with no immediate tangible benefits.

You want the good stuff that is helping your body, but if you don't know for sure that it's [AET] really helping your body, then why am I taking it? Do I really know that it's benefiting me? And that's probably why I wouldn't take it again. Or, I wouldn't do another five years. Because I haven't seen the benefits yet. (AET persistent)

For some non-persistent women, these beliefs contributed to their decision to forgo or discontinue treatment early. In contrast, for those women who persisted with AET despite holding negative beliefs about medications, a heightened perception of risk of recurrence outweighed their concerns about taking a long-term medication: “It's a drug in my body, doing things to me. There's nothing good about doing it, but do I want to get cancer again? No. I'm more scared to get cancer than I am to go on the pill” (AET persistent).

### **3.3.2 Social Factors**

#### **3.3.2.1 Social Support**

Most women had a supportive social network, however, they perceived AET as a woman's issue to be dealt with privately, shielding their family and friends from the challenges posed by AET. These women did not want breast cancer to continually impact their personal relationships and social interactions; instead, they wanted to move on with their lives, regain some sense of normalcy, and not be perceived as sick.

I want my life to be about other things. So, if people ask me how are you doing, I'm not shutting them out, but I don't want to bring them into the full depth of it. I've been awake since three o'clock this morning 'cause I woke up soaking wet and I'm grumpy and I don't want to bring that to my friends and family all the time. So, I don't talk about it as much with them. My husband knows. But I also don't want our marriage to be just about that.

(AET non-persistent)

In contrast, some women found the support from friends or family helped them persist with AET when side effects were bothersome and their commitment to AET waned, as did connections with fellow breast cancer survivors whose stories of overcoming difficulties and persisting with AET encouraged them to persevere with treatment. As well, anecdotal stories of

survivors who took AET and survived had a powerful influence on women's beliefs about the importance of AET, and consequently, their persistence.

### **3.3.2.2 Healthcare Provider Relationship**

Close to half of the women ( $n = 10$ ) continued to receive follow-up care from an oncologist throughout the course of AET. The remaining women ( $n = 12$ ) were discharged to their family physician following primary treatment or after completing the first few years of AET. Women who perceived a positive relationship with their physicians and had a high level of trust and confidence in their recommendations about AET were more likely to persist. Further, women who perceived their physicians as empathic, responsive, accessible, and knowledgeable about AET were more inclined to discuss AET concerns in consults, seek help in managing side effects, and persist with AET. A breakdown in the patient-HCP relationship, however, damaged women's trust in their physician, resulting in a perceived lack of support, poor symptom management, and for some women, influenced their decision to not persist with AET.

Oncologists were particularly influential in women's decisions about AET persistence. A few women in this sample declined primary cancer treatment, yet agreed to take AET in an effort to preserve their relationship and access to follow-up care with their oncologist. Gaining permission from their oncologist was also key to women's decisions to discontinue AET early, with some women sharing that if their physician had encouraged them, they would have tried to persist: "I said 'I've decided to stop [taking AET], what do you think?' And she [oncologist] shrugs and said 'Fine'. If she had said 'No, definitely not, I really don't think you should stop', I probably wouldn't have" (AET non-persistent).

Some women had a lengthy history with their family physician, which led to a high level of trust. Other women did not perceive their family physician as having the specialized knowledge

about breast cancer and AET required to provide adequate follow-up care. Their subsequent lack of confidence in their family physician prevented several women from seeking symptom management advice, resulting in unmet supportive care needs, which influenced some women's decision not to persist with AET.

I wouldn't go to the GP [family physician] because I don't feel that they're up on it [AET].

Well, I don't feel mine is up on all that. They don't have that knowledge. I think someone dealing with cancer, in the cancer setting, has more details on symptoms from one of those drugs. (AET persistent)

Disparities existed among women in terms of the support they received from HCPs with managing AET-related side effects. Women felt satisfied when their concerns were acknowledged and they were offered possible solutions. Some women were hesitant to ask their physicians about AET side effects because they feared their concerns would be met with resistance or apathy, or dismissed as being insignificant in comparison to the more severe side effects accompanying primary cancer treatment. As one woman shared:

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 a chemo every day, and so you just have to learn to deal with it. (AET persistent)

### **3.3.3 Structural Factors**

The transition from oncology to primary care was a key turning point for many women due to inequities in the provision of follow-up care. As mentioned, disparities existed regarding how breast cancer follow-up care was structured, with some women continuing to be followed by their oncologist for five years, while others were discharged earlier to a family physician. Some

women experienced a lack of continuity of care when transitioning from oncology to primary care: “When I did go back to the family physician, I said ‘[my oncologist] dismissed me and it was up to you to keep track of me.’ And he [GP] looked at me and said ‘We don’t do that’” (AET non-persistent). In addition, differences existed in the care women received from oncologists versus family physicians in terms of the frequency and type of follow-up care. Dissatisfaction with the frequency and perceived quality of follow-up care provided by family physicians contributed to some women’s decision to stop AET early.

It [transition to primary care] was annoying because you know that means you’re really getting nothing. No follow up. Because you don’t get any follow up from a GP [family physician]. They say they don’t know anything about cancer, it’s too complicated. (AET non-persistent)

Conversely, women who continued to see an oncologist reported greater satisfaction with the provision of follow-up care as well as a sense of safety and confidence. The specific focus on breast cancer during follow-up visits with an oncologist meant that the importance of AET and related symptom management issues were more frequently discussed than in follow-up visits with a family physician, when other health concerns took precedence.

Access to follow-up care was an additional issue for women residing in rural areas due to the limited number and availability of primary care providers. The inability to access HCPs with specialized knowledge of breast cancer and AET in a timely manner was disconcerting, especially when women’s worries felt immediate. One of the re-occurring issues most women struggled with was a perceived lack of time to discuss AET concerns with their physician.

The medical system is so overloaded and to deal with your GP [family physician] is difficult. They don’t give you much time. You wait two hours to see him [GP], and you get

to talk to him for about two minutes. You have to talk kind of fast, and you never get what you wanted to say all out, because you have about two or three minutes. It's not that conducive to getting a whole lot of help. (AET non-persistent)

Access to other HCPs, such as nurses and pharmacists with specialized knowledge of cancer and AET, provided a trusted, and often more accessible, resource for women. Inequities existed, however, in access to these supports. For instance, women participating in clinical trials had access to an interdisciplinary team who they relied heavily on to answer AET questions and provide help with managing side effects. Other women were not offered the same access to supportive resources. A lack of access to timely follow-up care meant some women felt abandoned during the survivorship period and were uncertain of how their breast cancer care would be provided, which in turn, influenced their decisions to stop AET early:

I wanted to be followed up. If they're going to start fiddling with your hormone levels, they should be checking you every three months. There's no checks and balances. If I had felt I was being followed and people knew what was happening to me, I would have felt much better. I felt totally alone. (AET non-persistent)

### **3.3.4 Balancing QOL and Quantity of Life**

Most women reported that over time, the decision-making process around AET persistence became a difficult balancing act between QOL and quantity of life (see Figure 3.2). The question, 'What if?' plagued women, who wondered if improved QOL and reclaiming a sense of normalcy was worth the increased risk of a breast cancer recurrence. For women who privileged quantity of life over QOL, positive beliefs about the necessity of AET and an acute perception of their risk of breast cancer recurrence tipped the scale towards persistence. For non-persistent

women, the tipping point in their decision about AET was the relative weight they placed on QOL in relation to other factors, particularly side effects.

You're counting the days and it becomes like you can't wait for the end [of AET]. I don't know what's going to happen. It may come back and I'm going to die anyway. So, I'd rather have a good QOL while I'm alive and not have side effects. (AET non-persistent)

While some persistent women were steadfast in their initial decision, others wavered throughout the course of AET. Several women reassessed their beliefs about the necessity of AET and their overall commitment when side effects intensified, concerns arose about potentially severe or late adverse effects of AET, perceived risk of recurrence decreased, a breakdown in the patient-HCP relationship occurred, and when they were dissatisfied with follow-up care.

The interrelationship among factors that influenced women to privilege either QOL or quantity of life, and to persist or not persist with AET, was complex and there was substantial variability in how women weighted the importance of various personal, social, or structural factors in their treatment decisions. For persistent women, social and structural factors, including support from family and friends and access to timely follow-up care with trusted HCPs who reinforced the value of AET, helped them persist when experiencing disruptive side effects and uncertainty about the necessity of AET. In contrast, non-persistent women struggled to continue with AET when their QOL was adversely affected, particularly in the face of insufficient support from their social networks and HCPs and beliefs that challenged the necessity and safety of AET.

### **3.4 Discussion**

The rate of AET persistence is low in breast cancer populations and tends to decrease over time (Barron et al., 2007; Hadji, Ziller, et al., 2013; Huiart et al., 2012; Owusu et al., 2008;

Partridge, Wang, Winer, & Avorn, 2003). Identification of patients at risk for non-persistence and the development of efficacious supportive care strategies are needed to improve women's persistence. If the efficacy of AET demonstrated in clinical trials is to be realized, the patient-reported factors influencing persistence in real-world settings must be addressed. In this study, a relational autonomy lens was used to explore how personal, social, and structural factors shape women's AET experiences, and how these factors interact to influence persistence throughout the AET trajectory. This study found that breast cancer survivors' decisions to persist with AET was a balancing act between QOL and quantity of life and was informed by a complex interplay of factors. The relative weight women attributed to QOL and quantity of life at different points in the AET trajectory was grounded in their personal experience and how social and structural factors influenced the broader context of their AET decisions and behaviours.

Several quantitative studies have linked the presence and severity of AET-related side effects to non-persistence (Aiello Bowles et al., 2012; Chim et al., 2013; Demissie et al., 2001; Kadakia et al., 2016; Kahn et al., 2007; Kidwell et al., 2014; Lash et al., 2006; Stanton et al., 2014). The results of this study echo these findings and further show the profound impact AET side effects can have on women's QOL. Similar to previous qualitative studies (Bender et al., 2014; Brett et al., 2018; Harrow et al., 2014; Moon, Moss-Morris, Hunter, & Hughes, 2017; Pellegrini et al., 2010; Verbrugghe et al., 2017; Wickersham et al., 2012), we found that physical side effects, including weight gain, joint pain, and menopausal-like symptoms, greatly impacted women's sense of self and body image and led some women to feel prematurely aged, which in turn influenced their decision to persist with AET. Given the significant value placed on youth and women's physical appearance in Western society, it is not surprising that these side effects

had an effect on AET persistence. This may be one area to address in future supportive care and lifestyle interventions offered to breast cancer survivors undergoing AET.

Research suggest that women's self-determination, necessity beliefs, and their ability to tolerate side effects, can greatly influence AET persistence (Brett et al., 2018; Lambert, Balneaves, Howard, & Gotay, 2018; Moon, Moss-Morris, Hunter, & Hughes, 2017; Verbrugghe et al., 2017). In this study, tenacity and a strong belief in the importance of AET appeared to help persistent women cope with side effects through lifestyle modifications and committing to a positive mindset. This finding is similar to previous studies that found persistent women held more positive attitudes toward AET than non-persistent women (Hershman et al., 2016; Lash et al., 2006). Translating these coping strategies into formal education resources (e.g., pamphlet, online resource, component of group education sessions) that could be shared with breast cancer survivors through oncology survivorship programs, primary care providers, and peer support groups could provide encouragement for women experiencing difficulty with AET. Given the limited pharmacological options available for treating AET-related side effects (Cella & Fallowfield, 2008), interventions such as cognitive behavioural therapy, hypnosis, yoga, and relaxation strategies that have been effective in managing cancer-related symptoms might assist women to better cope with the difficulties of long-term AET (Syrjala et al., 2014).

In this study, the importance women placed on influencing factors shifted over time. This finding is similar to the results of a recent study that examined the AET decision-making process and found concerns about AET can emerge at any point in the treatment trajectory, resulting in uncertainty and a subsequent reevaluation of AET decisions (Beryl et al., 2017). Similar to two recent qualitative studies (Brauer et al., 2016; Farias et al., 2017), we also found that some women's experience of AET-related side effects improved over time; however, the severity of

side effects for other women continued or increased. Like Moon et al. (2017), we found some women's necessity beliefs related to AET shifted throughout the treatment trajectory, leading them to question the importance of AET. Unique to this study was the finding that breast cancer survivors' perceived risk of recurrence can also shift over the course of therapy and influence women's overall persistence.

Identifying modifiable factors, such as women's perceived risk of recurrence and beliefs about the necessity of AET, provide potential avenues to explore the development of education and support strategies that promote AET persistence. The findings of this study suggest there might be key milestones in the AET trajectory when women are at higher risk for non-persistence that could offer critical opportunities for intervention. For instance, studies have shown that AET non-persistence increases sharply during the first year of therapy (Aiello Bowles et al., 2012; Hershman et al., 2016; Huiart et al., 2012; Kidwell et al., 2014). These results reflect the difficult adjustment period after initiating AET that cause some women to question their commitment to AET and may lead to non-persistence. It is important to note that while many women stop AET early in the treatment trajectory, the number of women who are non-persistent continues to increase over time (Ayres, Baldoni, Borges, & Pereira, 2014; Huiart et al., 2012), as was evident in the women in this study who discontinued AET around the four-year mark. Furthermore, evidence from clinical trials of tamoxifen suggest that side effects continue to persist with longer durations of treatment (Burstein et al., 2014), indicating the need for ongoing follow-up care throughout the entire course of AET, not only after initial onset. It is essential that HCPs assess AET persistence at each consultation, acknowledge women's concerns, and seek to address reasons for non-persistence. In addition, as some women's

perception of risk decreases over time, the benefits of persisting with AET for the full treatment duration should be reinforced.

While side effects were the primary reason for AET non-persistence, there were women in this study who persevered despite experiencing severe side effects. This highlights the importance of identifying how social and structural contexts, in particular, the quality of the patient-HCP relationship and women's trust in their physician, can either facilitate or hinder AET persistence. These findings are supported by previous research that suggests receiving adequate support from HCPs (Brauer et al., 2016; Brett et al., 2018; Cahir, Dombrowski, et al., 2015; Farias et al., 2017; Kahn et al., 2007; Moon, Moss-Morris, Hunter, & Hughes, 2017; Stanton et al., 2014; Verbrugghe et al., 2017; Wells et al., 2016), having frequent (Arriola et al., 2014) and effective communication (Farias et al., 2017; Liu et al., 2013), and trust in clinician advice (Brett et al., 2018; Harrow et al., 2014) might improve AET adherence and persistence.

Women reported greater satisfaction with care provided by oncologists compared to family physicians, which in turn facilitated persistence. Hadji et al. (2013) reported similar findings: women who received follow-up care from a specialist were more likely to be persistent with AET than women who received survivorship care within a general practice. As noted by Harrow et al. (2014) and Brett et al. (2018), we also found that women had concerns with the frequency and quality of follow-up care received from family physicians that influenced their decision to persist with AET. However, given the longevity of AET and the growing burden placed on oncology care programs, long-term breast cancer follow-up will need to increasingly occur in community settings. Alternative survivorship care models, such as nurse-led clinics (Grant, Economou, & Ferrell, 2010), may be one strategy to address the supportive care needs of women undergoing AET, improve overall continuity of care, and increase persistence (Albert et al.,

2011). As a result, primary care providers may require increased knowledge of AET and related practice guidelines (Luctkar-Flude, Aiken, McColl, & Tranmer, 2015), awareness of the factors influencing persistence, and strategies for managing AET-related side effects to facilitate persistence and increase women's QOL.

Standardized symptom management protocols for HCPs, telephone support lines, and peer support groups are just some of the possible strategies that might improve the experience of breast cancer survivors struggling with AET-related side effects. In addition, electronic resources such as evidence-based websites and online support groups might address the healthcare access issues and limited social support experienced by some women, particularly those living in rural and remote regions. Further to geographical differences, the discrepancy observed in this study regarding the provision of follow-up care (i.e., oncologist versus family physician) also speaks to the potential inequities in how cancer survivorship care is delivered.

These study results point toward a number of potential areas for further research. Identifying factors that influence AET persistence provide potential avenues to explore in the development of intervention strategies. Similarities between this study and the findings of recent research conducted across North America and Europe suggest that several factors found to influence AET persistence are not country specific, pointing toward the potential to develop universal intervention strategies that can be implemented across geographical regions (Brett et al., 2018; Lambert, Balneaves, Howard, & Gotay, 2018; Moon, Moss-Morris, Hunter, & Hughes, 2017; Verbrugghe et al., 2017). Given the recent guidelines recommending AET be taken for up to 10 years in certain populations (Burstein et al., 2014), further research is needed to investigate how personal, social, and structural factors influence persistence in the context of extended therapy. Gaining HCPs' perspectives will also be key to better understanding how the social and

structural factors intersect to influence survivors' AET persistence, and to inform the development of practical strategies for optimizing persistence. Most of the persistent women we interviewed experienced significant struggles related to AET side effects, indicating the importance of developing strategies to identify women facing AET-related challenges before they are lost to non-persistence.

### **3.5 Limitations**

The results of this study are limited by the small sample size comprised of predominately well-educated Caucasian women who reported a high socioeconomic status. There was some geographic variation within this study sample that revealed the unique challenges experienced by women that reside outside urban settings. We acknowledge that the percentage of non-persistent women (32%) did not equal the 40% non-adherence rate observed in the database used to recruit this study sample, which was due to difficulties in recruiting non-persistent women. Due to the large percentage of women who used both tamoxifen and an AI (41%) (see Table 3.1), we were not able to distinguish the study findings between these two categories of AETs. While tamoxifen and AIs differ in their side effects profiles, there may be other distinguishing factors associated with different regimens that could have influenced women's experiences in persisting with AET. The findings of this study only reflect women's perspectives and do not account for the experiences and perspectives of HCPs. Lastly, women may have experienced recall bias when reflecting on their experiences surrounding AET decisions and behaviours.

### **3.6 Conclusion**

The results of this study demonstrate that the personal, social, and structural factors influencing women's AET persistence are complex and can shift over time. There is a growing body of evidence to support the impact of personal factors, such as side effects and women's

beliefs, on AET persistence. Further exploration of how the social and structural context in which AET decisions and behaviours are enacted is needed to guide the development of novel supportive care interventions. As well, it will be important to gain the perspectives of HCPs who support women undergoing AET to inform practical intervention strategies that can be implemented into routine clinical practice. Addressing women's supportive care needs and ultimately AET persistence will help to ensure optimal survival outcomes for breast cancer survivors.

## **CHAPTER 4: ADJUVANT ENDOCRINE THERAPY ADHERENCE IN BREAST CANCER SURVIVORS: HEALTHCARE PROVIDER PERSPECTIVES**

### **4.1 Introduction**

AET, including tamoxifen and AIs, is part of standard of care treatment for women with HR+ breast cancer. AET reduces the risk of breast cancer recurrence by up to half when taken for at least five years (Early Breast Cancer Trialists' Collaborative Group (EBCTCG), 2011). In 2014, ASCO issued a guideline update that recommended AET be extended for up to 10 years to women at high risk for a breast cancer recurrence (Burstein et al., 2019, 2014). Despite the substantial clinical benefits, a significant portion (51%) of women are non-adherent to AET (Hershman et al., 2010). Non-adherence is associated with reduced survival, with a significant increase (49%) in mortality for women who are non-adherent to AET (Hershman et al., 2011).

AET non-adherence is a complex, multifaceted issue influenced by several factors. The demographic and clinical characteristics (e.g., age, disease severity, comorbidities, toxicity, type of care provider) associated with non-adherence are well documented in the literature (Gotay & Dunn, 2011; Moon, Moss-Morris, Hunter, Carlisle, & Hughes, 2017; Murphy et al., 2012). In recent reviews, our research and that of others have identified psychosocial factors linked to AET adherence, including women's perceived necessity for AET, self-efficacy, social support, the quality of the patient-HCP relationship, and continuity of follow-up care (Hershman et al., 2016; Lambert, Balneaves, Howard, & Gotay, 2018; Moon, Moss-Morris, Hunter, Carlisle, et al., 2017). More recently, researchers have also used qualitative inquiry to better understand breast cancer survivors' experiences and perspectives and their overall AET adherence (Brett et al., 2018; Harrow et al., 2014; Lambert, Balneaves, Howard, Chia, et al., 2018; Moon, Moss-Morris,

Hunter, & Hughes, 2017; Verbrugghe et al., 2017). This emerging body of work has sought to address a gap in the literature on the reasons why women struggle to adhere to AET.

Given the longevity of AET, the relationship between breast cancer survivors and their HCPs can span several years and multiple providers and healthcare settings. As such, exploring HCPs' experiences and perspectives in caring for women prescribed AET, including the structure and delivery of healthcare services, may identify broader social and structural factors that influence AET adherence. This evidence is foundational to the development of future interventions aimed at improving AET adherence, including identifying strategies that HCPs perceive as promising and feasible to implement.

The aims of this study were to: (1) explore HCPs' experiences and perspectives in providing care to breast cancer survivors prescribed AET, (2) identify how social and structural factors influence the provision of AET-related care; and (3) ascertain HCPs' recommendations for optimizing AET adherence and related care.

## **4.2 Methods**

In this qualitative study, an interpretive description (Thorne, 2016) approach to inquiry and the theoretical lens of relational autonomy was used to explore HCPs' experiences and perspectives related to women's adherence with AET. Relational autonomy is an interpretation of autonomy that considers not only the personal factors, but also the social and structural forces that influence behaviours and decision making (Sherwin, 1998). A relational autonomy lens focused the inquiry on the ways in which the broader social and structural contexts influenced the provision of AET-related care. Patient-reported factors associated with AET adherence (Lambert, Balneaves, Howard, & Gotay, 2018) and the experiences and perspectives of breast cancer survivors (Lambert, Balneaves, Howard, Chia, et al., 2018) are published elsewhere.

#### **4.2.1 Participant Recruitment**

Upon approval from the UBC Behavioural Research Ethics Board, HCPs providing care to women prescribed AET following primary cancer treatment were identified through the BC Cancer Breast Tumour Group, the BC Cancer Family Practice Oncology Network, and the BC Cancer nursing networks, including oncologists, general practitioners in oncology<sup>2</sup>, registered nurses, nurse practitioners, and pharmacists. These HCPs were involved in providing a range of services related to AET, including prescribing, managing symptoms, addressing questions, and providing follow-up care. HCPs received a study invitation and consent form (Appendix B.1) via email. Individuals who expressed interest were invited to contact the research team, who sought informed consent prior to the interview. Snowball sampling was also used to recruit additional HCPs to the study. Despite these recruitment efforts, no family physicians accepted our invitation to participate in the study.

#### **4.2.2 Data Collection and Analysis**

Semi-structured interviews (see Appendix B.2 for interview guide) ranging from 16 to 52 minutes in duration (36 minutes on average) were conducted with 14 HCPs (four in person and 10 by telephone), audiotaped, and transcribed verbatim. HCPs also completed a demographic form (Appendix B.3). Interview questions explored HCPs' initial and ongoing discussions and care experiences related to AET, including: (1) how they communicate the benefits and risks of AET; (2) how they provide AET-related follow-up care; (3) why they think breast cancer survivors experience difficulties with AET; and (4) what strategies they feel would be most effective at optimizing AET adherence. The project director, LKL, wrote field notes to document

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<sup>2</sup> In Canada, general practitioners in oncology are family physicians whose practices are focused on providing care to patients with a diagnosis of cancer.

observations, interactions with HCPs, and contextual information during the interviews. NVivo™ software was used to organize data. Data was collected and analyzed concurrently, with preliminary data analysis informing questions asked in subsequent interviews (Thorne, 2000). Three members of the research team (LKL, LGB, and AFH) independently reviewed several transcripts to confirm the preliminary coding structure and engaged in an iterative process of ongoing discussion and returning to the data throughout the analysis phase. Thematic analysis (Sandelowski, 2000) was used to analyze the interviews, beginning with reading transcripts line-by-line to organize data into broad codes. Data was then inductively analyzed to conceptualize ideas, comparing the thematic similarities and differences to understand the relationships among data (Thorne, 2016). To reflect the analytic process and keep track of methodological and analytical decisions, extensive analytical memos and conceptual diagrams were developed (Koch, 2006). These were reviewed during analysis, along with the field notes. Descriptive statistics summarized participant characteristics.

## **4.3 Results**

### **4.3.1 Sample Characteristics**

Participants included medical oncologists ( $n = 5$ ), radiation oncologists ( $n = 2$ ), nurse practitioners ( $n = 4$ ), a registered nurse, a pharmacist, and a general practitioner in oncology. Participants worked in cancer care settings from across the province, including urban and rural or remote regions (see Table 4.1).

**Table 4.1 Healthcare Provider Demographic and Practice Characteristics**

<b>Sample Characteristics <i>n</i> = 14</b>	<b>Frequency (%)</b>
<b>Discipline</b>	
Medical oncologist	5 (36)
Radiation oncologist	2 (14)
General practitioner in oncology	1 (7)
Nurse practitioner	4 (29)
Registered nurse	1 (7)
Pharmacist	1 (7)
<b>Practice Domain<sup>a</sup></b>	
Clinical practice	12 (86)
Research	3 (21)
Education	3 (21)
Professional practice	3 (21)
Administration	4 (29)
<b>Practice Context</b>	
Urban	6 (42)
Rural	4 (29)
Both urban and rural	4 (29)
<b>Years Worked as a Health Professional</b>	
<20	5 (36)
>20	9 (64)
Mean	19.6
<b>Years Worked as a Health Professional in Oncology</b>	
<5	4 (29)
5-14	3 (21)
15-19	4 (29)
>20	3 (21)
Mean	12.5

<sup>a</sup> Participants reported more than one domain, resulting in percentages adding to more than 100%

It is important to note that medication costs were not seen as a factor influencing adherence for women in BC, with AET being publicly funded and provided at no cost to patients for at least five years, and 10 years for tamoxifen. Access to AET, even in rural areas, was also not perceived to be a barrier. Rural HCPs described an established system for coordinating the delivery of AET across a vast geographical region, even in the most remote communities.

### **4.3.2 Main Components of Care**

HCPs focused on four main components of AET-related care in describing their experiences of providing care to breast cancer survivors. These components included: (1) the importance of having careful conversations about AET at the start of treatment; (2) difficulties in navigating transitions in care; (3) symptom management as a big part of their role; and (4) dealing with AET discontinuation. Within these components of care, HCPs identified social and structural challenges that influenced AET adherence among breast cancer survivors.

#### **4.3.2.1 Careful Conversations**

Oncologists in this study were responsible for prescribing AET and having initial AET treatment discussions with women. Their descriptions of these conversations revealed the structure and content of these discussions, including their approach to decision support, how they communicate the benefits and risks of AET, and the importance of addressing women's attitudes and beliefs in facilitating AET adherence.

Recognizing how HCP recommendations can influence women's treatment decisions, oncologists approached these conversations carefully. Most oncologists used a shared decision-making approach in which they personalized information based on women's age, risk profile, type of primary cancer treatment(s), and attitudes and beliefs toward AET and medication. They saw their role as providing the requisite information and decision support necessary to empower

women to make an informed choice, emphasizing that it was ultimately a woman's choice to initiate and adhere to AET. While differences existed in the level of detail shared with women, oncologists framed AET as an important and efficacious treatment, discussed the benefits and risks, treatment duration, and potential for sequential (i.e., switching from tamoxifen to an AI) and/or extended AET. Oncologists stressed the importance of accurately portraying AET benefits and risks in a way that conveys the importance of AET without being overly persuasive. As one medical oncologist shared, "don't try to oversell it."

*Understanding AET benefits and risks.* The oncologists reported that women's fear of cancer recurrence was not always commensurate with their actual risk, but rather was sometimes exaggerated or underestimated.

I think the human spirit is a mixture of fear, so there are lots of women who don't want a recurrence, of course, but also optimism. So, "It's not going to happen to me." I have had a number of women who have stated that and they've been right in some cases and they've been wrong in some cases. (Medical Oncologist)

Consequently, oncologists invested much time helping women understand their actual risk and the net benefit of AET for them personally. Oncologists also described how discussions with low risk women were often more involved because the benefits and risks of AET were not as clear for them as for women with high-risk disease.

I do have a careful discussion with them about the risks and the benefits. And quite often, it's a case where it's pretty even, so it's not a very clear-cut thing that they should take the medication. A lot of times, the woman's own personal views come into it. How they view the risks and the benefits. And sometimes, it's a much longer discussion than women with high-risk disease, because in high-risk disease it's very obvious that the benefits outweigh

the risks, but in low-risk women it's not as clear. It can often take a lot more discussion.

(Radiation Oncologist)

Almost all oncologists used numbers to quantify the benefits and risks associated with AET; however, some were concerned about what they perceived to be patients' "fixation" on numbers. To increase women's understanding, some oncologists chose to use absolute differences when presenting risk statistics because of their concern that women might over-estimate the benefits of AET when presented with relative numbers.

I'm very careful always to give women the absolute numbers, because it really tends to over-estimate the benefit if you just say I'm going to double your chance of not having a recurrence. That can be quite misleading. Five percent might go to 2–3% and some women would want that and other women would not want to take a medication for five years for that amount of benefit. (Radiation Oncologist)

I actually don't find numbers that helpful. I find people get fixated on the number. I only bring up the number if they're quite resistant to using [AET], because they bring up all the side effects. And then, I bring in numbers as to what the percentage of absolute risk is from side effects and from the other. I try to use it more as a comparison. I do provide them with more generalities, like around one quarter of women will relapse if they don't do this, or around 50%, that kind of thing. But, I don't say your risk is 33%. I give them a little bit more general fractions, and then, I try to tell them just what the additional benefit is...if half of the people were going to relapse without it, and then only a quarter of people will. That's a significant benefit. Or I'll turn it around, saying like this many people will stay

free of disease if they take it versus this many free of disease if they take nothing. (Medical Oncologist)

The protective effect of AET was also described by HCPs as a challenging concept for some women to embrace.

If you think about getting chemotherapy and [how it's] portrayed in movies and all sorts of media, how awful it is. So it must be the most important piece of your treatment, versus the little pill that you take every day. How could that possibly be as important? I think there is a bit of a misnomer out there about how important chemotherapy is and that the hormone piece really isn't that big a deal. (Pharmacist)

Oncologists described that when they carefully explained AET-related concepts (i.e., adjuvant treatment, risk of relapse, microscopic disease), most women ultimately understood the importance of AET. Structural factors, including a limited amount of time to discuss the pros and cons of AET and a lack of education resources for women, made these conversations further challenging, particularly when women held negative beliefs about medication.

***Managing expectations and fears.*** HCPs perceived that addressing women's expectations and fears at the start of AET impacted the decision to initiate and adhere to AET. Oncologists used various strategies during initial consults to manage women's expectation about therapy and ameliorate their fears about the potential side effects and longevity of AET. HCPs observed the side effects of AET were particularly concerning for women.

And then, of course, the side effect discussion is a problem and I think that ... the general side effects of hot flashes and joint symptoms, mood changes – and then, also getting into the sexual side effects. I think for a lot of women, whether they're young or they're old, that's a big deal. So, we talk about vaginal dryness, vaginal discharge, and loss of libido,

and all of those things. Being faced with those side effects...that's a problem. (Medical Oncologist)

However, some HCPs perceived that managing women's expectations of the potentially high likelihood of side effects at the time of AET initiation increased their tolerance of AET and resulting adherence.

In my experience, if you manage people's expectations in advance, then you get a better success rate. There's no point pretending or downplaying potential side effects because then they can experience a greater intensity or severity or spectrum of side effects and many women if they are not forewarned may then sort of balk. But if they're told to anticipate x and y and z and that they can report back and we can talk about ways to improve things and then they're often more accepting. (Medical Oncologist)

It's the intensity that gets them. And you don't know how intense it's going to be for anyone, until they're on it. But, I think if we can almost – without scaring them – give them the worst scenario. I think that it prepares people better. (Nurse Practitioner)

Depending on the type of AET prescribed, oncologists typically reviewed the common side effects that were not associated with risks of mortality, but could influence women's QOL and decision to discontinue AET. They also reviewed side effects that were rare, but medically more serious that would almost always result in AET being stopped.

HCPs also observed that the longevity of AET was a concern for many women who were not used to taking medication on a regular and long-term basis. When women were apprehensive about starting AET, some oncologists used various strategies to address women's concerns and encourage them to try AET. Some oncologists found it helpful to position AET as having

multiple benefits. For instance, they described tamoxifen as reducing the risk of recurrence and also preventing bone loss in menopausal women. To ease women's fears of serious risks, such as uterine cancer, one oncologists described reassuring women that serious side effects are often detected early because warning signs, like vaginal bleeding, signal to the patient something is wrong. Another strategy a few oncologists considered effective was to frame the initial decision to start AET as a decision women could revisit at any time, emphasizing their only commitment was to try it, not complete the recommended course of treatment.

Even five years is extended. Come on. You know, the minute you say to a person, "You're going to be on this for five years", it's like, their eyes go like this, you know? Like, [raising their eyebrows]. So, I always say, "Listen, it's one day at a time and we'll see." (Medical Oncologist)

Suggesting women ease into AET by taking it every other day for the first two weeks was an approach one oncologist said most women reportedly agreed to.

#### **4.3.2.2 Navigating Transitions in Follow-Up Care**

Oncologists were generally encouraged to follow practice guidelines recommending patients be discharged to the community following primary treatment (Guidelines and Protocols and Advisory Committee (GPAC), 2013). Routinely discharging women, however, was challenging for some physicians due to several factors, including HCP and patient preferences and access to primary care providers and uncertainty in their comfort with AET-related care.

***Variability in discharge practices.*** There was considerable variability in discharge practices among medical and radiation oncologists and across urban and rural practice contexts that did not always appear to be based on medical need.

So, we're very much encouraged to discharge our patients to their family doctors. Because 85% of women survive and once you've been in practice for 20 years, you have a huge practice, right? But there are issues. I'd say there's a lot of variability. It's definitely not a consistent approach across [the province] (Medical Oncologist)

Medical oncologists practicing in urban settings described commonly providing care to women for up to two years of AET and, in some cases, continued to see patients for five years and beyond. The medical oncologists described following women longer-term who were: (1) at a relatively 'higher' risk of recurrence; (2) enrolled in a clinical trial; (3) without a primary care provider; (4) having lingering issues related to side effects or outstanding tests (e.g., mammograms); and/or (5) vocal about their strong preference to remain under the care of their oncologist. Women discharged by medical oncologists in the first two years of AET were described as having a relatively low risk of recurrence, an established relationship with their primary care provider, and/or eligibility for referral to a nurse practitioner-led cancer survivorship program, if available. Radiation oncologists commonly discharged breast cancer survivors within a few weeks or months after initiating AET due to the low-risk profile of most of their patients.

The discharge practice patterns of oncologists based in rural areas differed from those in urban settings due, in part, to structural challenges. In rural practices with high patient volumes and relatively few oncologists, oncologists generally did not follow women for an extended period. Rural oncologists routinely discharged women to the community after at least one follow-up visit to assess their tolerance of AET.

After I've started them on [AET], I don't see them again, other than the first two-month visit. If they come back feeling well, there are just so many new patients coming through our doors, we have to discharge these patients. (Medical Oncologist)

***Challenges in transitioning follow-up to primary care.*** Some oncologists and the general practitioner in oncology found it difficult to transition care to primary care providers due to the availability of primary care providers and uncertainty in their comfort with AET-related care. The limited number of primary care providers, particularly in rural areas, challenged oncologists from routinely discharging women eligible for follow-up in the community. Some HCPs thought this led to a substantial number of women unnecessarily receiving survivorship care from oncologists and general practitioners in oncology in tertiary care settings, which they perceived to be an ineffective use of oncology resources.

I've found that some of the patients that are treated in Penticton or in Cranbrook, who I would discharge, I see notes going on and on, saying that the [general practitioner in oncology] was continuing to follow them on hormone therapy and I sort of asked why, and they say, "Oh well, there's a shortage of [general practitioners]." And I think, "Whoa. That shouldn't be [BC Cancer's] problem to suck up." (Medical Oncologist)

Another factor influencing care transitions was some HCPs' uncertainty in family physicians' comfort to provide AET-related care; as one medical oncologist shared, "some family doctors are just way better at this than others." HCPs who had confidence that their patients' breast cancer follow-up would be managed in the community were more likely to transfer care early on in the AET trajectory. The quality of women's relationship with their primary care provider was also perceived by some HCPs to influence AET adherence. A strong

relationship between women and a knowledgeable primary care provider was believed to result in the same level of adherence as women receiving care from an oncologist.

If the patient has an excellent relationship with a very good general practitioner, then they'll probably get as good adherence as staying with someone like an oncologist, right? So, a lot of it is what that primary care relationship is like. (Medical Oncologist)

When transitioning care to the community, oncologists shared a treatment summary and follow-up care plan with primary care providers that included information on AET prescription refills, date to re-refer women eligible for sequential AET, and surveillance instructions. The oncologists and general practitioner in oncology, however, reported what they perceived to be inconsistencies in the implementation of these recommendations evidenced by: a large number of patient re-referrals from family physicians for symptom management; unnecessary AET prescription refill requests; and delays in the start of the sequential AET strategy when women were not referred back to their oncologist on time. To mitigate unsuccessful transitions to primary care, some oncologists and the general practitioner in oncology offered to share follow-up care with family physicians. These physicians were responsible for AET-related care and the family physicians were responsible for women's general healthcare needs.

I'll often say to family doctors, "Listen, I've come to know this patient. This is a patient that will do well in your practice. I'll take care of the heavy lifting. Can you just be the family doctor?" And we've been very able to go on those doctors' empathy and sympathy for cancer patients and get them attached. (General Practitioner in Oncology)

As a result of the structural and social challenges of transferring care back to the community, HCPs highlighted the need for patients to be strong self-advocates in navigating the

healthcare system, particularly because follow-up related to AET can include multiple providers over several years.

If you're not a good self-advocate, if you're not pushy, if your family doctor retires, if you have some side effects and nobody's addressing them, then the adherence is going to be poor, you know? (Medical Oncologist)

#### **4.3.2.3 “A Big Part of the Job”: AET Side Effects**

The HCPs described AET side effects as a significant issue in their clinical practice and discussed some of the challenges associated with managing symptoms, including the large demand this placed on oncologists; disagreement over the responsibility of symptom management; and barriers and solutions to helping women manage their symptoms.

***Responsibility of symptom management.*** Given their specialized knowledge, oncologists found themselves responsible for the bulk of symptom management except when women were receiving follow-up from a general practitioner in oncology or nurse practitioner specializing in cancer care. Addressing AET side effects consumed a significant portion of oncologists' time and was described as “the number one task” of their week.

In fact, in the course of my week, I would say that that's the most common task for me to do, is to talk to people on the phone. Sometimes I'll see them in clinic. But usually, I'll just talk to them on the phone about their endocrine therapy side effects. That probably is the number one task of my week. It's a big part of the job, is dealing with hormone therapy.

(Medical Oncologist)

This demand came from several sources, including from women, primary HCPs seeking guidance on or re-referring previously discharged patients for symptom management, and patient callbacks from the general nursing support line.

I get a lot of referrals back. I've discharged a patient and six months later, the family doctor will send me back a referral – she's having a lot of symptoms, could you see her again? Or she wants to switch, or she wants to come off, or she wants to go down to half a tab, or she wants to do it every other day. There's lots of things. (Medical Oncologist)

I think it's very uncommon [for family physicians to address AET side effects]. Sometimes they'll call and they'll just take advice over the phone. And they'll say, "Oh, I could do that, if you want me to start them on Effexor. I have experience with that drug and we'll see how that goes." But I would say more than 90% of the time, I'll have to call patients, or have to see them back and I'll have to solve that. (Medical Oncologist)

Expectations about who was responsible for addressing AET side effects varied across disciplines. Some oncologists and nurse practitioners viewed symptom management as the responsibility of primary care providers. Other oncologists, however, did not expect primary care providers to have specialized knowledge of AET given their responsibility for a very broad range of healthcare issues.

I do hear things like, "Oh no, family doctors should be able to counsel women about their hormone therapy" and I don't agree with that. It's not something that is fair to put onto family doctors, because there's quite a lot to it and they have a huge range of things already that they have to discuss with patients. To the point where I wonder how they do it. So, I feel that that's my responsibility and I do not mind if they need to come back about their hormone therapy. Now, I think if you have [general practitioners in oncology], people who have extra training and are more sub-specializing in oncology, nurse practitioners would be another group who would be excellent for that. But, it just has to be a bit more

sub-specialized, rather than just someone like the family doctor. I just don't think that's fair. (Radiation Oncologist)

***Symptom management: challenges and solutions.*** Addressing women's symptoms was often challenging due to several factors, including a lack of symptom management guidelines, unclear symptom etiology, limited treatment options, and women's beliefs about medication. A lack of guidelines for managing AET side effects meant HCPs relied on the survivorship literature and their clinical experience, which resulted in an inconsistent approach in symptom management. Most HCPs emphasized how side effects were often hard to treat due to a lack of effective treatments options.

Other than Venlafaxine, the literature on all the other approaches, alternative and medically tested, there's not much success and most things that have been formally tested have been no better than placebo. (Medical Oncologist)

In addition to having few options, another key challenge to symptom management was the unknown and/or multifactorial etiology of side effects. Determining the cause of side effects was often problematic because of the difficulty in teasing apart potential confounding factors, particularly when symptoms occurred soon after primary treatment.

Emotional stuff is most prominent after they're finished chemo and radiation. They come to me for that three-month appointment after radiation. They've been on AI and they think everything's behind them, but that's when most of them emotionally have the hardest time. So, they tend to blame it on the AI, but it would happen in the patients who had triple-negative breast cancer, also. (Medical Oncologist)

As a result, HCPs often cautioned women against permanently discontinuing AET before exploring possible options for improving their symptoms.

I think it's not a single etiology, I think it's multifactorial, and so, you can't necessarily solve it by stopping hormone therapy, for example, or reverse it, even if the hormone therapy caused it or is a large part of it. (Medical Oncologist)

Medication breaks, in which AET was stopped for a period of time ranging from one week to a couple of months, were used by several HCPs to evaluate whether a pause in AET improved women's symptoms. This helped determine the etiology of symptoms and reset women's expectation about therapy, which often enabled them to resume AET. HCPs perceived that women were not keen to take additional medication to treat side effects; therefore, physicians preferred switching AET agents to prescribing supportive medication to alleviate symptoms. As the general practitioner in oncology said: "We don't want to have significant mitigation with several drugs, just to enable the patient to stay on tamoxifen."

There's lots of different options that they can try. If you don't like one, you can try the other, and you can try another. And there's at least three things that I try, right? I try a non-steroid AI, I try a steroidal AI, and then I try tamoxifen. (Medical Oncologist)

In some cases, HCPs supported dose reductions when women reported that taking AET every-other-day minimized their side effects. Not all HCPs, however, were supportive of these measures, citing the lack of data for alternative dosing in the adjuvant setting for invasive breast cancer. HCPs who acknowledged women's decisions to alter their AET dose did so from a risk-reduction perspective, assuming that patients would gain some benefit from AET rather than none.

A lot of women will instinctively, when things get unpleasant, they will start self-medicating – maybe skipping days, trying to see if that makes it more tolerable for them. I see that quite a lot actually. Once we find out that they may have been doing it every other

day and they're finding things to be much more tolerable, we will just support that.

Because ultimately, we're hoping that we try and get what compliance we can, so that we can get the benefit that it would be providing. (Registered Nurse)

We believe that getting some in you is better than none. But, we also don't want to affect your QOL so much that it's not worth really living. What's the point of living if you're so miserable? (Nurse Practitioner)

Many HCPs perceived AET adherence to be largely determined by a woman's mindset and the strategies she employed to cope with side effects. Consequently, communication and emotional support was considered to be one of the most effective tools for supporting AET adherence.

Our most useful or powerful tool is to support patients and reassure them that the hot flashes and menopausal symptoms are normal. I do think that supporting women, just through listening and encouraging and reassuring goes a very long way. (Nurse Practitioner)

#### **4.3.2.4 Dealing with AET Discontinuation**

Dealing with women's early discontinuation of AET was challenging for HCPs. Not only was AET adherence difficult to monitor across care settings, but also the decision to stop AET early was often hidden by women who were reluctant to disclose their decision. HCPs found themselves revisiting initial conversations with women about AET, adjusting how risks and benefits were discussed based on women's risk status and the amount of time that had passed.

While there was no standard practice for monitoring women's AET adherence in this sample, all HCPs routinely asked about AET use in follow-up visits. Oncologists reported that

unless primary care providers were asking about AET use, it was not monitored by oncology centres.

I think what you're doing is an important study and it's something that oncologists struggle with. It's one of those things where you see a patient for the last time, and you've said goodbye, and you've said all of the common sense stuff, and all of your best intentions are laid out, and the patient says, "Oh yes, I'll definitely do that." And you just know in your heart that a lot of them are not going to get their mammograms, and a lot of them are going to stop their hormone therapies, and nobody's going to know about it and talk to them about it, and I just don't have the ability to be the safety net for all of those things.

(Medical Oncologist)

Sometimes women who wanted to stop AET early sought input and permission from the HCPs before deciding to discontinue treatment. In other cases the HCPs were often surprised when they learned in scheduled follow-up visits women had already stopped AET. Women who were worried about ending AET early, and who had a good relationship with their HCP, were perceived as being more likely to ask about alternatives or seek permission to discontinue AET.

If they are discharged, they don't often call me back. But, some people do. Really, again, it depends on our relationship. It depends on language. It depends on how worried they are about stopping. So, if they're worried about stopping, they're going to call me and find out if there's alternatives. If they never wanted to take it in the first place, and their naturopath told them to take Indole-3-Carbinol, which is the latest thing that is being recommended,

I'm not going to hear about that. (Medical Oncologist)

When asked why they think women discontinue AET without consultation, HCPs suggested that a culture of patient compliance with HCP recommendations may prevent some women from

voicing their decision to stop. Some HCPs perceived that women felt guilty for not completing AET and were worried about how their decision would impact their relationship with a HCP, particularly their oncologist.

I think that's why they feel that they can't come and talk to you about stopping it, because it's almost like that "breast is best" motto, where women who can't breastfeed or choose not to, feel intimidated by that. And I think it's similar with the endocrine therapy, where they feel so – being such a high recommendation, that if they don't do it, it's that they're not doing due diligence. They don't want to upset their oncologists. And a lot of them will come to me and say, "I saw Doctor So-and-So yesterday. She's not very happy with me because I decided to stop the tamoxifen." (Nurse Practitioner)

When HCPs discovered women had discontinued AET, they were forced to review the implications of this decision with women and offer options for resuming treatment, if clinically appropriate. They observed some women were open to switching agents (e.g., tamoxifen to an AI) or re-starting AET if HCPs could offer options for potentially mitigating bothersome side effects that led to the decision to discontinue.

I assume that the drugs are always being taken and that's not always the case. It's funny, because they'll come to see me at the two-year time point, the time that they're supposed to switch from tamoxifen to an AI and they'll say, "Oh, you're going to be mad at me, but I stopped my tamoxifen six months ago." And I'll be like, "Did you tell anybody? Did you tell your family doctor? I don't recall getting a phone call about that." "Oh, I just kind of forgot." And so, we'll discuss that and we'll discuss the implications of that and discuss whether we're going to continue to switch over to something else or what we're going to

do. So, there are patients who will stop six months, even twelve months before they come back to see me and no one knows. (Medical Oncologist)

For low risk women, conversations about discontinuing AET were similar in nature to initial treatment discussions in which HCPs helped women weigh the protective effects of continuing AET against the burden of side effects. Oncologists did not necessarily discourage women from discontinuing AET when they experienced immediate and difficult side effects, describing the absolute benefit of AET for low-risk women as “a very borderline calculation.”

We’re just really talking about doing something reasonable to make that good outlook even better. But, being reasonable means that we don’t want them to be subjected to therapies that influence their QOL. So, if they end up taking tamoxifen and feeling depressed, that’s not worth it. If they end up going onto one of the aromatase inhibitors and being all sore and stiff and feeling like they’ve got bad arthritis all the time and not able to do their usual activities, that’s not worth it either. (Radiation Oncologist)

For women with high-risk disease, HCPs invested more time exploring ways to support AET adherence in the hope women would continue therapy. Yet, with the passage of time, some women’s perception of risk seemed to decrease and HCPs found it more difficult to convince them of the importance of long-term adherence. Supporting women in making an informed decision about stopping AET early appeared to be about respecting their autonomy while ensuring they understood the risks associated with their decision. Recognizing the power of HCP recommendations, some HCPs were unsure how strongly to encourage adherence: “Women who have much to gain will almost always persevere with treatment, but not always. And I’m never sure myself, if I should push harder” (Medical Oncologist).

### 4.3.3 Healthcare Provider Recommendations

HCPs made several recommendations about how to improve AET adherence, with emphasis placed on increasing education and support for both patients and clinicians and restructuring the delivery of AET-related care to breast cancer survivors. Foremost, some HCPs identified a need for more comprehensive AET education resources for clinicians and breast cancer survivors. For instance, these HCPs wanted concise, summarized information handouts to facilitate AET discussions and share with patients to take home. Given the limited time available in follow-up visits, HCPs highlighted the need for additional patient education as well a greater frequency of communication with patients, particularly at the start of AET. One suggestion was to offer nurse-led, group education sessions for women prescribed AET, followed by one-on-one consults with a nurse. Another suggestion was to develop an online, comprehensive information resource specific to AET that also offers a “symptom checker” function where patients can receive evidence-based suggestions for managing their side effects. Some HCPs also highlighted the importance of including lifestyle recommendations as part of these education initiatives. In response to the lack of guidelines, some HCPs recommended the development of AET-specific guidelines that include “a summary of up-to-date, proven treatments for any particular side effects, in a really easy to digest way” (Medical Oncologist).

When asked how they think AET adherence could be enhanced, HCPs emphasized the importance of personal connection; established patient-HCP relationships; and increased follow-up, particularly in the first three months of AET, to assess how women are tolerating therapy.

The best way is probably to contact them periodically and say, not in a sort of condescending or inquisitory way of saying, are you taking your medication? But more “Are you struggling with it? Are you having problems? Are you taking it every day?” And

if they're not, "Is it because you're so confident that you've been cured, or is it because you have side effects?" But probably some kind of questioning it would be best. (Medical Oncologist)

We are not supporting them once they leave here well enough. We're relying on them to contact us if they have an issue and we're not reaching out enough to check in with them. It relies on the patient to identify that there's an issue. (Nurse Practitioner)

This 'personal touch' of checking in either in person or by telephone was perceived to positively influence women's mindset and their overall commitment to AET. However, some HCPs also stressed the importance of implementing high-quality, efficient approaches to reducing oncologists' workload related to AET. Though oncologists were largely responsible for symptom management, some HCPs saw this model of care as unsustainable and a poor allocation of specialty resources. Some oncologists described themselves as an expensive and scarce option for providing long-term AET management, particularly in rural areas with relatively few oncologists.

Yeah, we just can't. We can't justify using up our [medical oncologists] to see people for adjuvant hormones, so that people can't get in for radical or concurrent chemotherapy and radiation. (Radiation Oncologist)

Instead, some HCPs recommended more effectively utilizing other HCPs, such as nurses with specialized knowledge, to deliver optimal AET-related care through survivorship clinics.

Survivorship clinics were seen as an ideal option for providing care to women undergoing AET akin to the services provided by other chronic disease clinics (e.g., diabetes).

I think it could be very helpful to have highly trained – either specialist practice nurses or advanced care, nurse practitioners who could even prescribe hormonal therapy. That would be helpful for us and then we would more stick to the radiation end of things. We're going to get this huge, big demographic bulge of cancer cases with not enough healthcare professionals – or not enough doctors, anyway. And doctors are a very expensive way to look after everybody. So, we are definitely going to have to make better use of nurse practitioners and advanced care professionals in different areas. And I think that would be a really good area for them, a really good area. It would be very helpful and very appropriate. (Radiation Oncologist)

Other recommendations for supporting AET adherence included: (1) developing visual aids to communicate absolute AET risks and benefits with patients; (2) translating education materials into other languages; (3) creating AET reminder systems; (4) conducting research on non-pharmacological options for improving side effects; and (5) upgrading the existing pharmacy system to generate automated alerts to indicate gaps in AET prescription refills.

There's actually systems out there, that if you got your prescription at three months you could put an automatic reminder in. And then so the problem is patients miss that, because there's no way for us to remind them. So, we don't have a pharmacy computer system that automatically does that. And that would be very helpful. (Pharmacist)

#### **4.4 Discussion**

This is the one of the first qualitative studies to explore HCPs' experiences and perspectives in providing care to breast cancer survivors prescribed AET. Other qualitative research with HCPs has mainly focused on investigating a single aspect of AET-related care, such as symptom management (Samuel et al., 2017; Turner et al., 2017) and physician

prescribing patterns (Wheeler et al., 2016). For instance, Wheeler and colleagues (2016) described some of the challenges HCPs encountered in AET discussions; however, their findings centred primarily on HCPs' perceptions of women's experiences and on identifying side effects that physicians attributed to AET. Our study builds on this beginning body of research to provide a more comprehensive portrayal of the unique challenges HCPs faced in caring for women undergoing AET, and their recommendations for improving AET-related care and adherence. HCPs highly invested in women's AET care and adherence and were challenged by personal, social, and structural factors that impacted four main components of AET care, including having careful conversations about AET, navigating transitions in care, managing side effects, and dealing with AET discontinuation. As a result, HCPs made several recommendations for improving support for patients and HCPs related to AET and adherence, which focused on identifying better ways of delivering high-quality, cost-effective care to women undergoing AET.

AET conversations were often quite involved and HCPs described investing a great deal of time and energy into this decision-making process to ensure women understood the benefits and risks of AET, while also respecting their values and beliefs. In particular, HCPs emphasized the importance of providing sufficient AET education to women at the outset of treatment. Some HCPs also observed that patient-centred communication was the most useful and powerful tool to support women in adhering to AET. These findings are consistent with previous research that found women's satisfaction with clinical support (Kroenke et al., 2018); the quality of the patient-physician relationship (Kahn et al., 2007), including frequent, patient-centred communication (Arriola et al., 2014; Liu et al., 2013); preparedness for the possibility of side effects; and physician involvement in decision making (Kahn et al., 2007) are significantly

correlated with greater AET adherence. These findings highlight the significance of HCP communication and support to AET adherence for women with breast cancer. However, the HCPs in this study struggled with the limited consultation time available and a lack of patient education resources. One recommendation for improving early AET communication and education was to offer nurse-led, group information sessions to provide breast cancer survivors with a comprehensive overview of AET and to address women's questions and concerns. It may also be worthwhile to evaluate if additional information sessions, offered at various points throughout the AET trajectory, would be of value to women and HCPs. Subsequent sessions could provide an opportunity to reiterate the benefits of AET and address challenges related to adherence that can emerge in the later stages of therapy, such as a decrease in women's perceived risk of recurrence.

The number of breast cancer survivors requiring long-term, AET-related follow-up care has progressively grown due to increased cancer incidence, as a result of an aging population; improved survival rates; and longer durations of AET. Consequently, oncologists will be increasingly constrained to provide AET-related care over an extended period of time, making it imperative to coordinate follow-up with primary care providers early in the AET trajectory. Several HCPs in this study, however, perceived challenges in transitioning follow-up to primary care. As a result, the provision of follow-up care varied widely across the sample and differences were observed among providers and geographical contexts. Intersection of social and structural factors was seen when breast cancer care was not successfully transferred to primary care providers. This was evidenced by a high number of patient re-referrals back to oncologists.

Previous research suggests that breast cancer survivors are not always confident their primary care providers have the specialized knowledge necessary to provide comprehensive

survivorship care (Easley et al., 2016; Lambert, Balneaves, Howard, Chia, et al., 2018; Mao et al., 2009; Roorda et al., 2015). Other researchers have also found that primary care providers themselves report having inadequate knowledge and training required to care for breast cancer survivors (Blanch-Hartigan et al., 2014; Luctkar-Flude, Aiken, McColl, & Tranmer, 2018; Potosky et al., 2011).

HCPs in this study made several recommendations to overcome challenges associated with providing AET-related care. Some HCPs highlighted the need to reevaluate the structure and delivery of follow-up, particularly related to symptom management. As suggested by the HCPs in this study, survivorship clinics led by nurses may be one way of delivering effective, patient-centred care while also decreasing the burden AET places on primary and oncology practices. Nurse-led clinics have shown effectiveness in reducing all-cause mortality and major adverse events, as well as improving medication adherence, QOL, and patient satisfaction in chronic disease populations (Al-Mallah et al., 2016; Larsson, Fridlund, Arvidsson, Teleman, & Bergman, 2014; Lewis et al., 2009; Wade et al., 2015). The results of a recent meta-analysis on the effectiveness of medication adherence interventions, among patients with coronary artery disease, found the most effective interventions used nurses (Chase, Bogener, Ruppar, & Conn, 2016). Yet, there are currently very few nurses involved in the management of AET in the province of BC.

If primary care providers, and other HCPs such as nurses, are to assume greater responsibility for long-term management of AET, they will require the knowledge, tools, and support to effectively and confidently care for breast cancer survivors. The high incidence of patient re-referrals to oncologists in this study, suggests that these HCPs will also need access to expert advice for more complex cases. One option is to expand the existing Rapid Access to

Consultative Expertise (RACE) and eCASE (electronic Consultative Access to Specialist Expertise) systems available to primary care providers in BC to include oncology as part of the specialty services offered (RACE, 2018). RACE and eCASE are innovative strategies to connect primary care providers with specialists for advice either through real-time telephone consults or conversations mediated through a web-based platform. In other illness populations, these systems have increased primary care providers' capacity to deliver care to patients and reduced emergency department visits and the number of patient re-referrals to specialists (Canadian Foundation for Healthcare Improvement, 2016). These interfaces are good examples of how better partnerships between oncology and primary care might be built.

The negative impact of side effects on AET adherence has been well documented in the literature (Cahir, Guinan, et al., 2015; Gotay & Dunn, 2011; Lambert, Balneaves, Howard, & Gotay, 2018; Murphy et al., 2012). HCPs in this study described symptom management as a substantial part of providing AET-related care. Yet, the lack of symptom management guidelines and the high rate of patient re-referrals back to oncologists suggest that HCPs may not have the necessary professional support required to manage AET-related symptoms in primary care settings. Nor did all oncologists expect primary care providers to provide this level of care. Disagreement among HCPs on who ought to be responsible for symptom management highlights a gap in the current system that needs to be addressed. This is consistent with the results of a recent study, which found that primary care providers expressed uncertainty about their ability to delivery AET-related symptom management and questioned if doing so was beyond their scope of practice (Samuel et al., 2017). The confusion surrounding AET-related symptom management is not surprising, since HCPs in this study who had specialized knowledge of breast cancer and AET described it as complex. The difficulty HCPs experienced in addressing AET-related side

effects was due, in part, to the unknown or multi-factorial etiology of some symptoms. This was further compounded by a lack of effective treatment options and women's own medication beliefs and preferences. However, despite the complexity of symptom management, HCPs need to be aware of the importance of asking about AET symptoms in follow-up consults to ensure women's side effects are not overlooked or poorly managed.

The results of this study have important implications for future research. The difficulty HCPs experienced in relation to care transitions suggests that research is needed to assess the information needs of primary care providers, and other HCPs such as nurses, who might be increasingly more involved in AET-related care. Research should also seek to identify the professional supports (e.g., guidelines for AET surveillance and symptom management) these HCPs require to deliver optimal AET-related care. One recommendation by some HCPs was to increase engagement of nurses in AET-related care. Further investigation is required to explore the feasibility and acceptability of optimizing nursing roles in the delivery of AET-related care. Research is also critically needed to identify and evaluate additional strategies for treating AET symptoms for which there are no effective management options. In particular, research into non-pharmacological approaches given women's apprehension to take additional medication will be important. Lastly, future investigations might also evaluate the impact of primary care initiatives and alternative models of care on healthcare utilization and costs, oncology discharge practices, patient satisfaction, and AET adherence.

#### **4.5 Limitations**

The results of this study are limited by the small sample size, including representation from only one nurse, pharmacist and, general practitioner in oncology and the absence of family physicians' perspectives. Study participants shared similar views on the importance of

supporting women in remaining adherent to AET and may not represent the perspectives of HCPs who did not express interest in participating in this study, such as family physicians. The study was conducted in a single Canadian province, which may limit the transferability of findings to other jurisdictions with different models of breast cancer care. The research findings and recommendations may need to be adapted for rural and remote healthcare contexts with unique challenges related to the structure and delivery of breast cancer care.

#### **4.6 Conclusion**

The high rate of non-adherence to AET in breast cancer is a complex, multifaceted issue. The results of this study demonstrate the pivotal role HCPs play in educating women about AET and supporting them to adhere to therapy. Greater support for HCPs is needed to improve the delivery and quality of care to the growing number of women undergoing AET. To ensure patients receive high-quality care, we will need innovations within the current healthcare system to meet the long-term needs of breast cancer survivors. New models of care and novel ways of addressing the current gaps in the healthcare system will need to be developed to enhance survivorship care, AET persistence, and ultimately ensure better outcomes.

## CHAPTER 5: CONCLUSION

This chapter begins with a summary of findings and key contributions of this research to the literature on breast cancer survivors' adherence<sup>3</sup> to AET. Next, potential applications of the research findings are discussed in the *Recommendations for Research and Practice* section. Finally, the dissemination of the research results is discussed in the *Knowledge Translation, Transfer, and Exchange* section, followed by study limitations and concluding thoughts.

### 5.1 Summary and Key Contribution of Findings

AET has significantly contributed to advancements in the treatment of breast cancer in terms of reducing women's risk of recurrence and mortality. Yet, despite substantial evidence of the efficacy of AET and the implementation of associated clinical practice guidelines, half of women are not adherent to these life-conserving therapies (Hershman et al., 2010; Owusu et al., 2008; van Herk-Sukel et al., 2010). This has significant implications for patient outcomes, including potentially increasing morbidity and mortality, and for society as a whole due to associated increased healthcare costs (WHO, 2003). The connection between adherence and survival outcomes emphasizes the importance of breast cancer survivors taking AET as prescribed and the need to identify factors that increase non-adherence. At the time this study began, the majority of research on AET adherence, however, focused on identifying demographic and clinical predictors of AET non-adherence, with very little known about the personal factors, such as women's beliefs and attitudes, and social and structural factors that shape the broader context of women's lives in which AET adherence is enacted. To ensure the

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<sup>3</sup> In this final Chapter, I return to using the WHO's (2003) definition of adherence, which encompasses the concepts of adherence and persistence. I will use 'persistence' terminology when referencing AET use for the breast cancer survivors I interviewed.

efficacy of AET demonstrated in clinical trials is realized in real-world contexts, it is important to understand *why* women make decisions and/or engage in medication-taking behaviours that could potentially cause them harm. As such, the overarching aim of this dissertation was to gain a better understanding of why a significant number of breast cancer survivors have suboptimal adherence to AET. Three research objectives were designed to address this overarching aim, and were presented in separate manuscripts in Chapters 2 through 4.

### **5.1.1 Integrative Review**

In Chapter 2, an integrative review was conducted to: (1) identify what was known quantitatively about the patient-reported factors associated with breast cancer survivors' AET adherence; and (2) explore the qualitative literature on the barriers and facilitators to AET adherence. The integrative review was the first to summarize these patient-reported factors in a way that paid particular attention to social and structural factors. Side effects of AET, women's beliefs about the necessity of treatment, their self-efficacy in taking AET and communicating with HCPs, the quality of patient-HCP relationships, social support, and a lack of continuity of follow-up care were all identified in previous research to influence AET adherence. These findings are consistent with the results of two recent systematic reviews that synthesized the psychosocial and healthcare factors associated with AET adherence (Moon, Moss-Morris, Hunter, Carlisle, et al., 2017; Van Liew et al., 2014). What was unique about the integrative review in Chapter 2 was the focus on patient-reported factors, and inclusion of qualitative data. This review identified additional factors (e.g., misconceptions about the hormonal nature of AET, concerns about premature aging) that were absent from most previous research on AET adherence, which collected data via questionnaires with pre-set questions.

Despite the unique perspective presented in the integrative review, the quantitative nature of most studies included, coupled with the small number of qualitative studies, provided limited insight into the nuances of women's real-world experiences and other socio-structural influences. In addition, the results of the integrative review identified features of AET non-adherence that required further investigation. For instance, more information was needed to understand how factors, such as women's medication beliefs, perceived need for AET, social relationships, and factors related the healthcare context, shape breast cancer survivors' beliefs about AET and their AET adherence.

### **5.1.2 Breast Cancer Survivors' Experiences and Perspectives**

In Chapter 3, the results from interviews with 22 breast cancer survivors offered a more person-centered perspective on factors that influenced women's AET persistence. These women revealed that persistence with AET, not adherence, was a challenge. It was not a matter of women forgetting to take their medication or changing the dose of AET; rather, they were challenged in continuing AET for the prescribed duration. While women did not report self dosing or forgetting to take AET (e.g., non-adherence) in this study, these medication taking behaviours have been cited as reasons for non-adherence in other qualitative research (Brauer et al., 2016; Cahir, Dombrowski, et al., 2015; Harrow et al., 2014; Wells et al., 2016; Wickersham et al., 2012).

One of the most significant contributions of this interpretive description study is the voice it gave to women's experiences related to AET and how these experiences impacted their persistence. Since beginning this study, it is encouraging to see that others have followed suit and more qualitative work has informed this emerging body of literature (Bluethmann et al., 2017; Brauer et al., 2016; Brett et al., 2018; Cahir, Dombrowski, et al., 2015; Farias et al., 2017;

Harrow et al., 2014; Humphries et al., 2018; Moon, Moss-Morris, Hunter, & Hughes, 2017; Simon et al., 2014; Verbrugghe et al., 2017; Wells et al., 2016; Wickersham et al., 2012; Wouters, van Geffen, et al., 2013). These studies provide valuable insight into women's AET experiences. What was unique about my study is how it illuminated the broader social and structural contexts that were central to shaping women's experiences in persisting with AET.

Some women described genuinely struggling to persist with AET and shared the profound impact side effects had on their QOL. Physical side effects, such as joint pain, muscle cramps, and hot flashes, kept some women awake all night and made activities of daily living difficult. Physical symptoms also prevented some women from doing activities they enjoyed before breast cancer (e.g., hiking) that were an integral part of their social connectedness with others. Side effects also took an emotional and psychological toll on some women, compromising their personal relationships, confidence in social situations, and occupational roles. Work-related changes altered some women's sense of identity and financially impacted their family. Quite simply, these were not just bothersome side effects – these were life-altering effects that many women endured on a daily basis and not surprisingly, largely contributed to some women discontinuing AET. Other qualitative studies have also identified that side effects can significantly impact women's QOL (Brauer et al., 2016; Harrow et al., 2014; Wells et al., 2016; Wickersham et al., 2012). My study, however, provided further insight into how these experiences affected many women not only physically and emotionally, but also how side effects impacted the social and occupational aspects of some women's lives.

Some women who were persistent with AET also experienced significant side effects – so what differentiated them from non-persistent women? The answer is not simple. Women's persistence with AET was influenced by a complex interaction of personal factors (e.g., beliefs

and values) and also broader contextual aspects (e.g., interactions with HCPs and access to care). For many women, AET persistence became a balancing act over the course of their treatment and the value these women placed on certain factors shifted over time and, ultimately, tipped the scales toward persistence or non-persistence (see Figure 3.2). These findings are similar to a recently published study that also found AET adherence was a “complex continuum of behaviours, appraisals, and decision points” throughout the duration of AET (Bluethmann et al., 2017, p. 109). Qualitative research has also shown that over time some women begin to question their initial beliefs about the importance of therapy (Brauer et al., 2016; Moon, Moss-Morris, Hunter, & Hughes, 2017). This continued reappraisal of AET benefits and risks suggests that while side effects are often a primary reason for non-adherence (Cahir, Guinan, et al., 2015; Humphries et al., 2018; Lambert, Balneaves, Howard, & Gotay, 2018; Moon, Moss-Morris, Hunter, Carlisle, et al., 2017; Murphy et al., 2012), there are other factors, that might also be highly influential in women’s adherence decisions and behaviours. Identifying these factors and understanding how they influence adherence is important to inform the development of person-centered strategies to improve support for women undergoing AET and increase adherence.

In this study, some women’s determination to persist with AET and overcome the difficult aspects of therapy was largely influenced by their beliefs about the necessity of AET; their perceived susceptibility of being diagnosed with breast cancer again; and ultimately, their fear of dying. This is consistent with recent quantitative research, which found women who hold positive beliefs about AET and the expected outcomes of therapy were statistically significantly more likely to persist with treatment (Bright et al., 2016; Hershman et al., 2016; Stanton et al., 2014). This study and those of others (Brauer et al., 2016; Cahir, Dombrowski, et al., 2015; Harrow et al., 2014), found that how women cognitively framed their AET experience directly

impacted their attitude toward AET and, in turn, their motivation to persist with treatment. This finding is consistent with the results of a recent survey of 1,371 breast cancer survivors that found 31% of women reported using positive “self-talk” (e.g., AET will reduce my chance of recurrence) as motivation to adhere to AET, which positively predicted their adherence (Bright et al., 2016, p. 249). In my study, although women’s beliefs had a substantial influence on their persistence, these women were also embedded in relationships with HCPs and faced with healthcare access issues that shaped their ability to persist.

In this study, HCPs were particularly influential in some women’s decisions about AET, which is consistent with previous research that has also acknowledged that HCP support impacts AET adherence (Cahir, Dombrowski, et al., 2015; Farias et al., 2017; Harrow et al., 2014; Humphries et al., 2018; Wells et al., 2016). For instance, qualitative evidence suggests that adequate clinical support, guidance, and information from HCPs can increase women’s self-efficacy and ability to continue with AET (Cahir, Dombrowski, et al., 2015; Farias et al., 2017; Humphries et al., 2018). Similarly, women in this study who had access to a knowledgeable HCP who validated their symptoms and provided options to alleviate side effects felt supported in persisting with AET. Other women, however, described that a lack of timely access to a knowledgeable HCP or the perceived inability of their family physician to manage their AET-related follow up influenced their decision to stop treatment early. Thus, one of the most important findings was the powerful impact of the broader socio-structural context on shaping breast cancer survivors’ willingness and ability to persist with AET by either enabling or constraining women’s agency.

### 5.1.3 Healthcare Providers' Experiences and Perspectives

The last phase of this research was an interpretive description study wherein I interviewed 14 HCPs who provided care to breast cancer survivors prescribed AET. HCPs are a key partner in women's adherence to AET and this interpretive description study gave voice to their perspectives, which was largely missing from the literature. The findings from this study built on insights from Chapters 2 and 3, which revealed that the nature of patient-HCP relationships and the structure and delivery of AET-related care influenced some women's AET use. The HCPs described their unique perspective on care relationships with women and features of the healthcare environment that influenced AET-related care, making social and structural barriers to AET adherence much more apparent. For instance, HCPs identified several challenges they encountered in clinical practice related to communication, transitions in care, symptom management, and addressing early discontinuation of AET.

The HCPs described the importance of having *careful conversations* with women about AET and articulated some of the challenges they encountered in navigating these discussions. HCPs expressed investing considerable time and energy in consults about AET to assist women in weighing the expected benefits of treatment against the risks and potential side effects. HCPs described tailoring their approach and presentation of information based on clinical factors (e.g., disease severity) as well as women's personal beliefs (e.g., medication beliefs). Some HCPs perceived that the more prepared women were for the possible reality of AET, the more likely they were to tolerate side effects and persist with treatment. This is consistent with previous research that found women who received information on side effects were more likely to adhere to AET (Heisig et al., 2015; Wuensch et al., 2015). Conversations with low-risk women were often much more involved because the benefits of AET were not always clear when weighed

against the disadvantages of taking a long-term treatment that could potentially result in a diminished QOL. Some HCPs voiced that sometimes they struggled with women's decisions to not initiate or continue with AET and were unsure of "how hard to push". Yet, they also recognized that while the current evidence suggests that they should promote complete adherence, increasing survival at the cost of QOL might not be a choice all women want to make, particularly women who have a low risk of recurrence.

In BC, after women complete primary breast cancer treatment, HCPs are strongly encouraged to transfer follow-up care from oncology settings to primary care. Several HCPs detailed why *navigating transitions in care* were often challenging because the structure of follow-up care was determined by factors that were not always based on medical need. Discharging women to primary care was often perceived as challenging by some HCPs due to several factors, including HCP and patient preferences, a scarcity of primary care providers, and HCPs' confidence their patients' needs would be met in primary care settings. Even when HCPs tried to discharge women to primary care, they received a large number of patients referred back for symptom management and, as a result, dealing with side effects in this survivor population became a large part of their work. Some HCPs identified this as an unsustainable and ineffective use of specialty resources.

The HCPs described how there is no formal monitoring of women's AET use beyond asking about it in follow-up visits. While some HCPs were consulted when women wanted to stop AET, many times women's decisions to discontinue treatment only came to light in a follow-up consult months later. When that happened, HCPs had to revisit the careful conversations they had previously with women, and try to address the reasons behind their non-persistence and offer potential options to resume therapy. HCPs made several recommendations

for improving education and healthcare services for breast cancer survivors prescribed AET that they thought would improve women's ability to adhere to AET, as well as better equip HCPs with the knowledge, tools, and resources to provide optimal care.

In terms of previous research, there is some quantitative evidence to support the significant association between AET non-adherence and elements of the patient-HCP relationship, including clinical support (Kahn et al., 2007) and patient-centred communication (Liu et al., 2013). Recent qualitative research also suggests that HCP support can have an influence on AET adherence (Cahir, Dombrowski, et al., 2015; Farias et al., 2017; Harrow et al., 2014; Humphries et al., 2018; Lambert, Balneaves, Howard, Chia, et al., 2018; Wells et al., 2016). Yet, only a few qualitative studies have explored HCPs' perspectives related to AET (Davidson et al., 2007; Samuel et al., 2017; Turner et al., 2017; Wheeler et al., 2016). These studies, however, primarily focused on examining a single aspect of AET-related care. For instance, one study evaluated the relative match between patients' and oncologists' perceptions of information discussed in healthcare visits (Davidson et al., 2007) and two manuscripts from another study focused specifically on HCPs' views about AET symptom management (Samuel et al., 2017; Turner et al., 2017). A third study explored physicians' prescribing patterns (Wheeler et al., 2016); however, the results centred on HCPs' perceptions of women's experiences and what they perceived to be the side effects of AET (Wheeler et al., 2016). My study builds on this nascent research to provide a more in-depth portrayal of the unique challenges HCPs faced, as well as, uncovering patient-, provider-, and system-related issues that constrained HCPs from providing optimal AET-related care. Furthermore, the recommendations made by HCPs for improving AET-related care and adherence, provide a unique contribution not previously evidenced in the literature.

#### **5.1.4 Understanding Adherence Through a Relational Autonomy Lens**

A final unique contribution of this research was the use of a relational autonomy lens, which illuminated how personal and socio-structural factors interacted to influence breast cancer survivors' AET experiences and adherence. A relational autonomy lens also helped uncover elements of the healthcare environment that were problematic for women and HCPs, including inequities in the provision of follow-up care. Limited access to timely care, a breakdown in the patient-HCP relationship, and the lack of symptom management options are three examples that limited women in their capacity to adhere to AET. Women's own agency was not always being supported; even some women who wanted to benefit from AET were not consistently receiving the support, the advice, and the follow-up care they required. This illustrates the need to look beyond the notion that women are solely responsible for their AET adherence and recognize that how care is provided also influences what women believe, what they understand, and how well they can manage the impact of AET on their QOL.

This research also identified new factors not previously known to influence AET adherence, such as concerns about the structure and delivery of care that made adherence difficult for women, which could foreseeably be modified within the healthcare system. This includes improving transitions in care and increasing the frequency of communication with women during the initial AET treatment period. These gaps represent points in the care trajectory wherein we can intervene to better meet women's supportive care needs so they are not lost to non-adherence. In the following *Recommendations for Research and Practice* section of this chapter, I provide a more detailed discussion of several additional issues that present opportunities for improvement.

Addressing non-adherence to AET is not going to be an easy fix. It will require looking beyond the personal reasons women do not adhere to how the system fails to support women in achieving optimal adherence. AET adherence is not only the responsibility of breast cancer survivors; women's adherence is a product of the environment in which care is provided and, therefore, is also the responsibility of the larger healthcare system. Conceptualizing AET adherence as situated in, and determined by, socio-structural conditions presents an opportunity to attend to the contextual factors that either enable or constrain women's adherence; rather than isolating the responsibility for change at the individual-level (Sherwin, 2011). Women need timely access to care that is evidence-informed and responsive, which also means that HCPs need the knowledge, tools, and time to provide this level of care. Hopefully, this dissertation will encourage us to ask: *“What can we do as HCPs and as a healthcare system to improve the delivery of patient-centred care that is responsive to breast cancer survivors' needs?”*

## **5.2 Recommendations for Research and Practice**

Clinical practice guidelines on the optimal duration of AET have emphasized the importance of identifying strategies to improve AET adherence, particularly given recommendations for longer durations of AET (Burstein et al., 2014). Medication adherence, however, is a long-standing issue in chronic disease populations that has not proven to be amenable to simple interventions, so it is not surprising that AET is no different. To date, no interventions have demonstrated statistically significant improvements in breast cancer survivors' AET use (Ekinici et al., 2018). Furthermore, the evidence on interventions aimed at enhancing adherence to oral anticancer agents is limited and inconsistent (Mathes, Antoine, Pieper, & Eikermann, 2014). In fact, the most effective methods for improving medication adherence in any chronic disease population remain unclear (Nieuwlaat et al., 2014). The results

of this dissertation suggest that interventions to improve AET adherence will likely take more than a one-dimensional approach to provide women with the information, support, and access to appropriate resources and care.

This section includes a discussion of recommendations for clinical practice and future research. Recommendations for research are woven throughout each sub-section, followed by *Overarching Research Considerations* and *Emerging Areas of Research*. *Recommendations for Research and Practice* are based on the results of this dissertation, as well as current research from the broader evidence base on AET, medication adherence, and cancer survivorship care. Recommendations include addressing factors related to the structure and delivery of follow-up care, nursing engagement in AET-related care, patient education and risk communication, frequency of follow-up communication, and symptom management. Similarities between the results of this study and research findings from across North America and Europe suggest that factors associated with AET adherence are not country-specific and the potential exists to develop AET interventions that might be suitable to be implemented in different geographical settings (Lambert, Balneaves, Howard, & Gotay, 2018).

Foremost, the results of this dissertation and research of others (Cahir, Dombrowski, et al., 2015; Farias et al., 2017; Harrow et al., 2014; Humphries et al., 2018; Wells et al., 2016) demonstrate that HCP support is particularly influential in women's decisions about AET. As such, these study findings are relevant to a range of HCPs, including specialist oncology HCPs and primary care providers. Dissemination of the study findings can be used to increase awareness among HCPs of the barriers and facilitators to AET adherence, including the importance of asking about women's AET use, assessing the presence of side effects, and discussing options for overcoming barriers to adherence. A simple strategy could involve HCPs

asking women “*What has your experience been in taking AET?*” “*Have you experienced any symptoms?*” “*Do you have any questions or concerns about AET?*” These questions could provide a mechanism for monitoring adherence, and also allow women to elaborate on aspects of AET that are important or concerning for them so that HCPs can begin to address any issues.

### **5.2.1 Structure and Delivery of Follow-Up Care**

There was considerable variability in discharge practices and the structure of follow-up care in this study. An increasing number of women are expected to undergo AET due to increased breast cancer incidence as a result of an aging population (Canadian Cancer Statistics Advisory Committee, 2018) and new guidelines recommending AET up to 10 years to eligible women (Burstein et al., 2019, 2014). Due to the growing demand placed on oncology centres, it will be increasingly important to transition care to the community early on in the AET trajectory. However, navigating transitions in care to the community was often problematic for both breast cancer survivors and HCPs in this study.

Research in Canada and the U.S. indicates that significant barriers exist to engaging primary care providers in cancer survivorship care, including issues related to a lack of knowledge, communication, and coordination of care (Grunfeld & Earle, 2010; Nekhlyudov, O’Malley, & Hudson, 2017). Other researchers have found that primary care providers themselves have reported feeling unprepared to provide survivorship care to breast cancer survivors due to a lack of formal education and professional tools to assist them to confidently deliver safe and effective care (Blanch-Hartigan et al., 2014; Luctkar-Flude et al., 2018; Potosky et al., 2011). In the context of AET, the results of a recent meta-analysis found that follow-up care provided by a general practitioner (e.g., family physician) versus an oncologist was significantly negatively associated with AET persistence (Cahir, Guinan, et al., 2015). More

specifically, a subsequent meta-analysis showed that the odds of persistence increased by 21 to 66% when care was provided by an oncologist or gynecologist than a general practitioner (Moon, Moss-Morris, Hunter, Carlisle, et al., 2017). If women are to persist with AET, regular follow-up care with a knowledgeable HCP in the community will be essential.

In the Canadian healthcare system, timely access to appropriate cancer-related care, and specifically symptom management, is an ongoing issue in community settings. According to the Canadian Partnership Against Cancer, *2018 Cancer System Performance Report*, one-third of cancer survivors waited over a year to gain help with their most difficult physical, emotional, or practical concerns encountered after completing primary cancer treatment (2018). These findings indicate there are substantial issues related to accessing timely and effective cancer survivorship care, which are not unique to AET or the healthcare system in BC. In 2018, the BC Patient Safety and Quality Council received a request from the provincial government to help inform improvements in care transitions for individuals diagnosed with cancer in BC (BC Patient Safety and Quality Council, 2019). What they found was that both patients and HCPs were frustrated with inconsistencies and a lack of communication as cancer patients transitioned through the healthcare system that left patients to coordinate their own care. The results of this dissertation echo these findings and demonstrate that care transitions between oncology and primary care settings were problematic for both HCPs and breast cancer survivors. Before proposing system changes and investing resources in efforts to improve the structure and delivery of breast cancer care across the AET trajectory it will be important to conduct additional foundational work.

Research is needed to identify the barriers that impede effective care transitions to inform the development and evaluation of health system initiatives to improve the coordination and continuity of care for breast cancer survivors. In particular, in relation to AET, research is needed

to explore primary care providers' unmet needs related to assuming responsibility of AET-related follow-up. A needs assessment using qualitative and survey research might be one mechanism to better understand primary care providers' needs and identify potential strategies to improve care transitions. A needs assessment could be structured to explore primary care providers' experiences with providing care to women undergoing AET; identify barriers and facilitators to effective care transitions; and assess primary care providers' education needs and perceived roles and responsibilities related to the management of AET. This needs assessment could include further consultation with oncology HCPs and engagement in practice observations to understand workflow processes and clinical care pathways that influence and intersect with different transition points in the breast cancer trajectory. The outcome of this needs assessment could be used to identify and make recommendations about potential strategies and initiatives to better support primary care providers (e.g., AET education module, guideline development, enhanced survivorship care plans) and potentially mitigate barriers that impede transitions in breast cancer care. This research could also explore virtual health approaches and technologies that could be leveraged to strengthen the connection between primary and oncology care providers. One of the goals would be to identify areas where communication practices and channels can be improved to facilitate better care delivery and reduce barriers for primary care providers and oncologists.

The results of this dissertation suggest that current models of AET-related care, especially those that rely primarily on oncologists, may need to be reevaluated. Evaluating current models of care delivery, and fostering effective and efficient interprofessional collaborations in care, are particularly salient and timely given the increasing demands on oncology healthcare systems. Recently, Canadian researchers have focused on exploring the most promising coordinated

cancer care models for patients transitioning to community-based providers within a publically-funded system (Grant, De Rossi, & Sussman, 2015; Mittmann et al., 2018; Sussman et al., 2017; Tremblay et al., 2017). For instance, in the Canadian province of Ontario three models of care for breast cancer patients transitioning from oncology-led care to primary care were developed and evaluated to examine the effects on patient experience, health system utilization, and mean costs (Grant et al., 2015; Mittmann et al., 2018). Models of follow-up care included: (1) direct discharge to primary care, (2) transition clinics led by nurses or general practitioners in oncology, and (3) shared care between primary care providers and oncologists. The results of this evaluation suggest that the transition of breast cancer survivors from oncologist-led care to primary care appears feasible and achievable and can result in high levels of patient satisfaction (Grant et al., 2015; Mittmann et al., 2018). Of note, is that most regions implemented a transition model, versus direct discharge to primary care; all regions used survivorship care plans; and all patients were provided specifically developed patient education materials. In terms of health system utilization and health care costs, compared to controls, breast cancer survivors who transitioned to primary care had fewer oncology visits, diagnostic scans, and lower healthcare costs over an average of 25 months of follow-up (Mittmann et al., 2018).

Until we identify the most effective healthcare delivery models to serve the majority of cancer survivors, there are actions we can take to improve the performance of our current system and to better support HCPs in delivering high-quality, patient-centred care. As some HCPs in this study suggested, optimizing oncology nurses' scope of practice with regards to survivorship care might increase support for breast cancer survivors and alleviate the heavy burden AET education and supportive care places on oncologists and primary care providers. Potential ways to increase nursing engagement in AET-related care are discussed in the following section.

### **5.2.2 Nursing Engagement in AET-Related Care**

Some HCPs and breast cancer survivors in this study advocated for further engagement of other HCPs, including registered nurses and nurse practitioners in education initiatives and follow-up care related to AET. Although few nurses were involved in the provision of AET care in this population, some breast cancer survivors named them as a trusted and, sometimes, more accessible resource. A growing body of evidence supports optimizing advanced practice nurses (i.e., nurse practitioners and registered nurses with advanced training and graduate education) to deliver high-quality, sustainable care in a number of contexts, including oncology (Canadian Nurses Association, 2008). Several systematic reviews have demonstrated the care provided by advanced practice nurses results in equivalent or improved care and patient outcomes (DiCenso, Bryant-Lukosius, Carter, & Harbman, 2014; Horrocks, Anderson, & Salisbury, 2002; Martin-Misener et al., 2015; Newhouse, Stanik-Hutt, White, Johantgen, & Bass, 2011). In 2017, an expert panel endorsed Canadian guidelines on recommended models of care for cancer survivorship, which indicated the discharge of breast cancer survivors from specialist-led care to nurse-led care in an institutional setting is a reasonable option for women with no ongoing treatment issues (Sussman et al., 2017). In terms of AET, other researchers have suggested that utilizing nurses in the delivery of AET-related care might provide breast cancer survivors with access to the support they need to remain adherent to AET for the full duration of treatment (Albert et al., 2011; Murphy et al., 2012; Wengstrom, 2008).

The Canadian healthcare system, however, has yet to optimize the expertise of advanced practice nurses in healthcare, particularly in oncology (Bryant-Lukosius et al., 2015). Coupled with increasing cancer incidence and demonstrated gaps in care, this suggests that an opportunity exists to increase engagement of nurses in cancer care by optimizing and expanding existing

nursing roles to improve access, quality of care, and patient outcomes (Bryant-Lukosius et al., 2015). Further investigation is needed, however, to determine how to best engage oncology nurses in practicing to their full-scope of practice with regards to providing AET-related care to breast cancer survivors. Based on the recommendation of some HCPs in this study, an initial starting point might be to evaluate the feasibility and effectiveness of nurse-led patient education and support sessions on AET, which I will discuss in the next section.

### **5.2.3 Patient Education and Risk Communication**

Enhancing patient education is one approach that has shown some effectiveness in increasing medication adherence. A recent systematic review of adherence interventions found that patient education that was personalized and repeated resulted in improved adherence to medications for chronic diseases (Kini & Ho, 2018). In relation to AET adherence, there is beginning evidence to suggest non-adherent women lack information about AET (Cahir, Dombrowski, et al., 2015). Clinical practice guidelines have also suggested that addressing women's beliefs about AET, helping them understand the rationale for treatment, and informing them of the high likelihood of side effects might lead to improved adherence (Burstein et al., 2014). Further supporting the importance of patient education, the research summarized in the integrative review indicated that women who were aware of potential side effects before initiating AET were more likely to be adherent (Lambert, Balneaves, Howard, & Gotay, 2018). Some HCPs interviewed also felt strongly that informing women about the possibility of side effects at the start of treatment better prepared them to manage side effects when they occurred and enhanced their ability to persist with AET. This highlights the important role patient education plays in women's AET experiences and adherence. Future research is, therefore, needed to identify breast cancer survivors' information needs in terms of the type, amount, and

preferred format of AET information and the most effective means of communicating this information (e.g., in person, online, patient handouts, mobile phone applications, visual representations). This evidence might best be ascertained through focus groups with women with breast cancer. Given the relationship between necessity beliefs and adherence, developing patient education initiatives that are comprehensive and target modifiable factors, such as women's beliefs and attitudes about AET, might be one means to enhance adherence.

HCPs in this study believed strongly that comprehensive, upfront AET education should be provided to women at the start of therapy. One specific recommendation was to offer nurse-led, group education sessions to women beginning AET, followed by individual consultations with a nurse. This model of care has reportedly worked well in another Canadian province (Vlahadamis, Danilak, Rawson, King, & Pituskin, 2013). The education sessions would introduce and provide a comprehensive overview of AET to women starting treatment and enable group facilitators (e.g., nurses) to address women's questions and concerns that often arise in the early phases of treatment. Preliminary research suggests group medical appointments, facilitated in part by a nurse practitioner, in which breast cancer survivors learn about AET options are a feasible and acceptable alternative to individual physician appointments (Trotter & Schneider, 2012; Vlahadamis et al., 2013). Furthermore, meta-analyses in other chronic disease populations (e.g., diabetes) suggest group medical visits can have a positive effect on clinical and patient-reported outcomes (Housden, Wong, & Dawes, 2013). There is also some suggestion that group medical visits have the potential to result in increased health system efficiencies, timely access to care, and decreased healthcare costs (Trento et al., 2005; Vlahadamis et al., 2013). A study to develop and pilot test group education sessions and consultations with a nurse thus

might be one strategy to evaluate the effectiveness of this approach in providing high-quality, efficient and cost-effective AET-related education and supportive care.

The findings from this dissertation highlighted how perceived risk of recurrence impacted women's AET persistence, including how a reduction in perceived risk over time influenced some women's decisions to discontinue AET prematurely. Some HCPs also described feeling challenged to support women in remaining adherent to AET after the acute diagnosis and treatment period was over and the immediate threat of breast cancer had passed. Thus, HCPs should discuss possible shifts in risk perception that individuals may face over the course of AET. It may be worthwhile to evaluate if additional education sessions, offered at key points throughout the AET trajectory (e.g., before the end of the first year when many women discontinue AET (Aiello Bowles et al., 2012; Hershman et al., 2016; Huiart et al., 2012; Kidwell et al., 2014)), would be effective to reinforce the importance of adherence. This might also provide an opportunity to reiterate the benefits of AET and the importance of full adherence to prevent a recurrence of breast cancer.

In terms of risk communication, best practice guidelines emphasize the importance of helping women to weigh the risks of treatment against the absolute benefits of therapy on an individualized basis (Burstein et al., 2019). This recommendation has implications for how treatment discussions are framed considering that HCPs in this study described using both absolute and relative statistics in AET consults. Some HCPs expressed concern that women might over-estimate the benefits of AET when presented with relative numbers. Instead, they found absolute terms helped women understand the benefit of AET for them personally and make an informed decision about AET. Furthermore, the apparent incongruence of women's

understanding of their actual and perceived risk in this study suggests that current methods used to communicate the benefits and risks of AET may need to be refined.

Accurate understanding of risk is particularly salient given the impact of perceived risk on women's beliefs about the necessity of AET, and in turn, the connection between positive necessity beliefs and AET adherence (Arriola et al., 2014; Bright et al., 2016; Grunfeld et al., 2005; Hershman et al., 2016; Stanton et al., 2014). There is some evidence to suggest that simplified, visual representations of benefits and risks may improve breast cancer survivors' comprehension of statistical information (Zikmund-Fisher, Fagerlin, & Ubel, 2008). Similarly, some HCPs in this study reported that visual representations of AET benefits and risks would help them better communicate these concepts to women. Further research is needed to establish how to most effectively communicate the benefits and risks of AET to breast cancer survivors, and to determine if visual representation tools might aid in AET treatment discussions.

Qualitative research could be used to explore patient and HCP preferences for this type of information. These results could then inform future intervention research; for instance using a pretest-posttest design to evaluate the effect of different risk communication strategies.

Outcomes of interest might include comprehension of risk statistics, the correspondence between women's perceived and actual risk, and the relationship between perceived risk and beliefs about the necessity of AET.

#### **5.2.4 Frequency of Follow-Up Communication**

Effective HCP communication is positively correlated with greater patient adherence to medical treatment, with meta-analysis results indicating poor physician communication is associated with a 19% higher likelihood of nonadherence (Zolnierrek & DiMatteo, 2009). The integrative review in Chapter 2 found that patient-centred (Liu et al., 2013) and frequent (Arriola

et al., 2014) patient-physician, communication, which included a discussion of side effects (Arriola et al., 2014; Kahn et al., 2007), was positively correlated with AET adherence. In addition, the findings of the interpretive description studies in Chapters 3 and 4 illustrated the positive influence communication and personal connection with a knowledgeable HCP had on women's AET adherence. As the HCPs in this study and others have suggested, more frequent communication with breast cancer survivors about their experiences and views related to AET may help shape patient beliefs, reinforce the importance of therapy, and improve AET adherence (Arriola et al., 2014; Cahir, Dombrowski, et al., 2015).

Although increasing the frequency of communication between patients and HCPs is not an easy task to accomplish in the fiscally and resource constrained Canadian healthcare system, improvements can be made to better meet the needs of breast cancer survivors. These findings suggest that additional points of contact with patients, perhaps by telephone, for early identification and management of symptoms and to address concerns that arise during the first few weeks of treatment might help women manage through this transition period and continue with AET. Additional communication in the early phases of AET may be particularly important for women receiving follow-up care in the community who find it challenging to access timely advice about their AET-related concerns. In the absence of an established system for monitoring adherence in BC, follow-up telephone calls might be an effective method for HCPs to assess AET adherence and monitor women's symptoms before side effects become intolerable. As others have argued, the most important adherence intervention might be to engage patients in ongoing care because patients who disconnect from the healthcare system are unlikely to receive, and thus not adhere to, medication (Nieuwlaat et al., 2014).

As others have also pointed out, further research is needed to evaluate the relationship between HCP communication, psychosocial factors (e.g., necessity beliefs, understanding of risk, patient satisfaction with HCP communication), and adherence (Arriola et al., 2014). Future prospective research, such as larger cohort studies, could include evaluation of the effects of HCP communication (e.g., frequency, type, quality) on AET adherence, and examine the potential interactions among communication and psychosocial and clinical factors. As stated above, a primary reason for increasing communication is to provide additional opportunities to assess for, and address AET-related side effects; however, this study revealed several challenges related to symptom management.

### **5.2.5 Symptom Management**

AET-related side effects are significantly negatively associated with non-adherence (Cahir, Guinan, et al., 2015; Gotay & Dunn, 2011; Lambert, Balneaves, Howard, & Gotay, 2018; Murphy et al., 2012), and for many women, poorly managed symptoms had a profound affect on their QOL (Brauer et al., 2016; Harrow et al., 2014; Lambert, Balneaves, Howard, Chia, et al., 2018; Moon, Moss-Morris, Hunter, Carlisle, et al., 2017; Wells et al., 2016; Wickersham et al., 2012). To support adherence, HCPs need to acknowledge the severity of women's symptoms, and assess for, and address side effects in all consultations. Recent research suggests that effective patient-provider communication about AET symptom management is associated with a HCP's ability to manage women's uncertainty, respond to their emotions, and exchange information (Farias et al., 2017; Turner et al., 2017). Yet, symptom management remains an ongoing challenge for HCPs due to a lack of effective treatments and the multi-factorial or unknown etiology of many symptoms that women attribute to AET.

In 2008, Cella and Fallowfield published evidence-based recommendations on pharmacological and non-pharmacological options for managing AET-related side effects. An update of this review is warranted to identify the most current and effective treatments for alleviating AET-related side effects and to translate these findings into symptom management guidelines. It would also be worthwhile to conduct an environmental scan of existing breast cancer and general cancer symptom management guidelines (e.g., pain) to determine if existing guidelines cover the full range of AET symptoms.

Another challenge with AET-related symptom management is there may not be effective interventions available for some side effects. If not, women may need self-management strategies that have shown effectiveness in reducing symptoms in other cancer and chronic illness populations (McCorkle et al., 2011). For instance, mindfulness-based stress reduction has demonstrated some benefit in improving broad-based, cancer-related symptoms (Lengacher et al., 2016). Yoga is another approach that has demonstrated effectiveness in reducing pain, muscle aches, and general physical discomfort among breast cancer survivors taking AET (Peppone et al., 2015). These are two promising lines of inquiry requiring further research that might help breast cancer survivors cope with AET-related symptoms, particularly those that are difficult to treat, such as general discomfort and fatigue.

To address the lack of treatment options for AET-related side effects, experimental studies are needed to evaluate new interventions to address problematic symptoms for which there are no effective management options. Investigation into non-pharmacological strategies, in particular, will be important given women's apprehension to take additional medication to treat side effects. In addition, future research should use innovative data collection techniques to collect 'real time' assessments of symptoms rather than retrospective reporting. This may be

possible through the use of a mobile phone application, or in healthcare settings that collect patient-reported outcomes through web-based portals linked to electronic medical records. Identifying effective treatments to alleviate women's symptoms and thus improve their QOL may be an effective method for improving AET adherence.

### **5.2.6 Overarching Research Considerations**

The integrative review in Chapter 2 described how most research on AET adherence has failed to distinguish between tamoxifen and AIs. Meta-analyses results indicate, however, non-persistence is significantly higher for women taking tamoxifen versus an AI (Huiart, Ferdynus, & Giorgi, 2013). As such, future research is needed to determine if factors associated with non-adherence differ across these two classes of AET. Similarly, the results of the integrative review highlighted that the concepts of non-persistence and non-adherence are often conflated in the literature. An aim of future research should be to examine adherence-related concepts (e.g., adherence, persistence, initiation) in isolation to distinguish if influencing factors are unique to each of these classifications. Non-adherence (e.g., forgetting, skipping doses) and non-persistence (e.g., stopping treatment early) are two distinct concepts that might require different intervention strategies. Furthermore, most research on AET adherence is based on five years of AET, and future research is needed to investigate if influencing factors remain significant in the context of extended AET. The integrative review also identified additional factors from qualitative literature that might play an important role in women's AET adherence (e.g., misconceptions about the hormonal nature of AET, body image), which warrant assessment in larger quantitative studies.

### **5.2.7 Emerging Areas of Research**

An interesting finding from this dissertation was the unexpected critique from a few HCPs who questioned the current blanket approach to prescribing AET for a minimum of five years to all women. Questions were raised about the potential of personalized medicine to identify women who do not need AET or are eligible for shorter durations to achieve optimal efficacy. The recently funded LA LEAST study (Lohrisch et al., 2017), which is examining whether biomarkers can be used to identify women at low risk who may qualify for shorter AET durations with minimal negative impact on survival, is an important step towards such personalized treatment decisions. The findings may allow oncologists to tailor AET decisions to each woman's risk profile and limit the negative impact on QOL while optimizing the protective effects of AET.

There is growing interest in the development and evaluation of interventions to target adherence, as well as women's coping skills related to side effects. New interventions that hold potential for enhancing AET adherence include a recent clinical trial designed to evaluate a cognitive behavioural training program to optimize breast cancer survivors' expectations about AET to improve their coping ability and QOL (von Blanckenburg, Schuricht, Albert, Rief, & Nestoriuc, 2013). Pilot testing is also currently underway to evaluate a brief telephone intervention using motivational interviewing that will help women explore their beliefs and attitudes about AET and motivate them to continue with treatment (Jones, 2018). A study protocol was also recently published that will develop and pilot test the efficacy of an intervention that combines an interactive smartphone application with personal support from a patient navigator to improve women's AET adherence (Chalela et al., 2018).

The results of a recent meta-analysis on the use of mobile text messages to improve medication adherence has demonstrated efficacy in improving adherence in chronic disease populations (Thakkar et al., 2016). In the context of AET, the results of a long-term randomized clinical trial evaluating the impact of text messaging aimed at reducing premature discontinuation of AIs, in 696 women diagnosed with breast cancer, were recently published (Hershman et al., 2019). Patients were randomly assigned to receive either bi-weekly text reminders about AET adherence or no text messaging for 36 months. This trial, however, found no difference in early discontinuation between the two groups, suggesting interventions to improve adherence will likely take more than a one-dimensional approach to address the multifactorial nature of AET non-adherence. The use of technology (e.g., text messages, smart phone applications) to deliver AET education, support, and adherence intervention strategies is an area requiring further research to evaluate the effectiveness of technology to potentially improve support for women taking AET and, possibly, adherence.

### **5.3 Knowledge Translation, Transfer and Exchange**

Dissemination of my research findings has been targeted to diverse audiences, including HCPs, researchers, and survivors. To date, a number of knowledge translation, transfer, and exchange activities have occurred. I have delivered several presentations at local and national conferences, including the Canadian Association of Psychosocial Oncology and the Canadian Association of Nurses in Oncology annual conferences. Most recently, I was invited to present at the Canadian Cancer Survivorship Research Consortium research rounds. This venue allowed me to present the results of my dissertation to a national, multidisciplinary audience of clinicians and researchers who work in cancer survivorship and represent a wide range of expertise in

epidemiology, psychology, sociology, economics, social work, nursing, oncology, and family practice.

With regards to publications, the integrative review of the patient-reported factors associated with AET non-adherence (Chapter 2) was published in a leading breast cancer journal, *Breast Cancer Research and Treatment*. This journal is targeted to oncology healthcare providers, including surgeons, medical and radiation oncologists, and endocrinologists and publishes articles that offer new perspectives on critical issues related to breast cancer. The article entitled, “Understanding AET persistence in breast cancer survivors” (Chapter 3), was published in the open access journal *BMC Cancer*. Choosing an open access publication was critical to making the results of this study available to a wide audience, including oncology and primary care providers, breast cancer survivors, their support networks, patient advocacy groups, and other researchers. These articles have also been shared and circulated to interdisciplinary groups at BC Cancer, where the research took place. Future dissemination activities will include presentations to breast cancer survivor groups and psychosocial, medical, and nursing rounds at BC Cancer and future national and international conferences. Finally, I plan to use these results to inform the development of a post-doctoral program of research that will develop, implement, and evaluate recommendations made in this dissertation. Specially, I have been awarded a Canadian Institutes of Health Research Health System Impact Post-Doctoral Fellowship in which I will interpret and address barriers impeding effective care transitions for women diagnosed with breast cancer in BC.

## **5.4 Limitations**

I outlined the limitations of each phase of this dissertation in the respective findings chapters. In this section, I discuss the overarching limitations of this research. Foremost, the self-

selection of participants who were either receiving or providing care related to AET in a single Canadian province has its limitations. As with all qualitative research, generalizations are understood to be tenuous and caution should thus be used when determining the relevance of findings to other jurisdictions given the small sample size and sample composition of the two interpretive description studies (Chapters 3 and 4). While these research results offer a preliminary understanding of breast cancer survivors' and HCPs' experiences and perspectives related to AET adherence, the generalizability of the findings to other geographical and practice contexts with differing models of breast cancer care is limited.

Resource constraints limited the scope of my study. For instance, the research budget did not allow for translation services to accommodate inclusion of non-English speaking participants who might have different experiences and perspectives related to AET, and unique communication challenges compared to English-speaking participants. As a result, this research excludes a large sub-sector of the cancer population in BC who speak Cantonese and/or Mandarin. The results also do not account for socio-cultural values, beliefs, and practices of sub-populations prevalent in BC, including Indigenous, Chinese, and South Asian breast cancer survivors that might influence AET-related care and adherence. Furthermore, while efforts were made to recruit women from diverse socio-economic backgrounds (e.g., random sampling methods), the voices of breast cancer survivors from underserved groups (e.g., lower socio-economic status) were missing from the findings. Consequently, the experiences and perspectives of women from underserved groups and the challenges they face in adhering to AET and accessing healthcare services are underrepresented.

Despite using purposeful sampling methods, and several follow-up strategies, recruitment of non-adherent and non-persistent women was very difficult. As a result, the sample of breast

cancer survivors did not represent the 40% non-adherence rate previously reported in this population (Chan et al., 2009). The high rate of non-adherence has been well documented in the literature; however, the women who participated in this study did not report experiencing issues with non-adherence, only persistence. Therefore, results from my interviews with breast cancer survivors do not account for the views of women who persist, but are non-adherent to AET. Furthermore, the results do not proportionately account for the experiences of women who do not experience side effects or difficulty adhering to AET. It will be useful to understand more about the facilitators of AET adherence from the perspective of these women.

Recruitment of HCPs to this study was difficult. Targeted efforts to recruit family physicians were unsuccessful and the absence of their perspectives represents a gap in our understanding of the challenges they face in primary care related to AET and adherence. It will be important to gain the perspectives of family physicians, who play a major role in the Canadian healthcare system in managing patients' general health problems, particularly when developing strategies for improving AET-related care and adherence in the community. Furthermore, only a small number of HCPs from each discipline participated in the study, which resulted in representation from only one registered nurse, pharmacist, and general practitioner in oncology. Perhaps the lack of interest in study participation may be a result of their limited engagement in AET care in BC.

Other overarching limitations include the lack of differentiation between AET agents throughout the findings that may warrant further investigation to determine if influencing factors and adherence differ between the type of AET agent prescribed. The results of this study also did not differentiate between the concepts of adherence and persistence, except in Chapter 3. It would be worthwhile for future research to investigate if variations exist among influencing

factors that affect AET adherence versus persistence. Lastly, the study design and resource and time constraints did not permit me to take preliminary conceptualizations back to study participants for confirmation before finalizing results.

## **5.5 Conclusion**

AET non-adherence is a significant clinical issue among breast cancer survivors that places women at an increased risk of recurrence and mortality. The findings from this dissertation provide unique insights into the AET-related challenges experienced by both breast cancer survivors and HCPs, including issues that exist in the healthcare system in one Canadian jurisdiction as to how AET-related care is provided. To ensure breast cancer survivors are able to maximize the potential benefit of AET, while still having a reasonable QOL, these challenges require attention. Novel ways of addressing current gaps in the healthcare system will need to be developed to optimize survivorship care, AET adherence, and also empower and enable HCPs across care settings to deliver optimal AET-related care that is responsive and patient-centred. Increasing adherence to AET in breast cancer has the potential to significantly impact individual patient outcomes by reducing the risk of breast cancer recurrence and mortality. As well, there exist clear societal implications of suboptimal adherence to AET in breast cancer populations related to recurrence and increasing the burden placed on an already over-stretched healthcare system. The goal is to meet the supportive care needs of breast cancer patients prescribed AET, including being able to offer women adequate strategies to reduce symptom burden and improve their QOL, and ultimately optimizing AET adherence and overall health outcomes.

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# Appendices

## Appendix A Breast Cancer Survivors

### A.1 Consent Form: Breast Cancer Survivors



a place of mind  
THE UNIVERSITY OF BRITISH COLUMBIA



**BC Cancer Agency**  
CARE & RESEARCH  
An agency of the Provincial Health Services Authority

**The University of British Columbia**  
School of Nursing  
Vancouver Campus  
XXX

Phone XXX  
Fax XXX  
[www.nursing.ubc.ca](http://www.nursing.ubc.ca)

### CONSENT FORM – Participants: Phase 1

**Study Title:** Understanding Adherence to Adjuvant Endocrine Therapy in Breast Cancer Survivors

**Principal Investigator:**

XXX

**Co-Investigators (alphabetical order):**

XXX

**Purpose:**

The purpose of this study is to explore women's experiences and perspectives related to endocrine therapy (aka hormone or hormonal therapy, such as tamoxifen and aromatase inhibitors). The specific aim of this study is to identify the factors associated with women's decisions to keep using or stop endocrine therapy early, with the aim of identifying strategies that may support women who are struggling to adhere to endocrine therapy. You are being asked to take part in this research study being conducted by XXX for a dissertation under the supervision of XXX at the UBC School of Nursing

**Study Procedures:**

If you choose to take part in this study, you will be asked to participate in one 60-minute interview at a place of convenience or by telephone, whichever is more convenient for you. The interview will be digitally recorded. You will be asked about your experience in being prescribed and/or taking endocrine therapy, what information you received, what difficulties related to endocrine therapy you may have experienced, your current knowledge about endocrine therapy (i.e., benefits and risks), and the support and resources you have used, would have liked, or require in supporting you in taking endocrine therapy. You will receive a \$15 honorarium to acknowledge your participation in the study and cover any related costs (i.e., parking, child care). You will also be asked to complete a demographic form and a survey to assess your

endocrine therapy use, perceived risk of breast cancer and severity of your symptoms that will take approximately 10 minutes to complete.

In the future we will be conducting a second follow-up phase to this study where participants will be sent a series of three short surveys to help us identify the best support strategies women taking endocrine therapy require. You do not need to participate in this phase; however, if you choose to participate in the second phase you will be provided a separate consent form for this part of the study.

You have a choice of not answering any questions or withdrawing at any time from the study. If changes are made to the study or new information becomes available, you will be informed.

**Risks and Potential Benefits:**

By taking part in this study, you will be sharing your experience of endocrine treatment and helping to identify the factors that are important to women who have been prescribed endocrine therapy for breast cancer. Your feedback will be used to inform the type of support available to women taking endocrine therapy. We anticipate there will be minimal risks associated with participating in the interview component of the study; however, some women may experience distress as a consequence of reflecting on their cancer experience.

**Confidentiality:**

We will keep your name and information you provide strictly confidential and it will not be shared with your health care provider(s). We will not use your name in research reports, and all data that is reported will be grouped data that will not identify you. You will be given a numerical identification number, which will be used to identify you in the database. The file linking your name, contact information, and identification number will be stored in a separate, password protected computer file. Any hard copies of study information will be stored in a locked file cabinet and the computer files will be password protected and stored on a secured network server at BC Cancer and at UBC after July 2013. Only the research staff directly involved in the data collection and analysis will have access to the information.

**Consent:**

Your participation in this study is entirely voluntary and you may withdraw from the study at any time by contacting the research team. Your choice on whether to participate in this study will NOT affect any care you may receive from BC Cancer or your family physician, or any invitations to participate in any future research projects at BC Cancer. Your signature indicates that you consent to participate in this study. Please keep a copy of this consent form for your records. If you have any questions or require information with respect to this study, you may contact XXX at XXX or by e-mail at XXX, or XXX, XXX's supervisor, at XXX or by email at XXX. If you have any concerns about your treatment or rights as a research subject, you may contact the Research Subject Information Line at the UBC Office of Research Services at XXX.

*I have read the above information and I have had a chance to ask any questions about the study and my involvement. I understand what I have to do and what will happen if I take part in the study. I freely choose to take part in this study and I have a copy of the consent form.*

\_\_\_\_\_  
Please Print Name

\_\_\_\_\_  
Signature of Participant

\_\_\_\_\_  
Signature of Witness

\_\_\_\_\_  
Date

-----  
Would you be willing to be contacted in the future for other studies related to breast cancer and endocrine therapy?

☐ Yes, I would like to receive information about future studies.

☐ No, I would not like to receive information about future studies.

\_\_\_\_\_  
Signature of Participant

\_\_\_\_\_  
Date

## **A.2 Interview Guide: Breast Cancer Survivors**

### **PARTICIPANT INTERVIEW GUIDE - Breast Cancer Survivors**

#### **Welcome and Introduction (5 minutes)**

- General introduction
- Review how we will spend the 60 minutes together
  - Discussion topics, 5 -10 min break if necessary, recording device, point out location of washrooms if conducting an in-person interview
- Confidentiality issues - name and information you provide related to the interview will be kept strictly confidential
- Ask if she has any questions before beginning

#### **Guiding Questions:**

1. What has it been like for you to take adjuvant endocrine therapy (AET) (aka hormone therapy)?
  - a. What has been easy?
  - b. What has been difficult?
  - c. Are you dealing with any side effects from therapy? If so, could you say a bit more about that experience?
  - d. Have you switched AET? (e.g., switching from tamoxifen to an AI) – Why? What was that like?
  - e. What has motivated you to take AET?
2. What were you told about AET?
  - a. What type of information were you given about AET (probe: studies, stories, etc.)
  - b. Was this enough information? Too much? What was missing?
  - c. Did you understand this information? If not, what are you uncertain about?
3. In your own words, can you tell me your understanding of how AET works?
4. What do you think are the pros and cons (benefits and risks) of taking AET?
5. How have you been followed up since taking AET?
6. What support have you received from your health care providers in taking AET?
7. Who has helped you make treatment decisions about AET?
  - a. Probe health professional, family, friends etc.
8. What is your current thinking about your decision to take AET?

- a. Probe thoughts about quitting or continuing.
- 9. *If applicable* - Why did you decide to stop taking AET, switch AET or alter the dose of your AET?
  - a. Did you consult with anyone in making the decision to stop/change/alter the dose of your AET?
  - b. What would make you change your mind and decide to start taking AET again?
- 10. What has or would have been helpful in supporting you to continue with AET?
  - a. If needed probe additional information, better communication with HCP, more information, educational resources, symptom management, reminders.
- 11. What strategies do you feel would be most helpful in supporting women in taking AET?
  - a. What would these look like?
- 12. What messages do you think would be particularly powerful for women that have stopped early?
- 13. How does your decision (to continue or stop) AET fit with your other treatment and health care decisions?
- 14. There is beginning evidence on extending AET to 10 years, what are your thoughts about continuing for 5 more years?
  - a. What kinds of things would you have to factor into that decision?
- 15. Is there anything else related to making a decision about AET you would like to share with me before we wrap up?

### A.3 Demographic Form: Breast Cancer Survivors

ID #: \_\_\_\_\_



#### DEMOGRAPHIC FORM (Participant)

*This form asks you some questions about yourself. This information will be helpful in understanding your experience of taking endocrine therapy (aka 'hormonal treatment' e.g., tamoxifen or aromatase inhibitors).*

1. What is your birth date (dd/mm/yyyy)? \_\_\_\_/\_\_\_\_/\_\_\_\_
2. What is your marital status?
  - ☐ Single
  - ☐ Married
  - ☐ Common-law
  - ☐ Divorced
  - ☐ Widowed
3. What is the highest level of education that you have achieved?
  - ☐ Less than high school
  - ☐ High school diploma
  - ☐ Some college/trade school
  - ☐ College/trade school diploma
  - ☐ Some university
  - ☐ Bachelor's degree
  - ☐ Graduate degree
4. Please indicate your employment status:
  - ☐ Employed, full-time
  - ☐ Employed, part-time
  - ☐ Self-employed
  - ☐ Student
  - ☐ Retired
  - ☐ Unemployed
  - ☐ Other (please specify) \_\_\_\_\_
5. What is your ethnic origin?
  - ☐ First Nations
  - ☐ Inuit
  - ☐ Métis
  - ☐ White (Western European, Eastern European, etc.)
  - ☐ Black (African, Caribbean, etc.)
  - ☐ East Asian (Chinese, Japanese, Korean, etc.)

- ☐ Southeast Asian (Vietnamese, Indonesian, Filipino, etc.)
- ☐ South Asian (East Indian, Pakistani, Sri Lankan, etc.)
- ☐ Latin American (Mexican, Chilean, Guatemalan, etc.)
- ☐ West Asian (Lebanese, Iranian, Egyptian, etc.)
- ☐ Other (please specify) \_\_\_\_\_

6. Because of the cost associated with breast cancer, income can be an important factor in making treatment decisions. What is your total household income before taxes (if unsure make your best guess)?

- ☐ Less than \$10,000
- ☐ \$10,000 to \$29,999
- ☐ \$30,000 to \$49,999
- ☐ \$50,000 to \$69,999
- ☐ \$70,000 to \$99,999
- ☐ \$100,000 or more

7. When were you diagnosed with breast cancer (mm/yyyy)? \_\_\_\_/\_\_\_\_

8. What is the estrogen receptor status of the breast cancer you have been diagnosed with?

- ☐ Estrogen receptor positive (ER+ve)
- ☐ Estrogen receptor negative (ER-ve)
- ☐ Uncertain

9. What is the progesterone receptor status of the breast cancer you have been diagnosed with?

- ☐ Progesterone receptor positive (PR+ve)
- ☐ Progesterone receptor negative (PR-ve)
- ☐ Uncertain

10. What endocrine (aka hormonal or hormone) treatments have you received for breast cancer? Please check all that apply

- ☐ Tamoxifen
- ☐ Aromatase inhibitors: (please specify): \_\_\_\_\_
- ☐ Other (please specify): \_\_\_\_\_

11. Are you still currently taking endocrine therapy?

- ☐ Yes
- ☐ No

12. Have you switched endocrine treatments since your diagnosis? If so, when and what treatment did you begin taking after switching?

- ☐ Yes
 

When switched (mm/yyyy)? \_\_\_\_/\_\_\_\_

New treatment that I switched to \_\_\_\_\_ (name of medication)
- ☐ No
- ☐ Uncertain

13. What health care provider(s) have you spoken with about endocrine therapy? Please check all that apply.

- ☐ Medical Oncologist
- ☐ Radiation Oncologist
- ☐ Surgical Oncologist
- ☐ General Practitioner (i.e., Family Doctor)
- ☐ General Practitioner in Oncology (GPO)
- ☐ Registered Nurse
- ☐ Pharmacist
- ☐ Other (please specify):  
\_\_\_\_\_

14. What treatments have you received for breast cancer? Please check all that apply.

- ☐ Surgery (i.e., lumpectomy, mastectomy)
- ☐ Chemotherapy
- ☐ Radiation
- ☐ Other (please specify): \_\_\_\_\_

15. When did you finish treatment (surgery, chemotherapy, radiation (*not including hormone therapy*) for your breast cancer? (mm/yyyy) \_\_\_\_/\_\_\_\_

16. Have you been diagnosed with any other types of cancer?

- ☐ Yes (please specify type of cancer): \_\_\_\_\_
- ☐ No
- ☐ Under investigation

#### A.4 Perceived Risk Question: Breast Cancer Survivors



#### PERCEIVED RISK QUESTION

**What do you think the chances are that you will have breast cancer again someday?** By again I mean either developing a new breast cancer tumor in your previously unaffected breast or suffering a recurrence of your prior cancer.

Please answer using a percentage scale where 100 means you will definitely get cancer again, and 0 means there is no chance you will get it again. **Answer:** \_\_\_\_\_ %

## **A.5 Standard Script: Breast Cancer Survivors**

### **STANDARD SCRIPT: ADDRESSING AET NON-ADHERENCE**

Thank you very much in sharing your experiences and thoughts with us about the use of hormonal therapy (e.g. Tamoxifen and aromatase inhibitors) following breast cancer treatment. Given the data supporting the long-term use of hormonal therapy for at least 5 years for the prevention of breast cancer recurrence, we would encourage you to consider discussing any decisions you have made or difficulties you have experienced related to your hormonal therapy with your health care provider. Decisions about treatments can be difficult and it is important you are fully informed and have had a chance to think about what is important to you. Talking with your health care provider about any decisions you have made or are thinking about making regarding continuing and/or stopping hormonal therapy may be helpful in your decision-making process.

## Appendix B Healthcare Providers

### B.1 Consent Form: Healthcare Providers



a place of mind  
THE UNIVERSITY OF BRITISH COLUMBIA



**BC Cancer Agency**  
CARE & RESEARCH  
An agency of the Provincial Health Services Authority

**The University of British Columbia**  
School of Nursing  
Vancouver Campus  
XXX

Phone XXX  
Fax XXX  
[www.nursing.ubc.ca](http://www.nursing.ubc.ca)

### CONSENT FORM – Phase 1

**Title of Study:** Understanding Adherence to Adjuvant Endocrine Therapy in Breast Cancer

Survivors

**Principal Investigator:**

XXX

**Co-Investigators (alphabetical order):**

XXX

#### Purpose

The purpose of Phase 1 of this study is two-fold: (1) to explore why breast cancer survivors' have suboptimal levels of adherence to prescribed adjuvant endocrine therapy (AET) and (2) to explore health care providers' and patient-advocacy representatives' experiences supporting breast cancer survivors undergoing AET. You are being asked to take part in this research study being conducted by Ms. Leah Lambert for a dissertation under the supervision of Dr. Lynda Balneaves at the UBC School of Nursing.

#### Study Procedures

You will be asked to take part in a brief 30-minute interview at a place of convenience in which we will ask you questions about your experience of talking to breast cancer survivors about endocrine therapies following breast cancer treatment. You will also be asked to complete a brief demographic form. The interview will be digitally recorded and transcribed verbatim.

In future we will be conducting a second phase of this study where participants will be sent a series of three short surveys as part of a Delphi process to help us identify and prioritize the best support strategies women taking endocrine therapy require to keep using these treatments. You do not need to participate in this second phase, however, if you choose to participate in the second phase you will be provided consent for this part of the study.

#### Risks and Potential Benefits

There are no direct risks or benefits from participating in this study. Potential long-term benefits from the study include providing valuable information about treatment discussions with breast cancer patients about their experiences in using AET, and the support needs of women struggling to adhere to treatment. This information will be used to identify strategies for optimizing breast cancer survivors' adherence to AET that will be later validated and prioritized through a series of surveys.

### **Confidentiality**

We will keep your name and information you provide strictly confidential. We will not use your name in the research reports and we will use pseudonyms and codes instead of your name or other personal information in our notes and typed copies of the interview transcripts. You will be given a numerical identification number, which will be used to identify you on the demographic form and in the database. The file linking your name, contact information, and identification number will be stored in a separate, password protected computer file. Any hard copies of study information will be stored in a locked file cabinet and the computer files will be password protected and stored on a secured network server at UBC. Only the research staff directly involved in the data collection and analysis will have access to the information.

### **Consent:**

Your participation in this study is entirely voluntary and you may withdraw from the study at any time by contacting the research team. Your signature indicates that you consent to participate in this study. Please keep a copy of this consent form for your records. If you have any questions or require information with respect to this study, you may contact **XXX** at **XXX** or by e-mail at **XXX**, or **XXX**, **XXX**'s supervisor, by email at **XXX**. If you have any concerns about your treatment or rights as a research subject, you may contact the Research Subject Information Line at the UBC Office of Research Services at **XXX**.

*I have read the above information and I have had a chance to ask any questions about the study and my involvement. I understand what I have to do and what will happen if I take part in the study. I freely choose to take part in this study and I have a copy of the consent form.*

\_\_\_\_\_  
Please Print Name

\_\_\_\_\_  
Signature of Participant

\_\_\_\_\_  
Signature of Witness

\_\_\_\_\_  
Date

Would you be willing to be contacted in the future for other studies related to endocrine therapy?

- ☐ Yes, I would like to receive information about future studies
- ☐ No, I would not like to receive information about future studies

\_\_\_\_\_  
Signature of participant

\_\_\_\_\_  
Date

## **B.2 Interview Guide: Healthcare Providers**

### **INTERVIEW GUIDE**

#### **Healthcare Providers and Patient-Advocacy Representatives**

##### **Welcome and Introduction:**

Thank you for agreeing to take part in an interview about the treatment decision-making process and experience of women who have been prescribed adjuvant endocrine therapy in breast cancer.

All the information we collect in the interview will be kept confidential and any identifying information will be removed. It should not take more than 30 minutes and will be digitally recorded. Do you have any questions before we begin?

##### **Guiding Questions:**

1. How are you involved/support in breast cancer survivors' decisions about AET?
2. How do you communicate the benefits and risks of AET to women? Could you give an example of a recent conversation you may have had with a woman about AET?
3. Who else, besides yourself and the breast cancer survivor, is usually involved in AET decisions?
4. From your experience, what difficulties do women face in taking AET?
5. How do you discuss the potential side effects of AET with women?
  - a. What do you tell them?
  - b. How do women usually manage these side effects?
6. In your experience, how is breast cancer survivors' adherence to AET monitored?
  - a. What health professional does the monitoring?
  - b. How is adherence monitored?
  - c. How could follow-up care related to AET be changed to enhance women's adherence to AET?
7. What do you think influences women in adhering to AET?
8. What do you believe would help breast cancer survivors in adhering to AET?
9. What would be helpful to support you in discussing AET with breast cancer survivors?
10. Given the recent expanded guidelines recommending breast cancer survivors use AET for 10 years, what changes have you seen in your practice/support around women's use of AET for an additional 5 years?

11. What is your current practice around extended therapy? (HCPs only)
  - a. How are you implementing the guideline, are you re-contacting patients or is it only being offered to patients going forward?
  - b. Are previous patients being 'grandfathered'?
12. When and how are you framing treatment discussions about extended therapy with patients? (e.g., what are you saying to convince women of the importance of extended therapy?) (HCPs only)
13. What are the responses and reactions you are seeing from patients about the expanded AET guidelines?
14. Do you think there needs to be different support for patients now that AET is being prescribed for 10 years? (e.g., symptoms management, more frequent follow-up care, greater adherence monitoring?)
15. Since the guidelines have expanded, have you seen any changes in healthcare programming or services to support breast cancer survivors over the recommended 10 years of therapy?

Is there anything else related to AET you would like to share with me before we wrap up?

### B.3 Demographic Form: Healthcare Providers

ID #: \_\_\_\_\_



#### DEMOGRAPHIC FORM (Healthcare Provider)

*Please complete the following questions that will give us some background information about you.*

1. Please indicate what type of health care provider you are.

- ☐ Medical Oncologist
- ☐ Radiation Oncologist
- ☐ Surgical Oncologist
- ☐ General Practitioner
- ☐ General Practitioner in Oncology (GPO)
- ☐ Registered Nurse
- ☐ Pharmacist
- ☐ Other (please specify): \_\_\_\_\_

2. Main type of work or practice. Please check all that apply.

- ☐ Clinical Practice
- ☐ Research
- ☐ Education
- ☐ Professional Practice
- ☐ Administration
- ☐ Other (please specify): \_\_\_\_\_

3. Place of employment:

- ☐ Vancouver Centre - BC Cancer
- ☐ Fraser Valley Cancer Centre - BC Cancer
- ☐ Private practice in community
- ☐ Other (please specify): \_\_\_\_\_

4. Total number of years worked as a health professional: \_\_\_\_\_(years)

5. Total number of years worked as a health professional in oncology: \_\_\_\_\_(years)

6. Type of work (please check one):

☐

Full-time

☐

Casual

☐

Part-time

☐

Other (please specify): \_\_\_\_\_