

# Living with Advanced Breast Cancer

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Survivors of advanced breast cancer (ABC), also known as metavivors, are often left with fewer treatment options in the landscape of a cure culture. Metavivors have unique psychosocial and physical needs distinct from patients with early-stage breast cancer.

metastatic breast cancer

side effects

metavivorship

breast neoplasms

## 1. Introduction

Breast cancer is the most common type of cancer in women, with a lifetime incidence of 12.9%. Additionally, it affects a small percentage of men. There were an estimated 281,550 new cases diagnosed in 2021 [1]. Of these patients, 6% will be diagnosed with de novo or recurrent advanced breast cancer (ABC). Historically, this group has faced a 5-year survival of just 29% [2]. Furthermore, 30% of those diagnosed with early-stage breast cancer will develop metastatic disease [3]. The short life expectancy for patients diagnosed with ABC has led to their exclusion from survivorship services frequently offered to patients with early-stage, localized breast cancer [4]. ABC survivors are left with fewer options in the landscape of a cure culture where treatment options aimed at eradicating disease are the main focus of treatment, research and funding. However, those living with ABC have unique psychosocial and physical needs distinct from patients with early-stage breast cancer, and they merit recognition [5]. The National Institutes of Health (NIH), American Society of Clinical Oncology (ASCO), and other entities have recognized that this limited focus has resulted in a dearth of research in the area of “metavivorship”, a focus on the well-being of patients with advanced cancer [6]. Novel treatments for this population have dramatically improved survival, particularly for patients with hormone receptor-positive and HER2-positive breast cancer [7]. It is critical that researchers consider the various side effects patients with advanced breast cancer experience in relation to their treatment. Furthermore, research has shown that supportive care, including early involvement of palliative care, improves outcomes for patients with metastatic cancer [8][9][10]. The results of these studies counter the conventional practice of providing palliative care only in end-of-life situations. They highlight the importance of conducting clinical research on the lived experience of patients with ABC. To this end, researchers must seek to mitigate or remove any barriers to participation patients may experience.

## 2. Known Side Effects

### 2.1. Fatigue

Fatigue can be debilitating for patients with ABC. A meta-analysis by Al Maqbali et al. of 129 clinical trials conducted between 1993 and 2020 estimated that 60.6% of patients with advanced breast cancer experienced fatigue [11]. Fatigue is common among those who have been treated with chemotherapy, immunotherapy, or hormone therapy [12], and can be associated with the site of metastasis [13][14]. While fatigue is inherently difficult to quantify, studies employ questionnaires beginning at the time of treatment and continuing at fixed intervals afterward to identify chronic treatment-related symptoms. These studies show that 30–60% of patients report moderate to severe fatigue during treatment, and up to a quarter of them still experience symptoms 10 years after treatment [15]. Studies have also uncovered correlations between reported fatigue and overall lack of motivation as well as negative mood [16]. Studies focused on patients with ABC are more limited but suggest that effective treatment strategies may be distinct from those known to be effective for patients with limited stage disease. For example, a trial conducted by Poort et al. evaluating patients with ABC found greater benefit with cognitive behavioral therapy (CBT) compared with exercise and usual care [17]. CBT in this entry addressed patients' sleep; coping strategies; self-efficacy; physical, social, and mental activities; and social support. These findings underscore the need for specialized treatment for ABC.

## 2.2. Anxiety

Anxiety among patients with metastatic cancer is an area frequently analyzed. Studies have found that those diagnosed with depression or anxiety have worse outcomes. Wang et al. performed a systematic review and meta-analysis of 2.6 million patients with any cancer diagnosis by assessing reports of anxiety/depression and measured outcomes. This analysis revealed higher cancer incidence, poorer survival, and higher cancer-specific mortality among patients with a diagnosis of anxiety and depression [18]. An Australian study of 227 patients with ABC found that over a third experienced anxiety, depression, or both, and 17% of these patients were ultimately diagnosed with an anxiety disorder [19]. Dobretsova and Deraskan found a link between anxiety, traumatic stress and decreased cognitive function. Recommending social support is an important intervention in buffering against these effects [20]. Given the broad availability of effective treatments for anxiety and depression such as psychotherapy [21], mindfulness [22], and anti-depressant medications [23], it is critical that patients are regularly screened using multimodal assessments (questionnaires, GAD10, PHQ, etc.) and subsequently referred for appropriate mental health services [24]. Unfortunately, relatively few studies have evaluated treatment for anxiety among patients with advanced cancer. Sakamoto and Koyama evaluated current medical management strategies and suggest that the medication quetiapine could be a better alternative to the more commonly prescribed benzodiazepines or selective serotonin reuptake inhibitors (SSRIs) [25]. Current guidelines therefore recommend a personalized and stepped model for treatment delivery [26].

# 3. Areas of Need for Future Study

## 3.1. Caregiver Support

Family-centered care is key to the health of patients with metastatic breast cancer. Emotional support is important for the well-being of all people, and vital for patients with ABC. It is clear from studies focused on caregivers that

they have unique needs, and the tremendous weight of their responsibilities as caregivers can lead to negative outcomes such as lower quality of life and impaired workplace productivity [27][28]. Northouse and others found that caregivers who employed maladaptive coping strategies such as alcohol use, affected the patient's quality of life [29]. Caregiver quality of life seems to benefit from patient referral to palliative care provided early in treatment [30]. Lack of access remains a key barrier. For example, qualitative studies focused on caregivers of patients living in rural areas have confirmed caregiver demand for palliative care services and highlighted lack of access to both in person and telehealth options [31]. Maslow, Allicock and Johnson's study of 41 Black cancer survivors and their caregivers consisted of a focus group to discuss cancer survivor and caregiver needs. Both survivors and caregivers expressed their concern about the availability of culturally appropriate support services [32]. There is a great need for community-based support structures, and it is healthcare centers' duty to explore ways to provide these services. Caregivers are an important part of the care team and should be included when considering treatment for patients with ABC. Deeper research into how best to support caregivers is warranted.

### 3.2. Financial Toxicity

There are substantial financial costs associated with any major illness, and cancer is no exception. Economically disadvantaged patients are not only lacking monetary wealth to overcome financial toxicity (FT) but are also less likely to have knowledge of financial fail-safes such as those listed in **Table 1**. FT can lead to decreased quality of life, and general cancer-related distress [33]. A recent study by Wan et al. evaluated the financial toxicity among patients with ABC by stratifying groups using an 11-item survey dubbed the Comprehensive Score for Financial Toxicity (COST). The groups most frequently experiencing FT included Black patients, hormone receptor-negative patients, low-income patients, and unmarried patients [34]. Lifelong continuous treatment for ABC continues to be as debilitating financially as it is medically. Expanded research and financial assistance programs directed toward patients with ABC will be crucial moving forward.

**Table 1.** Several financial assistance programs can allay financial strain resulting from extensive cancer therapy. However, many are geared toward short-term treatments provided for early-stage cancers. Here, researchers list resources tailored to assist with management of long-term cancer treatment.

Organization	Website	Phone	Assistance
American Cancer Society	<a href="http://www.cancer.org">www.cancer.org</a> (accessed on 22 April 2022)	800-227-2345	Reimbursements for costs associated with cancer treatment
Breast Cancer Assistance Fund	<a href="https://breastcanceraf.org">https://breastcanceraf.org</a> (accessed on 22 April 2022)	866-413-5789	Need-based financial assistance for non-medical costs of getting a patient to treatment and other living

Organization	Website	Phone	Assistance
Cancer Care	<a href="http://www.CancerCare.org">www.CancerCare.org</a> (accessed on 22 April 2022)	800-813- HOPE	expenses that may be incurred
Cancer Care Co-Payment Assistance Foundation	<a href="http://www.cancercopay.org">www.cancercopay.org</a> (accessed on 22 April 2022)	866-552- 6729	Counseling, education, support groups, need- based financial aid for treatments
Cancer Financial Assistance Coalition	<a href="https://www.cancerfac.org">https://www.cancerfac.org</a> (accessed on 22 April 2022)	not applicable	Copay assistance
Cancer Supportive Care	<a href="http://www.cancersupportivecare.com/drug_assistance.html">http://www.cancersupportivecare.com/drug_assistance.html</a> (accessed on 22 April 2022)	Not applicable	Coalition of financial assistance organizations joining forces to help cancer patients experience better health and well- being by limiting financial challenges.
The Health Well Foundation	<a href="http://www.healthwellfoundation.org">www.healthwellfoundation.org</a> (accessed on 22 April 2022)	800-675- 8416	Listing of pharmaceutical drug assistance programs with contact information.
Needy Meds	<a href="http://www.needymeds.com">www.needymeds.com</a> (accessed on 22 April 2022)	Not applicable	Need-based financial assistance with coinsurance, copays, premiums, and deductibles.
			Non-profit organization with a database of patient assistance programs to include drug discount programs and state assistance programs.

Organization	Website	Phone	Assistance
Susan G. Komen	<a href="http://www.komen.org">www.komen.org</a> (accessed on 22 April 2022)	877- 465-6636	Need-based financial assistance with treatment payments
Patient Access Network Foundation	<a href="http://www.panfoundation.org">www.panfoundation.org</a> (accessed on 22 April 2022)	866-316-7263	Need-based financial assistance with copays, deductibles, and medications.
Partnership for prescription assistant	<a href="https://www.phrma.org/patient-support">https://www.phrma.org/patient-support</a> (accessed on 22 April 2022)		Non-profit organization sponsored by Pharmaceutical Research and Manufacturers of America's (PhRMA), civic groups, and patient advocacy organizations. This group is dedicated to helping patients find free or low-cost brand-name prescriptions.
Patient Advocate Foundation on CoPay Relief	<a href="http://www.copays.org">www.copays.org</a> (accessed on 22 April 2022)	866-512-3861	Need-based financial assistance with copays for prescription drugs
Remember Betty [35]	<a href="http://rememberbetty.com">http://rememberbetty.com</a> [36] [37] (accessed on 22 April 2022)		Helps minimize the financial burden associated with breast cancer for patients and survivors so they can focus on recovery and quality of life. [38]
RxHope	<a href="https://www.rxhope.com/">https://www.rxhope.com/</a> (accessed on 22 April 2022)	Not applicable	Rx Hope advocates for patients and helps them navigate available

Emotional distress is a primary inhibitor of a patient's quality and enjoyment of life. While not quite synonymous with "fear of the future" [40], distress is often a result of helplessness stemming from a metastatic cancer diagnosis [41]. Left unmanaged, emotional distress can lead to decreased quality of life and is associated with several

Organization <sup>42</sup>	Website	Phone	Assistance
	[43]		ession and assistance programs.

advanced cancer experienced mood disorders [44]. It has also been found that patients who engage in active coping with a support person experienced fewer mood disorders [45]. While quality of life (QOL) surveys are ubiquitous in the study of patients with breast cancer, a more specialized and holistic analysis tailored to ABC would be valuable in helping future patients cope with their diagnosis.

### 3.4. Long-Term Immune Therapy Effects

Immunotherapy is standard of care for patients with triple-negative breast cancer and will likely play a larger role in the treatment of all cancers moving forward. As treatment with immunotherapy becomes increasingly commonplace, studies evaluating immune-related adverse events (irAEs) will be critical. Patients who experience a complete response to immunotherapy treatment and achieve long-term survival will likely have unique long-term needs resulting from their treatment. These may include treatment for new chronic conditions such as type 1 diabetes, Addison's disease, hypothyroidism, and others. IrAEs such as fatigue and anxiety present complex needs, and further study is needed to address their treatment.

### 3.5. Education

Patients with ABC have unique psychosocial, physical, and treatment needs distinct from those patients with early-stage breast cancer [46]. Previous studies illustrate that clinical trials are foundational to the improvement of healthcare delivery. However, clinical trials only succeed when patients have access to the opportunity and consent to become involved. Furthermore, inequities in clinical trial focus related to supportive care screening and lack of diversity in participant population further fuel a cycle of inequality.

As such, educating all eligible patients about clinical trial opportunities is key. The education should include what clinical trials are, why they are standard of care, and when they should be considered.

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