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The Association of COVID-19-Related Financial Difficulties and Adjuvant Endocrine Therapy Adherence in Women with Early-Stage Breast Cancer

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By

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2019

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An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health at Emory University
in partial fulfillment of the requirements for the degree of
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Abstract

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By: Sara Arshad

The COVID-19 pandemic heightened risks to health and financial stability, particularly for breast cancer patients. Adjuvant endocrine therapy (AET), a daily medication, is highly effective at reducing breast cancer recurrence risk, but burdensome side effects and financial hardship contribute to low AET adherence. We used data from the THRIVE study, a randomized controlled clinical trial examining the effect of a web-based remote monitoring app, and an electronic pillbox to measure real-time AET adherence.

Amid the pandemic, questions were added about COVID-related financial difficulty (CRFD), including changes/gaps in health insurance and difficulty accessing basic needs 12 months after study participation. Participants who reported any of these difficulties were categorized as having CRFD. Logistic regression analyses were used to estimate the association between sociodemographic characteristics and CRFD, as well as CRFD and AET adherence (≥80% adherence rate), controlling for sociodemographic and clinical characteristics.

The analytic sample contained 217 THRIVE participants who completed the 12-month follow-up survey after CRFD questions were added: 52% of patients were AET adherent and 40% reported CRFD. Patients who reported CRFD were more likely to be 50-64 or 65-83 years old (Ref. 31-49 years) and have a household income below the federal poverty level. Adjusted results show that CRFD is associated with a 19.3 percentage-point decrease in the likelihood of being adherent ($p=0.006$). Black women were 16.9 percentage points less likely to be adherent ($p=0.021$). The financial and racial disparities in adherence must be addressed in the clinic. Lower AET adherence associated with CRFD may have implications for downstream health outcomes. New approaches are needed to screen and address financial difficulty, particularly in times of widespread economic distress.

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INTRODUCTION

1 in 8 women in the United States will develop breast cancer in their lifetime.[1] 87% of women with breast cancer have hormone receptor-positive (HR+) tumors.[2] Adjuvant endocrine therapy (AET) is an umbrella term for a group of commonly prescribed oral medications for HR+ tumors. There is ample evidence of AET's efficacy with proper adherence to the medication regimen, which is typically prescribed after surgery, chemotherapy, or radiation, and needs to be taken daily for 5-10 years. Proper adherence to AET reduces risk of hospitalization, cancer reoccurrence, and death. However, adverse side effects of AET contribute to low medication adherence.[3] Other contributors to low AET adherence include worry about financial and/or health status, depression, and comorbidities.[4,5]

The COVID-19 pandemic brought on threats to both physical health and financial stability, to which cancer patients are already vulnerable. The pandemic's widespread unemployment and economic distress have significantly impacted vulnerable cancer patients.[6,7] Black and Hispanic women in particular face the greatest disparities in breast cancer outcomes and challenges in medication adherence. Low-income Americans were among the hardest hit from the pandemic's economic consequences.[8] Sociodemographic data is essential to address the disparities in cancer outcomes. This study utilizes survey data to understand participants' experience with COVID-19-related financial difficulties, and electronic pillbox data to capture real-time AET adherence.

Research Questions:

1) What sociodemographic characteristics are associated with COVID-19-related financial difficulties among early-stage breast cancer patients?
2) What is the association between COVID-19-related financial difficulties and adherence to adjuvant endocrine therapy among early-stage breast cancer patients?

LITERATURE REVIEW

The pandemic created large-scale financial hardship and psychological distress for many. Cancer patients have reported increased worry about accessing their cancer treatment during the COVID-19 pandemic.[9] Jones and colleagues introduced a theoretical model of financial burden after cancer diagnosis, emphasizing psychological financial burden, which includes financial worry.[10] The authors emphasize the difference between material difficulty and psychological worry about finances, both of which can contribute to outcomes. Financial worry is considered distinct from economic burden that can arise in part due to high out-of-pocket costs. A majority of cancer survivors in the United States reported some financial worry. Financial worry about affording healthcare is associated with less adherence to cancer treatment.[11] More financial worry was associated with poorer adherence to mammograms and clinical breast exams.[12] Additionally, research has shown that Black breast cancer patients reported more

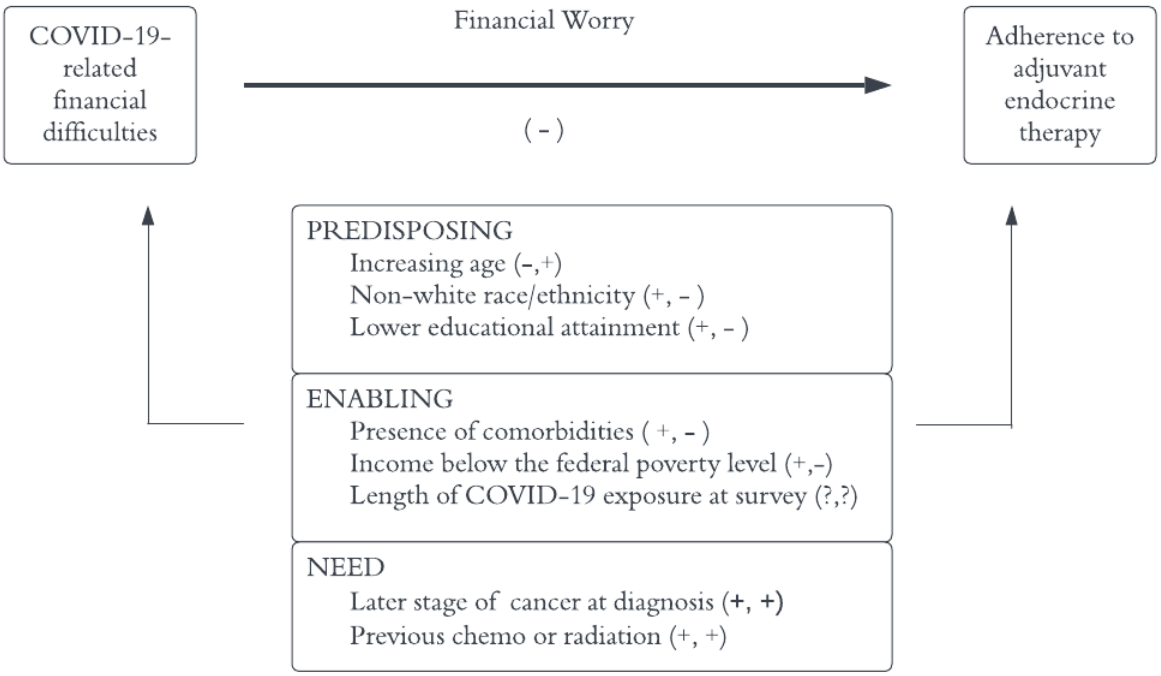
pandemic-related socioeconomic stress than their White counterparts.[14] There is still a need to explore how financial worry affects adherence to cancer drugs. Compared to traditional intravenous chemotherapy, oral drugs are both preferred by patients and becoming more common.[15] Oral medications rely on the patient's decision to take the medicine every day, which can be complicated by a variety of factors. This makes adherence especially important to study. In Carlos and colleagues' patient-centered model of systemic shock and cancer care adherence, in response to the COVID-19 pandemic, delaying or skipping medications is considered a coping behavior.[15]

Adjuvant endocrine therapy (AET) is a common class of oral treatment for HR+ breast cancer patients, among others. A perceived lower financial status and, notably, "a poorer relationship with the oncologist" was significantly associated with worse adherence to AET.[4]

Although AET is not one of the more expensive oral anticancer therapies, the financial strain brought on by a pandemic could be severe. It is also well understood in the literature that any copayments are associated with lower adherence to all medications, not just anticancer medications.[16] Previous analyses from the THRIVE study found that participants delayed prescriptions filled during the pandemic among this cohort of study participants, which indicates that the pandemic disrupted care specifically for these patients.[17] Studying the role of financial loss is necessary here. Research on psychological financial burden and perceived financial status among cancer patients is limited and only now emerging.

There are currently no studies that have examined the impact of the COVID-19 pandemic on financial loss and adherence to AET. There is a need to consider the pandemic's systemic stressors, particularly widespread depression, anxiety, and financial instability.[18] Patients with depression are less adherent to AET, and the financial impact of the pandemic is a predictor of depression in cancer patients.[5,6] Previous literature indicates that financial worry is associated with worse adherence to both preventative cancer screenings and cancer treatment.[12,11] There is a gap in the literature addressing pandemic-related financial difficulties and its association with adherence to AET, and this can be addressed with data from the THRIVE Study survey. THRIVE includes questions about COVID-19-related financial loss, changes or gaps in health insurance, and not having basic supplies such as food, water, and medications.[19] This data will provide insight into financial challenges, adherence, and demographic status of patients.

METHODS: Conceptual Framework



Andersen Model

The Andersen Behavioral Model for Healthcare Utilization is commonly used to model research questions centered around access to care, while modeling how individual and contextual characteristics affect people's abilities and health behaviors that affect their access to health services. The Andersen Model divides these factors into predisposing characteristics, enabling resources, and need-based variables that influence people's likelihood to access care.[20] Predisposing characteristics are demographic characteristics like age and gender that may influence a person's likelihood for utilizing healthcare services. Enabling factors determine a person's ability to access healthcare. Need-based variables include factors that affect health status and therefore influence the need to utilize healthcare.

Focal relationship

The focal relationship of this study is between COVID-19-related financial difficulties (CRFD) and adjuvant endocrine therapy adherence. Both variables were measured as dichotomous outcomes. A study participant was counted as experiencing CRFD if they reported pandemic-related financial loss, changes/gaps in health insurance, or not having basic supplies such as food, water, or medications. Participants were considered adherent to their AET if they took their medication as scheduled at least 80%

of the time during the study period as measured by the electronic pillbox WisePill. This 80% cutoff is consistent with previous medication adherence literature.[17,19]

Individual level confounders

Predisposing: Age, Race, Education

In this study, participant age refers to the age at which they enrolled in the study. Age was categorized into three groups: 31-49, 50-64, 65-83. As age increases, there is a negative association with CRFD and a positive association with AET adherence.[21,22]

The construct race refers to groups of certain physical characteristics while ethnicity refers to a person's cultural identification. Race and ethnicity were categorized as Non-Hispanic White, Non-Hispanic Black, and Other. Black women are disproportionately affected by the financial consequences of the pandemic and have lower adherence to AET.[22,23] Reporting race as Black will be positively associated with CRFD and negatively associated with AET adherence.

The construct education refers to the number of years of formal education attained by a participant. Education was categorized as having educational attainment of high school or less, or college/graduate school. The latter included people who attended some college, earned a four-year degree, attended some graduate school, or earned a graduate degree. As years of education increase, there is a negative association with CRFD and a positive association with AET adherence.[24]

Enabling: Comorbidity, Income, Length of COVID-19 exposure at survey time

The construct comorbidity refers to the presence of one or more diseases at a time. The presence of one or more comorbidities alongside the HR+ cancer diagnosis is positively associated with CRFD and negatively with AET adherence.[25,26]

Income refers to the total household income of the study participant. For this study, income was categorized as percentages (100%, 200%, 400%, >400%) of the federal poverty level, which was operationalized based on household income and size. An income at 100% or below the federal poverty level will be associated with poorer adherence.

Length of COVID-19 exposure at survey time refers to the length of time that participants were exposed to the pandemic when they completed their 12-month survey (12 months after enrollment). This will be operationalized as a binary variable, for one year or less, or more than one year exposure to the pandemic. The direction of the relationship with CRFD and AET adherence is unknown. Some may have felt the effects of the pandemic early on while others may have been hardest hit later on.

Need: Previous Chemotherapy/Radiation, Cancer stage

The construct of cancer stage refers to the severity and spread of the cancer that a patient has at diagnosis. In Stage I, the cancer is localized to one area of the body. In Stage II, the cancer has not spread but has grown larger than what would be seen in Stage I. In Stage III, the cancer has spread to surrounding tissues, and in Stage IV it has spread further to other organs.[27] This is a need-based characteristic. A later stage of cancer means the disease is more aggressive and therefore increases the need for use of healthcare, in this case, AET. Previous studies have shown that an earlier stage of cancer is associated with lower adherence to AET, in women with non-metastatic breast cancer. Also, previous chemotherapy and radiation are associated with better adherence, potentially due to a high motivation to remain adherent after undergoing previous treatment.[28]

Testable Hypotheses

H1: Younger, nonwhite participants with lower incomes are more likely to report CRFD.

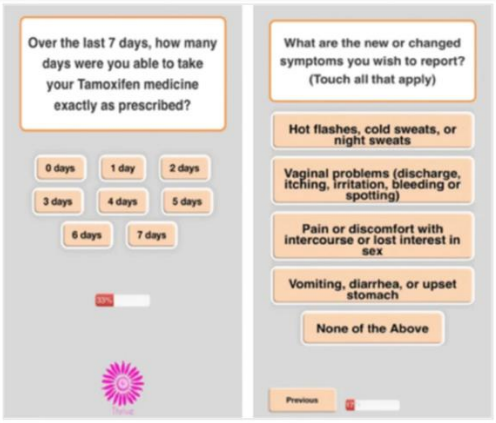
H2: The presence of any CRFD is associated with lower AET adherence.

Data Description

Data from this study came from participants enrolled in the THRIVE trial. THRIVE is a randomized controlled trial of 300 women with early-stage HR+ breast cancer that were prescribed AET no more than eight weeks prior to enrollment. The primary aim of the study was to assess the effect of a web-based symptom monitoring app on AET adherence. This study was conducted at the West Cancer Center & Research Institute (WCCRI) in Memphis, Tennessee. WCCRI is the largest cancer center serving West Tennessee, Northern Mississippi, and East Arkansas. 40% of patients at WCCRI identify as racial minorities, and the majority identify as Black. Memphis has one of the highest breast cancer survival rate disparities for Black women in the nation. WCCRI patients were recruited for THRIVE from November 2018 – June 2021. In this study, only patients that were recruited from April 2019 – June 2021 were included.

Study arms were “App” (n=96), “App+Feedback” (n=102), and Usual Care (n=102). The App group was given access to the THRIVE App where they could report their symptoms. The App+Feedback group, along with access to the THRIVE App, also received tailored text messages to use the App and to engage in healthy habits. The intervention lasted 6-months, and participants completed surveys at baseline and 12 months. Responses from the 12-month study were used for this study.

Figure 1: THRIVE App and Feedback Messages



a) Screenshot of THRIVE App

b) Feedback messages from THRIVE

Construct Measurement

COVID-19-related financial difficulty (CRFD). The construct CRFD comes from the THRIVE COVID-19 Survey in which patients were asked, "To what extent are you experiencing any of the following during the coronavirus pandemic? 1) Personal financial loss, 2) Changes or gaps in health insurance, 3) Don't have enough basic supplies (e.g., food, water, medications)." These questions were usually given Likert scale responses in the survey, where patients could select "not at all, slightly, moderately, considerably, a great deal" to describe the extent of their experience with any of the three challenges. CRFD was coded as a dichotomous measure for this study. The presence of any of the three concerns was defined as a CRFD.

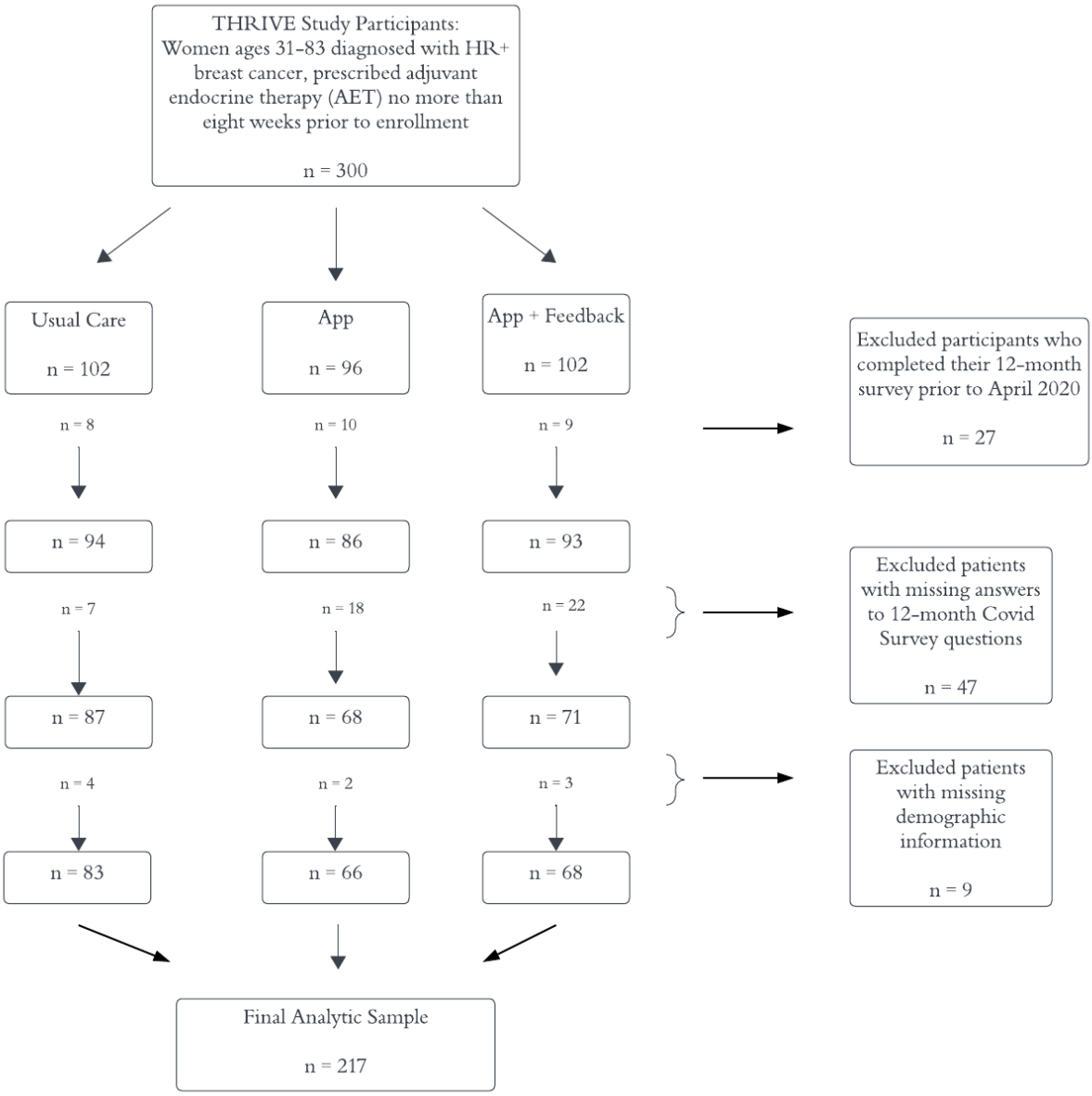
Adjuvant endocrine therapy (AET adherence). AET adherence was measured with WisePill, an electronic pillbox that records a dose each time it is opened. Every THRIVE participant was asked to use WisePill for 12 months. This allowed for complete, real-time adherence data.

Analytic Plan

This study utilized Stata 17 for all analyses. Descriptive statistics of the complete analytic sample were generated first. Next, adjusted logistic regressions were used to examine the association between sociodemographic and clinical characteristics with the presence of the three CRFD components. Then, additional unadjusted and adjusted logistic regressions were used to estimate the association between CRFD components and AET adherence. Marginal effects were generated using the "Margins" command

and can be interpreted as adjusted percentage point differences. Statistical tests were two-sided and $p<0.05$ was considered significant.

Analytic Sample Derivation



The recruitment period for the THRIVE study began in November 2018.[16] The inclusion criteria have been previously described: "a) adult female WCCRI patients (ages 18 years and older) with a diagnosis of ductal carcinoma in situ or Stage I-III hormone receptor-positive breast cancer; b) new prescription filled within the previous 8 weeks for an aromatase inhibitor (AI) or tamoxifen; c) have a mobile device with a data plan; d) have a valid email address; e) willing to complete brief surveys on a web-enabled device." Participants completed surveys at enrollment, then at six months, then at 12 months after enrollment. In

April 2020, additional questions about how the pandemic affected healthcare utilization, financial status, insurance coverage, etc. were added to the survey. For this study, the key predictor is COVID-19-related financial difficulties at 12 months, so analyses first excluded participants who completed their 12-month survey before April 2020, when the pandemic questions were added (n=27). Next, participants who had missing answers to any pandemic questions were excluded (n=47). Finally, patients who had any missing demographic information were excluded (n=9). The primary outcome of this study is adherence to AET, and because there are no missing values for the adherence variable, there are no further exclusions necessary (Final Analytic Sample, n = 217).

RESULTS

Figure 2: Percentage of Participants that Reported COVID-19-Related Financial Difficulties (CRFD)

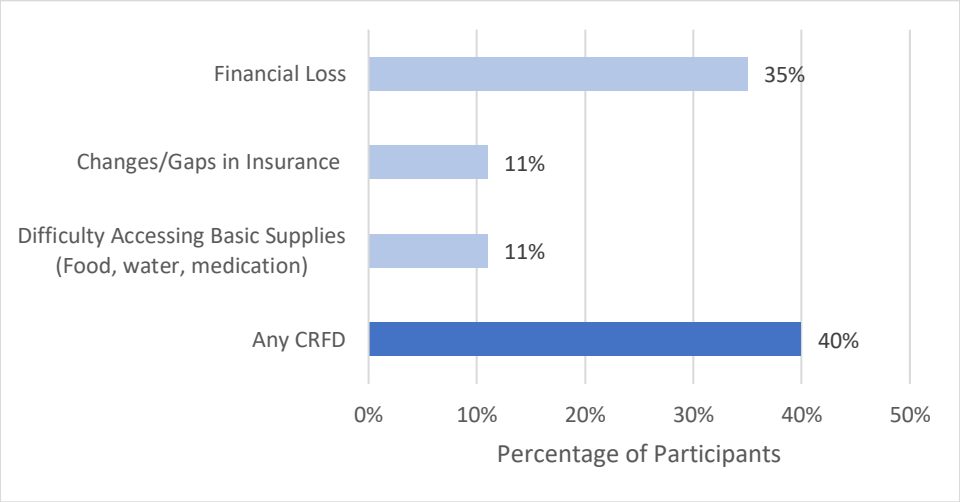


TABLE 1: Bivariate Analyses

	TOTAL N=217		COVID-19-RELATED FINANCIAL DIFFICULTIES			
			NO N=131 (60.3%)		YES N=86 (39.6%)	
Study Arm	**n**	**%**	**n**	**%**	**n**	**%**
Usual Care	83	38.25	47	35.88	36	41.86
App	66	30.41	40	30.53	26	30.23
App + Feedback	68	31.34	44	33.59	24	27.91
Adherent to AET **(p=0.007)**						
Yes	113	52.07	78	59.54	35	40.70
No	104	47.93	53	40.46	51	59.30
Demographic & Clinical Characteristics						
Age Group at Enrollment						
31-49 Years	53	24.42	32	24.43	21	24.42
50-64 Years	99	45.62	55	41.98	44	51.16
65-83 Years	65	29.95	44	33.59	21	24.42
Race/Ethnicity						
Non-Hispanic White	141	64.98	91	69.47	50	58.14
Non-Hispanic Black	68	31.34	37	28.24	31	36.05
Other[b]	8	3.69	3	2.29	5	5.81
Education (p=0.011)						
College or Graduate School[c]	177	81.57	114	87.02	63	73.26
High School or Less	40	18.43	17	12.98	23	26.74
Income (% of Federal Poverty Level)						
100% (p=0.000)	15	6.91	3	2.29	12	13.95
200%	42	19.35	17	12.98	25	29.07
400%	57	26.27	38	29.01	19	22.09
>400%	103	47.47	73	55.73	30	34.88
One or More Comorbidities						
Yes	76	35.02	89	67.94	52	60.47
No	141	64.98	42	32.06	34	39.53
Cancer Stage at Diagnosis						
1	158	72.81	98	74.81	60	69.77
2 or 3	33	15.21	17	12.98	16	18.60
Other	26	11.98	16	12.21	10	11.63
Previous Chemo or Radiation						
Yes	156	71.89	88	67.18	68	79.07
No	61	28.11	43	32.82	18	20.93
Length of Pandemic Exposure						

One year or less	87	40.09	50	38.17	37	43.02
More than one year	130	59.91	81	61.83	49	56.98

TABLE 2: Adjusted Logistic Regression Estimating the Association between Sociodemographic & Clinical Characteristics with Personal Financial Loss (n=217)

	Adjusted Percentage Point Difference	*p*-value	95% CI	
Age Group at Enrollment				
31-49 Years	Ref.			
50-64 Years	-2.74	0.735	-18.6	13.1
65-83 Years	-9.34	0.300	-27.0	8.34
Race/Ethnicity				
Non-Hispanic White	Ref.			
Non-Hispanic Black	-8.73	0.222	-22.8	5.28
Other[b]	15.24	0.373	-18.3	48.8
Education				
College or Graduate School[c]	Ref.			
High School or Less	10.74	0.249	-7.53	29.0
Income (% of Federal Poverty Level)				
100%	Ref.			
200%	-11.55	0.434	-40.5	17.4
400%	-35.50	0.015	-64.2	-6.81
>400%	-39.12	0.009	-68.3	-9.87
One or More Comorbidities				
No	Ref.			
Yes	6.69	0.383	-8.3	21.7
Cancer Stage at Diagnosis				
1	Ref.			
2 or 3	1.70	0.847	-15.5	19.0
Other	4.76	0.631	-14.7	24.2
Previous Chemo or Radiation				
No	Ref.			
Yes	10.23	0.139	-3.32	23.8
Length of Pandemic Exposure				
One year or less	Ref.			
More than one year	-9.05	0.226	-23.7	5.59

TABLE 3: Adjusted Logistic Regressions Estimating the Association between Sociodemographic & Clinical Characteristics with Changes or Gaps in Health Insurance (n=217)

	Adjusted Percentage Point Difference	*p*-value	95% CI	
Age Group at Enrollment				
31-49 Years	Ref.			
50-64 Years	8.34	0.045	0.2	16.5
65-83 Years	9.55	0.096	-1.7	20.8
Race/Ethnicity				
Non-Hispanic White	Ref.			
Non-Hispanic Black	4.35	0.399	-5.8	14.5
Other[b]	5.57	0.668	-19.9	31.0
Education				
College or Graduate School[c]	Ref.			
High School or Less	2.18	0.691	-8.6	13.0
Income (% of Federal Poverty Level)				
100%	Ref.			
200%	-5.09	0.680	-29.3	19.1
400%	-19.4	0.104	-42.7	4.0
>400%	-19.7	0.106	-43.5	4.2
One or More Comorbidities				
No	Ref.			
Yes	-3.07	0.516	-12.3	6.2
Cancer Stage at Diagnosis				
1	Ref.			
2 or 3	0.1	0.859	-9.8	11.8
Other	-1.42	0.819	-13.6	10.7
Previous Chemo or Radiation				
No	Ref.			
Yes	11.4	0.001	4.73	18.2
Length of Pandemic Exposure				
One year or less	Ref.			
More than one year	-4.98	0.351	-15.4	5.5

TABLE 4: Adjusted Logistic Regression Estimating the Association between Sociodemographic & Clinical Characteristics with Not Having Basic Supplies (n=217)

	Adjusted Percentage Point Difference	*p*-value	95% CI	
Age Group at Enrollment				
31-49 Years	Ref.			
50-64 Years	0.03	0.941	-8.8	9.5
65-83 Years	-0.06	0.921	-11.4	10.4
Race/Ethnicity				
Non-Hispanic White	Ref.			
Non-Hispanic Black	9.21	0.080	-1.1	19.5
Other[b]	27.54	0.075	-2.8	57.9
Education				
College or Graduate School[c]	Ref.			
High School or Less	12.52	0.068	-0.9	25.9
Income (% of Federal Poverty Level)				
100%	Ref.			
200%	-15.58	0.233	-40.6	9.49
400%	-26.78	0.043	-52.7	-0.08
>400%	-24.65	0.078	-52.0	2.74
One or More Comorbidities				
No	Ref.			
Yes	-3.41	0.457	-12.4	5.59
Cancer Stage at Diagnosis				
1	Ref.			
2 or 3	2.32	0.681	-8.8	13.4
Other	-7.37	0.083	-15.7	1.0
Previous Chemo or Radiation				
No	Ref.			
Yes	5.02	0.179	-2.30	12.3
Length of Pandemic Exposure				
One year or less	Ref.			
More than one year	1.44	0.770	-8.2	11.1

TABLE 5: Adjusted Logistic Regression Estimating the Association between Sociodemographic & Clinical Characteristics with any CRFD (n=217)

	Adjusted Percentage Point Difference	*p*-value	95% CI	
Age Group at Enrollment				
31-49 Years	Ref.			
50-64 Years	5.71	0.473	-9.9	21.3
65-83 Years	-6.07	0.496	-23.6	11.4
Race/Ethnicity				
Non-Hispanic White	Ref.			
Non-Hispanic Black	-4.08	0.585	-18.7	10.5
Other[b]	27.0	0.086	-3.8	57.8
Education				
College or Graduate School[c]	Ref.			
High School or Less	10.2	0.280	-8.3	28.7
Income (% of Federal Poverty Level)				
100%	Ref.			
200%	-14.52	0.282	-41.0	11.9
400%	-42.49	0.002	-68.7	-16.2
>400%	-49.11	0.000	-75.6	-22.7
One or More Comorbidities				
No	Ref.			
Yes	1.23	0.870	-13.5	15.9
Cancer Stage at Diagnosis				
1	Ref.			
2 or 3	-0.38	0.966	-17.8	17.0
Other	-0.57	0.953	-19.6	18.4
Previous Chemo or Radiation				
No	Ref.			
Yes	13.3	0.055	-0.3	26.9
Length of Pandemic Exposure				
One year or less	Ref.			
More than one year	-9.8	0.181	-24.2	4.6

TABLE 6: Unadjusted & Adjusted Logistic Regressions Estimating the Association between Distinct COVID-19-Related Financial Difficulties and AET Adherence

	Unadjusted Percentage Point Difference	*p*-value	95% CI		Adjusted Percentage Point Difference	*p*-value	95% CI	
COVID-19-Related Financial Difficulties								
Financial Loss	-16.4	0.020	-30.2	-2.6	-10.6	0.137	-24.7	3.37
Changes/Gaps in Insurance	-24.2	0.018	-44.3	-4.1	-15.6	0.196	-39.3	8.1
Difficulty accessing basic supplies	-44.5	<0.001	-59.5	-29.5	-43.4	<0.001	-61.0	-25.9
Study Arm								
Usual Care	Ref.							
App	0.33	0.968	-15.8	16.4	-5.2	0.493	-19.9	9.6
App + Feedback	-7.16	0.380	-23.1	8.8	-13.0	0.083	-27.7	1.7
Age Group at Enrollment								
31-49 Years	Ref.							
50-64 Years	21.5	0.008	5.5	37.4	20.0	0.013	4.17	35.9
65-83 Years	34.1	0.000	17.0	51.1	29.7	0.001	11.9	47.5
Race/Ethnicity								
Non-Hispanic White	Ref.							
Non-Hispanic Black	-22.8	0.001	-36.8	-8.8	-12.6	0.113	-27.8	3.23
Other[b]	-9.57	0.598	-45.2	26.0	13.8	0.353	-15.4	43.1
Education								
College or Graduate School[c]	Ref.							
High School or Less	0.05	0.952	-16.6	17.6	13.0	0.145	-4.5	30.4
Income (% FPL)								
100%	Ref.							
200%	-11.0	0.461	-40.1	18.2	-26.9	0.047	-53.4	-0.4
400%	16.5	0.251	-11.7	44.7	-18.2	0.153	-43.1	6.77
>400%	6.7	0.625	-20.2	33.8	-22.2	0.088	-47.6	3.28
One or More Comorbidities								
No	Ref.							
Yes	4.9	0.489	-9.0	18.8	1.08	0.888	-13.9	16.1
Cancer Stage at Diagnosis								
1	Ref.							
2 or 3	-12.6	0.182	-3.1	5.9	-12.5	0.177	-30.7	5.64

Other	-8.9	0.398	-29.6	11.7	-11.6	0.229	-30.5	7.3
Previous Chemo or Radiation								
No	Ref.							
Yes	-0.5	0.943	-15.3	14.2	8.12	0.268	-6.24	22.5
Length of Covid Exposure								
One year or less	Ref.							
More than one year	-9.00	0.190	-22.5	4.5	-8.3	0.250	-22.5	5.86

TABLE 7: Unadjusted & Adjusted Logistic Regressions Estimating the Association between COVID-19-Related Financial Difficulties and AET Adherence

	Unadjusted Percentage Point Difference	*p*-value	95% CI		Adjusted Percentage Point Difference	*p*-value	95% CI	
COVID-19-Related Financial Difficulties	-18.8	0.006	-32.2	-5.5	-19.3	0.006	-33.0	-5.7
Study Arm								
Usual Care	Ref.							
App	0.03	0.968	-15.8	16.4	-4.6	0.546	-19.8	10.3
App + Feedback	-7.1	0.380	-23.1	8.8	-11.7	0.128	-26.8	3.37
Age Group at Enrollment								
31-49 Years	Ref.							
50-64 Years	21.5	0.008	5.5	37.4	19.1	0.021	2.88	35.3
65-83 Years	34.1	0.000	17.0	51.1	28.4	0.003	9.93	47.0
Race/Ethnicity								
Non-Hispanic White	Ref.							
Non-Hispanic Black	-22.8	0.001	-36.8	-8.8	-16.9	0.032	-32.3	-1.43
Other[b]	-9.57	0.598	-45.2	26.0	5.8	0.730	-27.3	39.0
Education								
College or Graduate School[c]	Ref.							
High School or Less	0.05	0.952	-16.6	17.6	7.8	0.399	-10.4	26.0
Income (% FPL)								
100%	Ref.							
200%	-11.0	0.461	-40.1	18.2	-12.6	0.410	-40.7	16.6
400%	16.5	0.251	-11.7	44.7	0.4	0.979	-29.1	28.3
>400%	6.7	0.625	-20.2	33.8	-6.4	0.678	-36.4	23.7
One or More Comorbidities								
No	Ref.							
Yes	4.9	0.489	-9.0	18.8	1.5	0.852	-13.9	16.8
Cancer Stage at Diagnosis								
1	Ref.							
2 or 3	-12.6	0.182	-3.1	5.9	-12.6	0.176	-30.8	5.7
Other	-8.9	0.398	-29.6	11.7	-9.3	0.355	-28.9	10.4
Previous Chemo or Radiation								
No	Ref.							
Yes	-0.5	0.943	-15.3	14.2	6.8	0.233	-7.8	21.4
Length of Covid Exposure								
One year or less	Ref.							

More than one year	-9.00	0.190	-22.5	4.5	-9.0	0.233	-23.9	5.8

Sample Characteristics

In the complete sample of 217 participants, 52.07% were adherent to their prescribed adjuvant endocrine therapy (AET). Among those that reported CRFD, 40.70% were adherent. Participants that did not report CRFD had a higher adherence rate, 59.54%. 86 participants (39.6% of the sample) reported some CRFD. These participants were 58.14% Non-Hispanic White, 36.05% Non-Hispanic Black, and 5.81% Other. 24.42% were between 31-49, 51.16% were between 50-64, and 24.42% were between 65-83 years of age. Most had completed some college or graduate school (73.26%). 34.88% of participants reporting CRFD had incomes at or above 400% of the Federal Poverty Level, and the majority did not have comorbidities (65.09%). The majority also had Stage I breast cancer at the time of diagnosis (72.17%) with some previous chemotherapy or radiation (71.70%). The majority (59.91%) of participants were also exposed to the pandemic for more than one year at the time they completed their 12-month survey (Table 1).

Outcome and Key Predictor Comparison

Figure 2 shows the percentage of patients that reported any of the components of CRFD, as well as overall CRFD. 35% reported some personal financial loss, 11% reported changes/gaps in insurance, and 11% reported not having basic supplies like food, water, and medication. Overall, 40% of the sample reported at least one of these (Any CRFD).

Regression Analyses

The first set of regressions estimate the association between sociodemographic and clinical characteristics with the different components of CRFD. Participants with incomes at or above 400% of the federal poverty level were significantly less likely to report financial loss (p=0.015 and p=0.009, respectively) **(Table 2)**. Older participants (p=0.045) and those with previous chemotherapy or radiation (p=0.001) were significantly more likely to report changes or gaps in insurance **(Table 3)**. Participants with income at 400% of the federal poverty level were significantly less likely (p=0.043) to report not having basic supplies like food, water, and medications **(Table 4)**.

Patients who reported any CRFD were more likely to be 50-64 years old, and Other race/ethnicity **(Table 5)**. They were also more likely to have an education level of high school or less. However, of these characteristics, only poverty status was statistically significant. Comorbidities, cancer stage at diagnosis, and previous chemo or radiation had no significant impact on CRFD.

However, in unadjusted comparisons of adherence **(Table 6)**, patients who reported any CRFD were significantly less likely to be adherent to AET (Financial Loss Marginal Effect = -16.4 percentage points, p=0.020); (Changes/Gaps in Insurance Marginal effect = -24.2 percentage points, p = 0.018); (Basic Supplies Marginal effect = -44.5 percentage points, $p < 0.001$). In the adjusted analyses, only the basic

supplies component remained significant. After controlling for covariates, patients who reported not having basic supplies had a 43.4 percentage-point reduction in adherence ($p < 0.001$) compared to their counterparts who did not report this issue. The 50-64 and 65-83 age groups were significantly associated with higher adherence, as were those at 200% of the federal poverty level.

In the adjusted regression for adherence with the combined CRFD variable (**Table 7**), the presence of any CRFD (Marginal effect = -19.3, $p = 0.006$) and being Black (Marginal effect = -16.9, $p = 0.032$) were associated with lower adherence. Alternately, being age 50-64 (Marginal effect = 19.1, $p = 0.021$) or 65-83 (Marginal effect = 28.4, $p = 0.003$) was associated with an increased likelihood of being adherent.

DISCUSSION

Key Findings

Each CRFD factor was associated with lower adherence, and not having basic supplies was statistically significant. Of the three CRFD factors, not having basic supplies was the most severe. In this sample of mostly college-educated, higher-income women, even a small percentage reporting difficulties with accessing food, water, or medications is surprising, but speaks to the severity of the economic consequences of the pandemic. When patients do not have their basic needs met, they are likely unable to focus on the importance of taking their medication every day. Additionally, the presence of *any* CRFD was significantly associated with lower adherence. These findings suggest the influence of both material difficulty and financial worry in lower AET adherence.

Older participants were significantly more likely to be adherent to their AET. This adds to the understanding that younger women are generally less adherent to AET. Younger women may be more susceptible to worse symptom burden due to the menopausal side effects of AET as well as financial difficulties.

Finally, there was a significant racial disparity in adherence. Non-Hispanic Black participants showed significantly poorer adherence than their White counterparts, although they were not more likely to report CRFD. This suggests some unmeasured mechanism driving the low adherence. Given previous research in which Black women's higher association with socioeconomic stress during the pandemic, financial worry may very well be a mechanism driving lower adherence. This highlights the need for additional resources to support adherence for Black patients. This is especially important considering that these disparities persist after controlling for poverty status.

Limitations

This study had some limitations. First, the participants were from one cancer center in Tennessee, so the results may not be generalizable to all breast cancer patients taking AET. Second, it would not be ethical to randomize people to CRFD, so we must rely on observational data instead. Therefore, the findings from this study are associations and should not be interpreted as causal. The differential follow-up rates by study arm should also be considered. Each study arm lost a different number of participants to follow-up. Third, the study was limited to English speakers and may not capture the experience of women with limited English, who may have experienced more CRFD effects due to various accessibility issues. Additionally, there were some omitted variables that could not be included. Data about the participants' belief in the efficacy of their treatment was not included due to a high percentage of missing values. Also, a direct question about financial worry was not included in this survey but was added to other similar studies by the same research group.

Conclusions

Despite these limitations, this is the first study of CRFD and AET adherence. Major strengths of this study are the variables of the focal relationship—the THRIVE survey data with direct questions about pandemic-related financial challenges, and the complete, real-time adherence data for all participants. This study's findings suggest that AET adherence improvement interventions should consider more than just symptom burden. Promoting better adherence to AET is crucial given its' effectiveness at reducing risk of hospitalization, cancer reoccurrence, and death. Future treatment approaches and prescribing practices must consider broader contextual level factors and promote better adherence to AET. New approaches are needed to screen for and address financial difficulties, particularly for patients who are younger, Black, and/or do not have access to their basic needs. This study reinforces that a complete understanding of patients' financial situation should be an important factor in cancer treatment. Finally, this study provides further evidence for how distress associated with global events affects health-related behaviors.

The lower AET adherence in patients with CRFD could have downstream effects on health outcomes and should be studied further. This could be accomplished with a nationally representative sample. The psychological component of this research would benefit from mixed methods approaches, ideally a comprehensive, qualitative "financial worry" survey coupled with

detailed questions about basic needs being met. Patients' access to patient navigators and community support should be considered. This, along with screening to identify financial difficulties, is especially important to consider, especially in times of widespread economic distress.

References

1. American Cancer Society. *Breast Cancer Statistics.* https://www.cancer.org/cancer/types/breast-cancer/about/how-common-is-breast-cancer.html

2. National Cancer Institute. *Female Breast Cancer Subtypes - Cancer Stat Facts*. SEER. https://seer.cancer.gov/statfacts/html/breast-subtypes.html
3. Berry DA, Cronin KA, Plevritis SK, Fryback DG, Clarke L, Zelen M, et al. Effect of screening and adjuvant therapy on mortality from breast cancer. New Engl J Med. 2005;353(17):1784–92. https://www.nejm.org/doi/full/10.1056/NEJMoa050518
4. Stanton, A. L., Petrie, K. J., & Partridge, A. H. (2014). Contributors to nonadherence and nonpersistence with endocrine therapy in breast cancer survivors recruited from an online research registry. *Breast Cancer Research and Treatment*, *145*(2), 525–534. https://doi.org/10.1007/s10549-014-2961-3
5. Mausbach, B. T., Schwab, R. B., & Irwin, S. A. (2015). Depression as a predictor of adherence to adjuvant endocrine therapy (AET) in women with breast cancer: a systematic review and meta-analysis. *Breast Cancer Research and Treatment*, *152*(2), 239–246. https://doi.org/10.1007/s10549-015-3471-7
6. Kirby, A., Drummond, F.J., Lawlor, A. *et al.* Counting the social, psychological, and economic costs of COVID-19 for cancer patients. *Support Care Cancer* **30**, 8705–8731cleve (2022). https://doi-org.proxy.library.emory.edu/10.1007/s00520-022-07178-0
7. Leach, C. R., Kirkland, E. G., Masters, M., Sloan, K., Rees-Punia, E., Patel, A. V., & Watson, L. (2021). Cancer survivor worries about treatment disruption and detrimental health outcomes due to the COVID-19 pandemic. *Journal of Psychosocial Oncology*, *39*(3), 347–365. https://doi.org/10.1080/07347332.2021.1888184
8. Parker K, Minkin R, Bennett J. Economic Fallout From COVID-19 Continues to Hit Lower-Income Americans the Hardest (2020). Pew Research Center.
9. Dee, E. C., Nipp, R. D., Muralidhar, V., Yu, Z., Butler, S. S., Mahal, B. A., Nguyen, P. L., & Sanford, N. N. (2021). Financial worry and psychological distress among cancer survivors in the United States, 2013—2018. *Supportive Care in Cancer*, *29*(9), 5523–5535. https://doi.org/10.1007/s00520-021-06084-1
10. Jones, S. M., Henrikson, N. B., Panattoni, L., Syrjala, K. L., & Shankaran, V. (2020). A theoretical model of financial burden after cancer diagnosis. *Future Oncology*, *16*(36), 3095–3105. https://doi.org/10.2217/fon-2020-0547
11. Jones, S. M. W. (2022). Financial worry in people with cancer: Relationship to employment and outcomes. *Psycho-Oncology*, *31*(11), 1835–1842. https://doi.org/10.1002/pon.6034
12. Jones, S. M. W., Schuler, T. A., Padamsee, T. J., & Andersen, M. R. (2021). Financial Anxiety is Associated With Cancer Screening Adherence in Women at High Risk of Breast Cancer. *Annals of Behavioral Medicine*, *55*(12), 1241–1245. https://doi.org/10.1093/abm/kaab010
13. Wu Y, Liu X, Maculaitis MC, Li B, Berk A, Massa A, Weiss MC, McRoy L. Financial Toxicity among Patients with Breast Cancer during the COVID-19 Pandemic in the United States. Cancers (Basel). 2023 Dec 21;16(1):62. doi: 10.3390/cancers16010062.
14. Ruddy, K., Mayer, E., & Partridge, A. (2009). Patient adherence and persistence with oral anticancer treatment. *CA: A Cancer Journal for Clinicians*, *59*(1), 56–66. https://doi.org/10.3322/caac.20004

15. Carlos, R. C., Lowry, K. P., & Sadigh, G. (2020). The Coronavirus Disease 2019 (COVID-19) Pandemic: A Patient-Centered Model of Systemic Shock and Cancer Care Adherence. *Journal of the American College of Radiology*, *17*(7), 927–930. https://doi.org/10.1016/j.jacr.2020.05.032
16. Sinnott SJ, Buckley C, O'Riordan D, Bradley C, Whelton H. The effect of copayments for prescriptions on adherence to prescription medicines in publicly insured populations; a systematic review and meta-analysis. PLoS One. 2013 May 28;8(5):e64914. doi: 10.1371/journal.pone.0064914.
17. Paladino, A. J., Pebley, K., Kocak, M., Krukowski, R. A., Waters, T. M., Vidal, G., Schwartzberg, L. S., Curry, A. N., & Graetz, I. (2022). An examination of health care utilization during the COVID-19 pandemic among women with early-stage hormone receptor-positive breast cancer. *BMC Health Services Research*, *22*(1), 1403. https://doi.org/10.1186/s12913-022-08705-9
18. Fortune, E. E., Zaleta, A. K., & Morris, V. G. (2023). Perceived COVID-19 pandemic impact and protective factors predicting patient-reported depression and anxiety in individuals living with cancer. *Journal of Patient-Reported Outcomes*, *7*(1), 29. https://doi.org/10.1186/s41687-023-00571-1
19. Paladino, A. J., Anderson, J. N., Krukowski, R. A., Waters, T., Kocak, M., Graff, C., Blue, R., Jones, T. N., Buzaglo, J., Vidal, G., Schwartzberg, L., & Graetz, I. (2019). THRIVE study protocol: a randomized controlled trial evaluating a web-based app and tailored messages to improve adherence to adjuvant endocrine therapy among women with breast cancer. *BMC Health Services Research*, *19*(1), 977. https://doi.org/10.1186/s12913-019-4588-x
20. Andersen R, Newman JF. Societal and individual determinants of medical care utilization in the United States. Milbank Mem Fund Q Health Soc. 1973 Winter;51(1):95-124. PMID: 4198894.
21. Chlebowski RT, Kim J, Haque R. Adherence to endocrine therapy in breast cancer adjuvant and prevention settings. Cancer Prev Res (Phila). 2014 Apr;7(4):378-87. doi: 10.1158/1940-6207.CAPR-13-0389.
22. Barron TI, Connolly R, Bennett K, Feely J, Kennedy MJ. Early discontinuation of tamoxifen: a lesson for oncologists. Cancer. 2007 Mar 1;109(5):832-9. doi: 10.1002/cncr.22485. PMID: 17243168.
23. Taylor MG, Carr DC, Jason K. Financial Hardship and Psychological Resilience During COVID-19: Differences by Race/Ethnicity. J Gerontol B Psychol Sci Soc Sci. 2022 Jul 5;77(7):e117-e122. doi: 10.1093/geronb/gbab173. PMID: 34604902; PMCID: PMC9653000.
24. Murphy CC, Bartholomew LK, Carpentier MY, Bluethmann SM, Vernon SW. Adherence to adjuvant hormonal therapy among breast cancer survivors in clinical practice: a systematic review. Breast Cancer Res Treat. 2012 Jul;134(2):459-78. doi: 10.1007/s10549-012-2114-5. Epub 2012 Jun 12. PMID: 22689091; PMCID: PMC3607286.
25. Whitney RL, Bell JF, Reed SC, Lash R, Bold RJ, Kim KK, Davis A, Copenhaver D, Joseph JG. Predictors of financial difficulties and work modifications among cancer survivors in the United States. J Cancer Surviv. 2016 Apr;10(2):241-50. doi: 10.1007/s11764-015-0470-y.

26. Yussof I, Mohd Tahir NA, Hatah E, Mohamed Shah N. Factors influencing five-year adherence to adjuvant endocrine therapy in breast cancer patients: A systematic review. Breast. 2022 Apr;62:22-35. doi: 10.1016/j.breast.2022.01.012. Epub 2022 Jan 24. PMID: 35121501; PMCID: PMC8818734.
27. Cleveland Clinic. Cancer (2022). https://my.clevelandclinic.org/health/diseases/12194-cancer
28. Wulaningsih, W., Garmo, H., Ahlgren, J. et al. Determinants of non-adherence to adjuvant endocrine treatment in women with breast cancer: the role of comorbidity. Breast Cancer Res Treat 172, 167–177 (2018). https://doi.org/10.1007/s10549-018-4890-z