Review Article

EXPLORATION OF CONTRIBUTING FACTORS FOR NONADHERENCE TO BREAST CANCER TREATMENT – A SYSTEMATIC REVIEW

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Abstract

Background: Poor adherence to breast cancer treatment often poses the patient towards unfavourable health outcomes. On the contrary consistencies in following treatment protocols have proven to flag up the manifold benefits of adherence. Breast cancer survivors do forego treatment at times for various reasons that exposes them for the risk of cancer recurrences. This systematic review aims to explore the contributing factors for non-adherence to breast cancer treatment. **Methods:** The study has been registered in PROSPERO. The review included major database searches from PubMed, Ovid Medline and Web of science for relevant articles. The articles were meticulously screened following PRISMA guidelines 2020 and a total of 21 studies which met the inclusion criteria were included out of the 113127 for the review. Zotero reference manager was used to import and retrieve the studies. The included studies were assessed for methodological quality using MMAT (mixed method appraisal tool) version 2018. **Results:** The collective findings of the studies have brought to focus the factors for nonadherences such as side-effects of treatment, cost, accessibility to health care, comorbidities, older age, beliefs & preferences, knowledge about treatment, online information overload, forgetfulness, use of multiple medications, educational level and patient healthcare provider relationship. **Conclusion:** Nonadherences to breast cancer treatment is multifactorial. Health care providers team-based approach is essential to manage the diverse factors influencing nonadherence to breast cancer treatment. Nurses catering for patients can collaborate develop strategies, policies and manage individual patient concerns to ensure adherence and improve treatment outcomes.

Keywords: Nonadherence, Noncompliance, Breast cancer, treatment, Factors influencing, Contributing factors, Breast cancer survivors.

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INTRODUCTION

Adherence to treatment protocols is crucial among cancer patients to avert recurrences and to lower morbidity rates. Breast cancer is one of the worlds highly prevalent type of cancer in women. An estimate of about 2.3 million new cases and 764000 deaths were reported in 2023[1]. A study by ICMR-National centre for disease information and research (NCDIR) has projected a 5.6% annual increase in breast cancer cases, owing to 50000 new cases each year[2].

Vast majority of breast cancer patients undergo a combination of treatment modalities over a lengthy span of time. Hence, patient's adherence and persistence to treatment schedules is vital for a better outcome.

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treatment is evident and has been commonly reported among breast cancer patients.According to World Health Organization (WHO) nonadherence to treatment is defined as the failure to follow agreed-upon medical recommendations by the patient prescribed by the health care provider[3].

A cohort study conducted in France on 229 695 patients with early breast cancer, reported that nearly 17.0% developed non-persistence and 41.0% developed nonadherence. The 20% most at-risk patients accounted for 45% of nonadherence and all patients with a risk higher than the median accounted for 76% of nonadherence to treatment[4]. A study conducted in Mumbai, India examined socio-economic variations of breast cancer treatment and discontinuation among 500 breast cancer patients. The study findings projected that a total of 71 (14%) of the breast cancer patients discontinued their treatment. The study also emphasized on provision of free treatment for low socio-economic patients to lower the risk of discontinuation to treatment among breast cancer patients[5].

Nonadherence to breast cancer treatment has become one of the notable and significant issues in health care practices. It impacts patients in a way that increases the risk of recurrences of breast cancer and lessen the survival and quality of life among patients. On the contrary substantial reports have shown that, adherence to treatment protocol enhances higher

survival rates reducing the mortality rates and also provides an optimal treatment efficacy among breast cancer patients[6].
Despite the fact that the benefits of treatment adherences to breast cancer underscore the risk, nonadherences to treatment are likely reported among patients challenging their recovery and maximum therapeutic effectiveness of the treatment.

A retrospective cohort study was conducted to examine the association between endocrine therapy adherence trajectories and breast cancer recurrence risk in nonmetastatic breast cancer survivors in the US. The study reported that nearly 7% of breast cancer survivors who discontinued before completing 6 months of their treatment schedule were associated with an increased treated breast cancer recurrence risk compared to those with complete adherence to treatment[7].
Multiple factors influence nonadherences to breast cancer treatments and patient reported narratives portrayed in studies best outlines the reasons for foregoing treatment protocols. therefore, identifying and addressing these determinants is pivotal to prevent from cancer progression to enhancing clinical outcomes[8]. The primary objective of this review is to explore the various factors contributing to nonadherences to breast cancer treatment.

METHODOLOGY

A systematic review process was selected to explore the contributing factors for non-adherence to breast cancer treatment and registered in PROSPERO (ID-CRD42024616911). Through this strategy the relevant available literature was identified and examined. The review followed the guidelines of PRISMA (Preferred reporting items for systematic reviews and meta-analyses). We conducted searches from databases such as PubMed, Ovid Medline, Web of sciences, from case reports and other articles. The first and the second author conducted initial literature searches and screening of articles from databases and from internet sources. While additional searches were conducted by the third and fourth authors to find out for any missing studies. 21 studies were selected out of the total 113127 which fulfilled the inclusion criteria. Majority of the studies 7 were cross-sectional studies, 5 retrospective studies, 4 qualitative studies, 4 survey studies and 1 prospective study (Figure-1). The articles were assessed for methodological quality using MMAT (mixed method appraisal tool) version 2018. The tool comprises screening questions and methodological quality criteria for all studies with responses scored as yes, no and can't tell (Table-2). The included studies were assessed for quality by two reviewers.

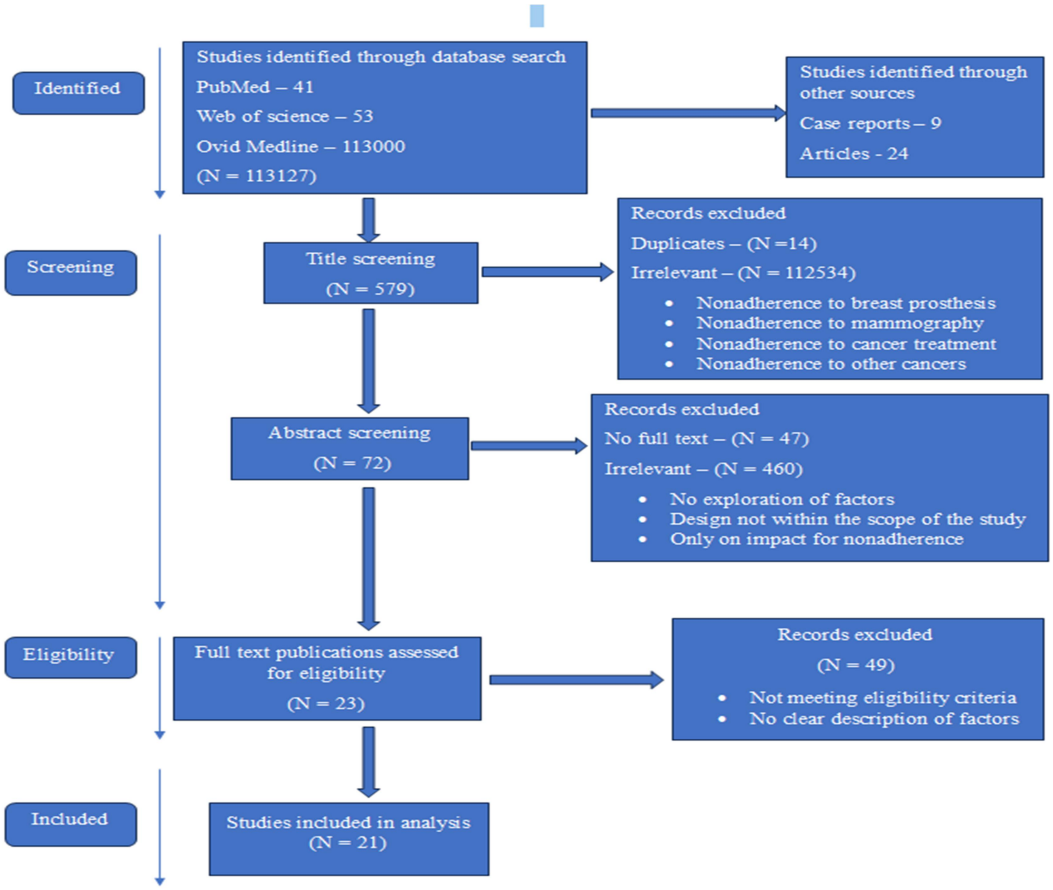


Figure 1: Prisma 2020 Flow Diagram For Systematic Review

Table – 1: Characteristics of included studies on contributing factors for nonadherences to breast cancer treatment for methodological review

Study no	Author, Year, location	Study design	Objectives	Participant characteristics	Sample size	Method of data collection	Definition of nonadherence	Factors that contributed to nonadherence	Outcome
1	Chang CY *et al*. 2024, US	Retrospective cohort study	To examine the association between endocrine therapy adherence trajectories & breast cancer recurrence risk	- Nonmetastatic breast cancer survivors. -Endocrine therapy initiated between 2010-2019. -Stage 0-III	Stage 0-I N=28042 Stage II-III N=7781 Total-35823	Surveillance, epidemiology, Medicare data	Breast cancer survivors discontinuing before completing 6 months of treatment	-Side effects	high recurrence risk was reported in 7 % of breast cancer survivors
2	Eraslan P & Tufan G. 2022, Turkey	Cross-sectional observational descriptive study	To investigate whether an online search on cancer treatments creates information overload and to determine the effect of online search on treatment adherence in postmenopausal breast cancer (BC) patients receiving adjuvant aromatase inhibitor (AI) treatment.	-Post menopausal women with surgically treated breast cancer -Received adjuvant AI therapy at least 1 year - From January 2021 to August 2021	103	Cancer Information Overload (CIO) scale, Hospital Anxiety Depression Scale (HADS), and Modified Medication Adherence Questionnaire (MAQ).	Breast cancer patients on adjuvant AI therapy dis continuing treatment within 1 year without consulting a physician	- Cancer Information Overload (CIO) is one of the main determinants for non-adherence - co-morbidity(s) -additional internet information searches - AI side effects -depression -anxiety	Not reported
3	Zheng C & Chagpar AB. 2022 US	Population based survey	To assess the prevalence of contribution of cost to treatment non adherence in breast cancer survivors	-People diagnosed with breast cancer within past 5 years surveyed in 2018 National health interview survey (NHIS)	24,858	Survey, interview	Breast cancer survivors foregoing treatment due to cost within the first 5 years of diagnosis	-Cost of treatment -not able to afford -family income - insurance status	~12 % breast cancer survivors on prescribed medications for first 5 years discontinued treatment
4	Haji-Hersi *et al*. 2022, US	Survey study	To identify factors that contribute to non-adherence to endocrine therapy in breast cancer patients.	-Women with breast cancer	32	Medication Adherence Rating Scale (MARS-8)	Nonadherence to endocrine therapy in breast cancer treatment plans	-Drug allergies -patient ability to pay -poor personal beliefs about the prescribed therapy - low education level -adverse drug events -poor patient-	59% of patients were non-adherent to endocrine therapy

								provider relationship	
5	Wheeler *et al.* 2019, US	Prospective cohort study	To examine endocrine Therapy (ET) Nonadherence and Discontinuation in Black and White Women with breast cancer	-Women aged 20–74 years with a first primary, stage I–III, hormone receptor–positive (HRþ) breast cancer -At 2 years postdiagnosis	1280	Patients' medical records and tumor (stage, grade, HRþ status) and blood samples. - patient-reported data were collected via telephone and mailed questionnaire	nonadherence, defined as not taking ET every day or missing more than two pills in the past 14 days, discontinuation, and a composite measure of underuse	-forgetting to take ET -cost related barriers -side effects burden -older age -Low recurrence risk perception - lack of a shared treatment decision making	black women more often reported nonadherence than white (13.7% vs 5.2%) but not discontinuation (10.0% vs 10.7%)
6	Leonhardt *et al.* 2024, Austria	retrospective study	To assess the guideline adherence of MTB (Multidisciplinary tumor boards) recommendations & identify predictors for non-adherence	-patients with breast & colorectal cancer between 01/2019 and 03/2024	579 patients breast cancer (n = 451 & colorectal cancer (n=128)	Information extracted from the electronic health record and the tumor board information system	Noncompliance with guidelines of MTB recommendations.	-patient preferences -lack of surgical treatment recommendation - comorbidities -older age at diagnosis	Most MTB recommendations were adherent to guidelines (n = 453, 78.2%)
7	Lee *et al.* 2025, Florida	qualitative study	To explore the influence of race and socio -economic status on ET (endocrine therapy) adherence through the perspectives of Black breast cancer survivors (BCS) and oncology providers.	-Black BCS with non-metastatic breast cancer on ET (n = 24) and medical oncology providers (n = 9)	24 Black BCS and 9 providers	Semi-structured individual interviews through videoconference using semi-structured guides.	Not defined	-medication costs -costs of managing symptoms - endocrine therapy side-effects -time toxicity -access to care -patient distrust.	Black BCS face a myriad of costs which potentially impact ET adherence.
8	Biggers *et al.* 2016, US	cohort study	To investigate the role of out-of-pocket cost supports through the Medicare Part D Low-Income Subsidy on disparities in breast cancer hormonal therapy persistence and adherence by race or ethnicity	women aged ≥ 65 years with a breast cancer surgery between 2006 and 2007 and were on at-least one prescription for oral breast cancer hormonal therapy	25,111	all Medicare D enrollees	Patient with a medication possession rate (MPR) of less than 0.80 (or 80%) were defined as nonadherent Non-persistence (or discontinuation) was defined as 90 consecutive days with no claims for a hormonal therapy prescription	-No subsidy	Unsubsidized women were 60% to 200% more likely to discontinue hormonal therapy in the first 35 months compared to the Low-Income Subsidy women of the same race or ethnicity.
9	Yusufov *et al.* 2020, US	Cross sectional study	To examine Predictors of increased risk for early treatment non-	Patients on oral anti-estrogen therapies (AET)	73	Patients self-reported treatment adherence after 3 and	Discontinuing oral AET after 3 and 6 weeks on AET initiation.	- Psychological and menopause symptoms	Patients nonadherent were (*n* = 19; 26.0%) and adherent were

			adherence to oral anti-estrogen therapies in early-stage breast cancer patients			6 weeks on AET		-depression, -generalized anxiety - insomnia - hot flashes	(*n* = 54; 74.0%) at 6 weeks. Adherence consistent at 3 weeks
10	Moon *et al*. London, 2025	Qualitative study	To understand women's experiences of taking tamoxifen and to identify factors which may be associated with non-adherence.	breast cancer survivors who had been prescribed tamoxifen	32	semi-structured interviews conducted face to face or over the telephone	Non-adherence can consist of missing or altering doses and/or taking medication "holidays"	-side effects of tamoxifen - beliefs on costs and benefits of treatment -lack of support -inadequate information	Women who believed tamoxifen use is important than its cost were more likely to be adherent, but women who believed benefits did not outweigh the side-effects were likely to discontinue treatment.
11	Antonini *et al*. 2025, Brazil	cross-sectional observational ecological study	To determine the migration rate of BC patients in Brazil and specifically to analyse migration rate by stage and treatment modality, its costs and possible reasons for delays	Breast cancer patients' data extracted from SISCAN between 2017 and 2022	275,140	Using retrospective data, information obtained from the DATASUS-SISCAN/Cancer Information System database.	Not defined	-Regional inequalities in healthcare infrastructure - limited availability of medical resources - Patients who travel long distances for treatment -financial hardship - accommodation challenges - family separation - psychological distress	lack of access to treatment causes nonadherence to treatment, unfavourable outcomes and poorer prognosis
12	Zuo *et al*. 2025, Canada	Cohort study	To assess the Impact of early discontinuation of adjuvant endocrine therapy on survival in breast cancer (BC)	women aged 50–80, diagnosed with first primary ER+ (Estrogen positive) BC between 2010–2015 and underwent surgery	6823	based on the Alberta Cancer Registry (ACR) database	Early discontinuation (ED) consisted of patients whose adjuvant endocrine therapy (AET) treatment duration was less than 48 months and stopped more than 6 months prior to death.	-older age (>70 years) - early-stage disease -HER2 negative status -lack of chemotherapy or radiotherapy	one-third (27.3 %) of ER+ BC patients discontinued AET early, which was associated with increased risks of recurrence and mortality
13	Lubas *et al*. 2026, US	Retrospective study	To identify predictors of low ET (endocrine therapy) adherence and evaluate the role of RT	Older patients with hormone receptor-positive, human epidermal growth factor receptor 2	1,488	US-based, electronic health record	Low ET adherence was defined as ET use for <80% of the 5-year post surgery follow-up period.	-older age -treatment at academic centres	l ET adherence is associated with an higher risk of death for older HPEsBC patients. 23%

			(radiation therapy) in modifying survival among patients with low ET adherence.	(HER2)-negative early-stage breast cancer (HPEsBC) undergo breast-conserving surgery (BCS) followed by adjuvant RT and/or endocrine therapy (ET)					demonstrated low adherence
14	Assad-Suzuki *et al*. 2025, Brazil	cross-sectional, observational study	To evaluate adherence to Adjuvant Endocrine Therapy in Patients with Nonmetastatic Estrogen Receptor–Positive Breast Cancer	Women with nonmetastatic ER+ invasive breast carcinoma who underwent ET for at least 6 months Betw een June 2021 and September 2023	726	Morisky Medication Adherence Scale-8 (MMAS-8) -specific questions were developed to explore return to work (RTW) - European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire C30 and BR23 instruments	patients with scores below 8 in MMAS scale were classified as nonadherent to ET	-use of ovarian function suppression therapy -difficulty in RTW -low QOL were associated with nonadherence to adjuvant ET.	only 58.7% showed adherence to ET treatment with a duration of 3.3 years -Patients who were adherent had significantly high global health status, role, emotional, cognitive and social functioning, body image, and future perspective scores than those with low adherence
15	Brett *et al*. 2018, UK	Qualitative study	To explore factors that influence adherence and nonadherence to AET (adjuvant endocrine therapy) following breast cancer to inform the development of supportive interventions.	women who had been prescribed AET, 2–4 years following their diagnosis of breast cancer	32	Semi-structured interviews	Nonadherence were defined as having initiated AET but now had stopped taking the medication.	-burden of side effects -feeling unsupported -concerns about long-term AET use - valuing the quality of life over length of life - risk perception	Improving adherence to AET by timely information on its efficacy and providing support to manage side effects will reduce recurrence and mortality patients
16	Nicolett i & Damin. 2023, Brazil	cross-sectional study	Factors influencing the first and the fifth years adherence and nonadherence to adjuvant endocrine therapy in breast cancer patients	Female patients diagnosed with HR-positive breast cancer, stages I to III, and with indication of AET were included	463	Brief Medication Questionnaire . interviews	Not defined	-use of aromatase inhibitors - polypharmac y of at least 3 mediations -previous diagnosis of DM or SAH have contributed to low adherence	failures in maintaining adherence to treatment increased from 23% of patients in the 1st year of treatment to 35% of patients in the 5th year. Educate on benefits of

								among patients	treatment, manage comorbidities, limit multiple medication, importantly detect and treat early the side effects of AET to decrease nonadherence
17	Wheeler *et al*. 2016, US	Qualitative research study	To understand Oncology providers' perspectives on endocrine therapy (ET) prescribing and management	oncology providers who saw five or more breast cancer patients per week which includes oncologists, surgeons, physicians' assistants, and oncology nurses	20	telephone interviews, using a semi-structured guide	clinically eligible females fail to initiate ET or discontinued by 5 years	- persistent unresolvable side effects (hot flashes, night sweats, and joint pain)	adherence to ET reduces in breast recurrence by ~40% & mortality by a third when taken as recommended for at least 5 years. limited options and evidence for successfully managing side effects. Management of side effects should be a priority for research for developing best practices and disseminate knowledge to providers
18	Ali *et al*. 2017, Singapore	cross-sectional survey	To measure the Prevalence and determinants of adherence to oral adjuvant endocrine therapy (OAET) among breast cancer patients	Breast cancer patients receiving OAET for at least 6 months	157	face-to-face interview with a semi-structured questionnaire and review of medical records using a structured check list. Morisky Medication Adherence Scale-4 items	Not defined	- Forgetfulness 63 (67.7%) was the main reason for nonadherence . -long duration of therapy (19.4%) - attempts to avoid potential side effects. (15.1 %)	OAET adherence rate was 40.8% among breast cancer patients. 93 patients were nonadherent.
19	Agnew *et al*. 2024, Scotland	cross-sectional survey	To explore the impact of symptom clusters on endocrine therapy adherence in patients with breast cancer	Participants aged 18 or over, had previously received a breast cancer diagnosis, and had internet access	1051	online survey With 6 standardized questionnaires to measure adherence (MARS-5, sleep (Sleep Condition Indicator (SCI)), depression (Patient Health Questionnaire	Nonadherence may be intentional (deliberately not following prescription instructions) or unintentional (forgetting a dose or misunderstanding instructions)	- treatment side effects, insomnia (73.83 % displayed probable insomnia disorder)	Nonadherence was high and more likely in patients reporting severe symptoms. nonadherence was 50.8 % (unintentional) and 31.01 % (intentional). relieving overall side effect burden

						(PHQ-9)), anxiety (General Anxiety Disorder Assessment (GAD-7), fatigue (Flinders Fatigue Scale (FFS), and menopausal symptoms (Breast Cancer Eight Symptom Scale (BESS)			for better medication adherence
20	Rahimi *et al*. 2023, US	retrospective study	To assess adherence to oral endocrine therapy in racial/ethnic minority patients with low socioeconomic status before and during the COVID-19 pandemic	Patients on appropriate doses of OET for prevention or treatment of Breast cancer	258	Data collected during the 6 months before and 6 months after the start of the pandemic. Patients of Harris Health System with at least one OET dispensed record from June 2019 through September 2020 was extracted from the EPIC Electronic Health Record (EHR) system.		nonadherence before the pandemic - Black/African American - obesity -prevention setting -tamoxifen therapy -4 or more years on OET During the pandemic -prevention setting -those not using home delivery were more likely to be nonadherent	Adherence was significantly lower during the pandemic (44%) compared to before the pandemic (57%).
21	Mitchell *et al*. 2023, US	retrospective cohort study	To examine adjuvant chemotherapy (AC) non-adherence, patient-centered communication, and patient-level factors in elderly breast and colon cancer patients	stage I–III breast cancer or stage III colon cancer between 2005 and 2013 who had surgery and completed a CAHPS survey within 2 years following their diagnosis. -Patients aged ≥65 years at diagnosis and have continuous Medicare coverage	577	SEER-CAHPS database	Not defined	-Older age -uninsured patients -greater number of comorbidities	At all 3 levels of AC nonadherence was higher in patients with (69%, 81%, and 89% for primary nonadherence and non-persistence at 3 and 6months, respectively than colon cancer patients (43%, 46%, and 62%, respectively

Table -2: Assessment of risk of bias of the included articles using Mixed method appraisal tool (MMAT) version 2018

Authors & Year	Screening questions		Category of study designs				
			1. Qualitative Methodological quality criteria				
	S1. Are there clear research questions?	S2. Do the collected data allow to address the research question?	1.1. Is the qualitative approach appropriate to answer the research question?	1.2. Are the qualitative data collection methods adequate to address research question?	1.3. Are the findings adequately derived from data?	1.4. Is the interpretation of results sufficiently substantiated by data?	1.5. Is there coherence between qualitative data sources, collection, analysis & interpretation?
Lee *et al*, 2025	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Moon *et al*, 2025	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Brett *et al,* 2018	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Wheeler *et al,* 2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes
			4. Quantitative descriptive Methodological quality criteria				
			4.1. Is the sampling strategy relevant to address the research question?	4.2. Is the sample representative of the target population?	4.3. Are the measurements appropriate?	4.4. Is the risk of nonresponse bias low?	4.5. Is the statistical analysis appropriate to answer the research question?
Chang CY *et al*, 2024	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Eraslan P & Tufan G, 2022	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes
Zheng C & Chagpar AB, 2022	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Haji-Hersi *et al,* 2022	Yes	Yes	Yes	Yes	Yes	Yes	Can't tell
Wheeler *et al,* 2019	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Leonhardt *et al*, 2024	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Biggers *et al*, 2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Yusufov *et al*, 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Antonini *et al*, 2025	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Zuo *et al*, 2025	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Lubas *et al*, 2026	Yes	Yes	Yes	Yes	Yes	No	Yes
Assad-Suzuki *et al*, 2025	Yes	Yes	Can't tell	Yes	Yes	No	Yes
Nicoletti & Damin, 2023	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Ali *et al*, 2017	Yes	Yes	Can't tell	Yes	Yes	Can't tell	Yes
Agnew *et al*, 2024	Yes	Yes	Yes	Yes	Yes	No	Yes
Rahimi *et al*, 2023	Yes	Yes	Yes	Yes	Yes	No	Yes
Mitchell *et al*, 2023	Yes	Yes	Yes	Yes	Can't tell	No	Yes

ELIGIBILITY CRITERIA

Studies that fulfilled the following inclusion criteria were selected 1) studies that explored factors for nonadherence to breast cancer treatment 2) qualitative study, cross sectional study, prospective & retrospective studies, survey studies 3) studies published in English between 2015 to 2025 4) Published online from peer reviewed journals. The exclusion criteria were 1) studies that explored only adherence but not nonadherence to breast cancer treatment 2) studies that only assessed nonadherence to breast cancer treatment but did not explore the contributing factors 3) Review articles, commentaries, editorials

SEARCH STRATEGY

The systematic review was conducted using electronic

database searches in PubMed, Ovid Medline & Web of science. Boolean operators were used such as "AND", "OR", "NOT" and various search terms like "Nonadherence", "Breast cancer treatment", "Factors influencing", "Contributing factors", "Determinants", "Causes for nonadherence" for obtaining relevant articles. All searches of the electronic databases were conducted using MeSH terms, key words, text words and search strings appropriate to each database. The search was limited to articles published in English between January 2015 to December 2025.

DATA EXTRACTION

The selection process started by carefully reading the title, followed by the abstract, objective & the full text of each article & paper. Each paper was evaluated in accordance with PRISMA-P 2020 guidelines. The title of the papers that have mentioned factors for non-adherence to breast cancer treatment was identified and potentially relevant articles were further evaluated by reading their full text, objectives, methods, approaches & population/subjects, results and inferences. Studies which were not eligible based on the examination of full text were excluded and the reason for the exclusion is documented. The selection process flow diagram is presented based on PRISMA statement. Zotero was used to import and retrieve the articles from databases. The information extracted from the articles included the author, year and place, study design, objectives, participant characteristics, sample size, method of data collection, factors that contributed to nonadherence and outcome and summarized using MS Excel spread sheet (Table - 1). The overall selected search results were complied.

RESULTS

We identified 113127 articles through database searches and 579 were retained from the title screening after removing duplicates and irrelevant articles. Further 72 articles were selected from abstract screening excluding irrelevant and no full texts. 23 full text published articles were identified and assessed for eligibility. After reviewing the full text, a total of 21 studies were included in the analysis that fulfilled the inclusion criteria. We examined the 21 studies exploring factors for nonadherence to breast cancer treatment with the total sample of 374531.

Chang *et al*, Eraslan & Tufan, Haji Hersi *et al*, Wheeler *et al*, Lee *et al*, Moon *et al*, Brett *et al*, Ali *et al*, Agnew *et al* have all collectively highlighted that the side effects experienced by breast cancer patients during treatment process is one of the most influential factors for nonadherence to treatment. [7.9,11,12,15,18,23,25,26] Zheng & Chagpar, Wheeler *et al*, Leonhardt *et al*, Biggers, Antonini *et al*, Mitchell *et al*, Rahimi *et al*, Nicoletti & Damin have reported many other factors for nonadherence to breast cancer treatment such as costs of treatment (affordability), lack of insurance/subsidy, lack of accessibility to treatment (inequal availability of medical resources, travel long distances for treatment), patients on longer duration of therapy, older patients (>70 years), patients with comorbidities, lower educational level, psychological issues, obesity, polypharmacy (prescribed at least 3 mediations), individual beliefs and preferences to treatment choices.[10,12,13,14,19,27,28] Ali *et al* and Wheeler *et al* underscored that forgetfulness to take medication contributed to nonadherences among patients.[24,25] Haji Hersi spotlighted that poor patient health care provider relationship significantly affects adherences to treatment protocols.[11] Eraslan and Tufan identified that internet searches to cancer information and overload is an important determinant for nonadherences[9] while Moon *et al* have reported that inadequate information about treatment as the contributing factor for nonadherences.[18] However, lack of information about treatment and online searches for cancer treatment (information overload) has been emphasized as contributing factors for nonadherences to treatment.

DISCUSSION

The consolidation of the 21 studies on exploring the contributing factors for non-adherence to breast cancer treatment in this systematic review has elicited multidimensional facets for nonadherences among breast cancer patients, pointing out to variations between patients. Zheng C & Chagpar, Haji-Hersi *et al*, Yusufov *et al*, Zuo *et al*, Ali et al, Agnew et al. underscored the prevalence of nonadherence between 12% to 89 % especially with breast cancer patients on endocrine therapy.[10,11,17,20,25,26] Chang *et al,* Antonine *et al,* Zuo *et al*, Lubas *et al* and Brett reported that the consequences of nonadherences to treatment mounts to significant rates of breast cancer reoccurrences, higher risk for mortality, poor prognosis and unfavourable outcome.[7,19,20,21,23] Assad-Suzuki *et al* and Wheeler *et al* showcased the benefits of adherences to treatment as contributing to potentially satisfactory health status and overall patient clinical outcome. Promoting quality of life in all aspects pertaining to physical, psychological, cognitive and social functioning, substantially reducing breast cancer recurrence by approximately 40% & lowers mortality rates. [22,24] This indicates that promoting adherence to treatment is remarkable and vital which can be achieved by meticulously identifying and initiating strategies to promote adherence. Brett *et al*, Nicoletti & Damin emphasized that educating the patients on the benefits of treatment, managing comorbidities effectively, reducing polypharmacy and above all detecting and treating early the adverse effects of treatment is of prime importance to enhance adherence. [23,14] However, Wheeler *et al* and Agnew *et al* have indicated that limited options and evidence for successfully managing side effects challenge the implementation of evidence-based practices in health care. Further the studies highlighted that side effects management in particular should be a priority for research to identify best practices and disseminate knowledge to providers to promote adherences to treatment among breast cancer patients. [24,26]

CONCLUSION

In the recent years breast cancer has emerged as the major type of cancer in women with a steady and significant inclination in morbidity & mortality rates. Nonadherence to treatment protocols has always been a challenging issue among health care providers to deal with. Nonadherences to treatment schedules among breast cancer survivors are highly variable owing to multiple influencing factors. This systematic

review provides a comprehensive broader view on the contributing factors for nonadherence to breast cancer treatment with an emphasis for collaborative team work to focus on care tailored to patients need, develop structured strategies, policies, proactive side effects management through evidence-based practices, providing accessible and affordable treatment across communities to ensure consistency in adherence to treatment and to achieve optimal clinical outcomes.

Ethical approval
The study does not require Institutional ethical approval.

Declaration of patient consent
As the study reviews previously published articles, therefore patients' consent is not required.

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Nil.

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Conflicts of interest
The authors declare no conflicts of interest related to this study.

Use of AI assisted technology for manuscript preparation
The authors confirm that AI assisted technology was not used for manuscript preparation.

AUTHORS CONTRIBUTIONS

Evangelene G: Developing protocol, PROSPERO registration, database searches & screening, data extraction, interpretation of results & design, final write up and quality assessment. **Dr. Bindhu Mathew**: Conceptualization, developing protocol, database searches & screening, design writing, review & editing. **Dr. Rakesh S Ramesh**: Conceptualization, quality assessment. **Dr. Sumithra Selvam**: Data extraction & quality assessment.

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