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Racial/Ethnic and Socioeconomic Disparities in Endocrine Therapy Adherence in Breast Cancer: A Systematic Review

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Abstract

We examined the current literature to understand factors that influence endocrine therapy (ET) adherence among racial/ethnic and socioeconomic subpopulations of breast cancer patients. We searched PubMed and PsycINFO databases for studies from January 1, 1978, to June 20, 2014, and January 1, 1991, to June 20, 2014, respectively, and hand-searched articles from relevant literature reviews. We abstracted and synthesized results within a social ecological framework.

Fourteen articles met all inclusion criteria. The majority of included articles reported significant underuse of ET among minority and low-income women. Modifiable intrapersonal, interpersonal, and community-level factors are associated with ET use, and these factors vary across subgroups.

Both race/ethnicity and socioeconomic status are associated with ET use in most settings. Variation in factors associated with ET use across subgroups indicates the need for more nuanced research and targeted interventions among breast cancer patients.

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Contributors
All authors participated in the conceptualization and design of the systematic review, participated in data analysis, contributed to the article through iterative revision, and approved the final article. M. C. Roberts led the systematic review, including article selection (title selection, abstract selection, and full-text review) and data abstraction, and drafted the article. When there was uncertainty regarding article selection, a decision was made through discussion and consensus between S. B. Wheeler and M. C. Roberts.

Human Participant Protection
This systematic review used secondary data with no individual identifiers; therefore, human participant protection was not necessary.

Low medication adherence is common among patients taking oral drugs; an estimated half of all patients are nonadherent to a medication regimen across multiple chronic disease areas.[1] This low medication adherence is problematic because it is associated with poorer prognosis for many common conditions.[2] Evidence has demonstrated that non-White patients are less likely to adhere to medication regimens than White patients,[3,4] suggesting that medication adherence may be an important lever for targeting racial disparities in health care outcomes. Medication adherence has become a particularly important issue in cancer care because the use of oral anticancer drugs in clinical practice has increased.[3] Endocrine therapy (ET) for breast cancer is among the most common oral anticancer therapies, and racial variation in ET adherence may play a role in racial disparities in breast cancer care outcomes.

Breast cancer is the most common cancer among women in the United States: of the 232 570 women diagnosed with invasive breast cancer each year, approximately three quarters will have hormone receptor–positive breast cancer.[5,6] Typically, women with this type of breast cancer undergo surgery with or without radiation, some will take adjuvant chemotherapy, and nearly all will be eligible for ET.[7,8] ET is most commonly given in the adjuvant setting to prevent recurrence of curable cancers.[5,9] ET consisting of at least a 5-year course of tamoxifen or an aromatase inhibitor (AI), is the gold standard for adjuvant treatment of these cancers, and it reduces 5-year breast cancer recurrence by 40% and breast cancer mortality by one third.[10]

However, evidence from observational and patient-reported sources has suggested that many women underuse ET because of noninitiation (i.e., never starting ET), nonadherence (i.e., not taking ET as prescribed), or nonpersistence (i.e., not taking ET for the recommended duration).[11–15] ET underuse is associated with shorter time to recurrence, lower quality of life, and increased medical costs.[16] Approximately one third of women who initiate adjuvant tamoxifen discontinue the drug before the 5-year, guideline-recommended duration.[12,13,15] Of those who continue taking tamoxifen, 16% to 28% do not fully adhere to the therapy.[12,13,17–19] Furthermore, adherence and persistence decline over time.[19] Thus, by the end of the 5-year course of therapy, only about half of women have taken tamoxifen as prescribed.[12,13] AI data have shown similar patterns of underutilization;[12] at 5 years, 19% to 25% of women have discontinued their AI,[20,21] and 20% to 31% of women have been nonadherent.[18,22]

Minority populations may be disproportionately affected by ET noninitiation, discontinuation, and nonadherence.[12,23–28] Minority and low-income populations are less likely to be integrated into the health care system; thus, they may face unique barriers to care, such as poor access to providers, that influence receipt of ET and other cancer-related treatment.[29,30] Among minority women who are also low income or who experience high levels of social stressors, competing social and economic demands may take priority over medication adherence, leading to suboptimal medication use.[31] Patterns of ET utilization among minority women are understudied and may contribute to the well-recognized and persistent racial, ethnic, and socioeconomic disparities in outcomes. Despite advances in breast cancer prevention and treatment, breast cancer mortality remains 37% higher among Black women than among White women.[32] Biological differences are important but cannot fully explain this racial/ethnic variation in mortality.[9,33] Thus, the observed disparities likely arise from a combination of factors, including incomplete or omitted ET treatment.

In several studies of insured women, non-White race[11,12,22,24–28] and low socioeconomic status (SES)[34] have been associated with lower ET initiation, adherence, and persistence; however, reasons for this variation have not been well described. Although previous literature reviews have described factors that are associated with ET utilization broadly, none have detailed racial variation in the use of ET. We addressed this literature gap by conducting a systematic review of the adjuvant ET literature that is focused on barriers to ET use among low-income and minority populations.

METHODS

Our review methods followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (Figure 1).[35]

Data Sources and Searches

We conducted systematic literature searches of the PubMed and PsycINFO databases for articles dated January 1, 1978, to June 20, 2014, and January 1, 1991, to June 20, 2014, respectively. We also hand searched the bibliographies of relevant literature (Figure 1).

The precise search terms used for all searches were as follows: (breast cancer[MeSH Terms]) AND (aromatase inhibitor* OR tamoxifen[MeSH Terms]) AND (adherence OR compliance OR persistence OR maintenance OR discontin* OR initiat*). We chose broad search terms to capture all ET utilization articles, including all types of ET (e.g., tamoxifen and AIs) and utilization terms (e.g., initiat*, persist*, adhere*). To complement these searches, we hand-searched bibliographies of key studies and other relevant review articles to identify additional articles that were not captured in the database searches.[9,21,22,34,36–72]

Study Selection

Studies with both experimental and nonexperimental study designs, with or without a comparison group, were included. We included studies that explored both (1) racial/ethnic or socioeconomic variation in ET initiation, adherence, or persistence and (2) barriers to ET that varied by race/ethnicity or SES through the use of interaction terms for race, ethnicity, and SES with other factors (e.g., modifiers) or through analyses of ET use among racial/ethnic or socioeconomic subgroup populations. Most of these studies used self-reported race/ethnicity data.

We excluded studies with the following characteristics:

1. The primary focus was not ET utilization (e.g., efficacy trial data without utilization data presented);
2. the study was conducted outside of the United States;
3. ET was delivered as chemoprevention or palliative treatment of metastatic disease;

4. the article was a literature review, letter to the editor, editorial, or thought piece; and
5. the article examined diverse patient populations but did not include racial/ethnic or socioeconomic subgroup analyses or interaction terms. We did not exclude studies on the basis of duration of follow-up or clinical setting.

We used EndNote X4 (Thompson Reuters, New York, NY), a citation management software system, to organize and manage our citation database for the review. EndNote enabled us to de-duplicate the individual searches and create a database of unique articles. Using our inclusion and exclusion criteria, we conducted title searches to identify which articles should undergo abstract review.

Next, 1 author (M. C. R.) reviewed abstracts to determine which articles were eligible for full-text review. In this phase, we excluded literature review articles from further analysis; however, we hand searched their bibliographies and added relevant references to the abstract search.[9,36–48] We conducted full-text reviews to determine which articles would be abstracted. Study selection and review were conducted by 1 reviewer (M. C. R.). However, if the decision to include an article was unclear after the full-text review, a second reviewer (S. B.W.) assessed the article, and the final inclusion decision was resolved by discussion and consensus between the 2 reviewers.

Data Extraction

Applying the PICOTS framework,[73] 1 author (M. C. R.) extracted the following data from each article: population, intervention (i.e., types of ET included), comparator group (if applicable), outcomes, timing (duration of follow-up), and setting. We categorized study outcomes into 4 groups: provider discussion, recommendation, and prescribing; initiation; adherence; and persistence.

Definitions of utilization varied from study to study. Thus, we classified ET use outcomes according to our prespecified definitions of initiation, adherence, and persistence. For the purposes of this review, we defined *ET initiation*, or *initial ET use*, as whether the patient began ET. *ET adherence* referred to whether the patient took the prescription at the recommended dose and on the recommended schedule. Typically, studies defined nonadherence as having less than 80% of days covered by prescription fill records. Finally, *persistence* or *continuation* referred to whether the patient continued to take the medication for the recommended duration of therapy (regardless of whether the patient took it correctly according to recommended dosing and schedule).We further divided these groups by ET type (i.e., amoxifen, AIs, or both). AIs included letrozole, anastrozole, or exemestane.

Data Synthesis and Analysis

We did not conduct meta-analyses because significant heterogeneity existed among

1. study populations,
2. ET type,
3. outcomes assessed,

4. independent variable measurement,
5. duration of follow-up, and
6. study setting.

This was a qualitative decision made after data extraction and review. However, we did analyze studies within a well-known theory-driven conceptual framework, the social ecological framework.[74]

The ecological perspective of the social ecological framework acknowledges that multiple-level factors in the social system (i.e., intrapersonal, interpersonal, and community factors) influence health behaviors such as ET utilization (Figure 2).[75,76] Findings from the abstracted articles were organized into intrapersonal, interpersonal, and community levels. We report descriptively on the included studies and their implications. Results from regression analyses and *P* values were abstracted directly from the included studies.

RESULTS

Of 142 abstracts, 14 articles met final inclusion criteria (Table 1).[19,22,60,77–87] Five of these studies examined socioeconomically disadvantaged populations. These 5 studies included publicly insured patients who were enrolled in state Medicaid programs[19,60,81,87] or Medicare's low-income subsidy program.[22] Of all included articles, 6[77,78,80,81,83,86] examined primary data collected through the use of surveys, interviews, or focus groups; of these, 3[77,80,83] included self-reported barriers to care (Table 2). Eight studies[19,22,60,79,82,83,85,87] used large secondary data sources or medical records to examine racial/ethnic and socioeconomic disparities in ET use; of these, 3[77,79,86] examined adjuvant breast cancer therapy broadly, including not only ET use but also either chemotherapy, or chemotherapy with radiation therapy. Although these studies evaluated chemotherapy and radiation therapy as dependent variables, some studies included these treatment variables (i.e., surgery, chemotherapy, radiation) as predictor variables of ET use[19,22,60,81,82,84,87] and other studies[78,80,83], did not include treatment variables in their analyses. One study stratified results by chemotherapy receipt.[85] Finally, of all included studies, only 1 used a qualitative approach.[77]

Intrapersonal Characteristics

Multiple intrapersonal characteristics were associated with ET use: race/ethnicity, medication side effects, patients' health beliefs, and cost of medications, as well as other person-level characteristics.

Overall effect of race/ethnicity on endocrine therapy use—The effect of race/ethnicity on ET use varied by study; however, the majority of the studies indicated that there was significant racial/ethnic variation in ET use (Table 3). Several studies indicated that Black women had lower odds of initiating ET[77,79,85] and being adherent to ET[19,22] than other racial/ethnic groups. One study found no significant racial/ethnic differences in ET persistence by race/ethnicity; however, the authors did note racial/ethnic variation in reported barriers to care.[83] For example, the most commonly cited barrier to ET use among minorities was lack of physician recommendation, and this barrier was more commonly reported among Black women (17%) than among Hispanic women (3%; P = .038).[83] In another study, although being Black was not associated with ET adherence among women receiving the Medicare low-income subsidy, among those who did not receive this subsidy, Black women had increased odds of being non-adherent to tamoxifen (odds ratio [OR] = 2.60; 95% confidence interval [CI] = 1.39, 4.87) and increased odds of being nonadherent to an AI (OR = 1.86; 95% CI = 1.35, 2.55) compared with White women.[22]

Among high-risk patients (defined as women with increased genetic susceptibility to breast cancer; e.g., bilateral breast cancer before age 50 years), no racial/ethnic differences emerged in ET initiation; however, the opposite was true for women with sporadic (non–high-risk) breast cancer—Black women had lower odds of initiating ET (OR = 0.20; 95% CI = 0.06, 0.60) and non-Hispanic White women had lower odds of using ET (OR = 0.40; 95% CI = 0.17, 0.94) than Asian women.[84] This same study demonstrated that racial/ethnic differences in ET use decreased as the diffusion of ET into clinical practice increased over time.[84]

Hispanic or Latina ethnicity was also associated with differential ET use in certain studies, but the direction of association varied by study. Compared with non-Hispanic Whites, low-income Latina women participating in the California Breast and Cervical Cancer Treatment Program were more likely to be persistent with ET at 36 months if they were less acculturated (adjusted odds ratio [AOR] = 9.08; *P* = .001), where acculturation was defined as being more comfortable with the English language.[81] Interestingly, this association between ethnicity and persistence was nonsignificant among Latina women who were more acculturated. Other studies, which were not conducted in low-income study populations specifically, found that Hispanic women were less likely to initiate adjuvant therapy than non-Hispanic White women.[79,82] Specifically, 1 study[82] indicated that Hispanic women had decreased odds of ET initiation compared with White women (AOR = 0.82; CI = 0.71, 0.96). Asian race was also associated with ET use. One quantitative study[82] found that Chinese patients had 22% lower odds of initiating ET compared with White patients, and one qualitative study[77] also indicated lower ET initiation among Chinese women compared with other racial/ethnic minorities.

Several studies, however, did not find an association between race/ethnicity and ET use. Although a New Jersey Medicaid study indicated lower odds of adherence among non-Whites compared with Whites,[19] 2 studies conducted within a North Carolina Medicaid population found no association between race/ethnicity and initiation,[60,87] adherence,[60] or persistence.[60] Instead, these studies demonstrated low ET use across the board among low-income women in North Carolina. Another study found no racial differences in ET adherence; however, this was a small study conducted in 1 academic medical center.[78] The authors noted that low power and high insurance coverage rates among Black women in the study may explain the nonsignificant findings.[78] A study using self-report and Surveillance, Epidemiology, and End Results registry data (Los Angeles, CA, and Detroit, MI, regions) found that race was not associated with persistence; furthermore, the study found that Black and Latina women were more likely to initiate ET than Whites.[80] The authors suggested that peer support, patient navigator programs, and other important contextual factors may explain improved ET use among Black and Latina women.[80] Overall, variation in the effect of race/ethnicity on ET use likely arises from variation in study designs, populations, ET types, outcomes and measurement of other variables, and settings.

Side effects—Side effects were strongly associated with ET use across quantitative and qualitative studies. Among low-income women, those who experienced side effects had lower odds of persistence at 36 months (AOR= 0.26; *P* = .003; Table 4).[81] Furthermore, side effects emerged as an important concern during patient focus groups.[77] In particular, changes in body image and sexual concerns as a result of ET use were noted as common concerns across all racial/ethnic groups.[77] In 1 study, fear of side effects was reported as a barrier among 28.8% of noninitiators: 40%of women who discontinued therapy reported side effects a reason for discontinuation, and 25%of women who discontinued therapy reported being worried about risks associated with ET.[80]

Racial/ethnic variation existed in the reporting of side effects as a barrier to ET use. For example, in 1 study, the most commonly cited barrier to ET use among Hispanic patients was side effects, whereas side effects were the least commonly cited barrier among Black women (16% vs 8%; non-significant).[83] Regardless of racial/ethnic variation in reporting, however, side effects were among the top reported barriers to ET.[83] Interestingly, 1 small prospective study did not find an association between concerns about side effects and ET adherence; this study instead found a positive association with ET adherence when women reported increased value in their provider’s opinion and when women had a higher perceived importance of ET, suggesting these factors may be the drivers for ET adherence, not concerns about side effects.[78]

Health beliefs—Several health beliefs were associated with ET use. Higher perceived efficacy of patient–physician interactions was associated with increased ET persistence among low-income women (OR = 1.04; *P* = .04).[81] Worry about recurrence was associated with increased odds of ET initiation; however, this association was not found with ET persistence,[80] suggesting that different factors influence different types of ET behavior.

A dislike for medication (23.2%), being unsure whether ET was helping (22.3%), feeling as though they had taken ET long enough (17.9%), and wanting to move on from cancer (16.1%) were all reported reasons for discontinuing ET by 4 years.[80]

Endocrine therapy–related costs—Costs were reported as a barrier to ET use across racial/ethnic groups in both qualitative and quantitative studies. Out-of-pocket costs among Medicare beneficiaries influenced ET use regardless of ET type and SES (including both patients who received low-income subsidies and those who did not across racial/ethnic groups).[22] In a qualitative study, financial burden and access to affordable breast cancer care were recurring themes among both key informants (i.e., community health workers and advocates in diverse breast cancer populations) and breast cancer survivors.[77]

In particular, Latinas noted job disruptions and financial hardships as barriers to ET initiation and adherence.[77] However, another study found that cost was a barrier to ET use among only 5% of women.[83] In yet another study, costs were rarely reported as a reason for noninitiation (5%); however, cost was reported more often as a reason for discontinuation among women who stopped ET before 4 years of therapy (18.8%), and a small proportion stopped for insurance-related reasons (7%).[80] Thus, it is unclear to what extent costs are a barrier specific to minorities in the use of ET across settings and populations. Variation in results regarding cost may be explained by changes in generic availability for tamoxifen and AIs over time during the different study periods.

Other person-level characteristics—Associations between other person-level characteristics and ET use were also observed. Education was not associated with ET use among a diverse, low-income population.[81] However, in a qualitative study, Latinas reported that, broadly, low education and language presented barriers to breast cancer care.[77] These differences may be explained by the inclusion of provider–patient communication factors, potentially suggesting that good communication, not education level, influences ET use.

Mixed evidence was found regarding associations between ET use and age, income, health care utilization (e.g., number of office visits), prescription use (e.g., number of other prescriptions), insurance status, clinical characteristics, tumor characteristics, and treatment characteristics. This variation is likely the result of variation in study designs and analysis methods, patient populations and settings, and ET use measures.

Interpersonal Characteristics

Several interpersonal characteristics were associated with ET use. In particular, studies reported that provider referral, patient–provider communication, and social support played a role in the use of ET.

Provider referral and recommendation—One study investigated the relationship between receiving a referral to a medical oncologist, race/ethnicity, and ET use.[79] Race/ethnicity was not associated with receiving a medical oncologist referral.[79] Furthermore, among women who saw a medical oncologist, race/ethnicity was not associated with receipt of adjuvant therapy (including radiation, chemotherapy, or ET). However, among women who did not see a medical oncologist, racial/ethnic differences in receipt of adjuvant therapies persisted, in that non-Hispanic White women were more likely to use ET than non-Hispanic Black or Hispanic White women.

Overall, these results suggest that referral to a medical oncologist may ameliorate disparities in the use of appropriate breast cancer care, perhaps by bridging knowledge gaps or provider network gaps through medical oncology consultation.[79] Another study indicated that women whose primary oncology provider was a medical oncologist had a higher likelihood of ET initiation than those whose primary provider was a surgeon; this association did not hold for ET persistence.[80] The authors suggested that patients who see a medical oncology provider may have clearer indications for ET use than those who see a surgeon or other provider, which may explain why there were differences in ET initiation by provider type, but not in persistence.[80]

Among ET-eligible women who did not initiate ET, 33.8% reported not taking ET because their provider said they did not need to, because the doctor left the decision up to them (21.3%), or because the doctor never discussed ET (7.5%).[80] However, some women reported not initiating ET despite a doctor's recommendation (18.8%).[80] Finally, of women who discontinued ET, 25% who stopped within 4 years after ET initiation reported doing so because of a doctor's recommendation.[80]

Patient–provider communication quality—The quality of communication between provider and patient appears to influence ET use across qualitative and quantitative studies. Patient-centered communication increased ET use among low-income Latina women, where patient-centered communication was defined as communication that explores "patients' ideas and concerns, and assesses and responds to their emotions and understanding" (AOR = 1.22; $P = .006$).[81(p830)] The effect of patient-centered communication on ET use did not vary by ethnicity in this low-income population.[81] Although quality of communication was important to patients, this study found that provider–patient discussion specifically about the hormonal activity of ET and how ET works biologically was not associated with ET use.[81]

Results from another survey indicated that communication about ET was rated lower among Black patients than among White patients ($P \leq .001$).[86] Quality of provider communication, extent of provider's involvement, and level of trust in the medical system were all rated lowest among Black patients.[86] Emergent themes from qualitative interviews and focus groups showed that patients and key informants believed there was "an urgent need for health care providers to become more culturally sensitive" during patient–provider interactions with respect to adjuvant treatment discussions.[77(p425)] Women who felt they received adequate information about ET were more likely to initiate ET than those who did not.[80]

Social support—In our review, we found that social support was not strongly associated with ET use. Hispanics (32%) were significantly more likely than were Whites (18%) and Asians (13%) to report being helped by parents, children, or grandchildren during ET-related decision-making, whereas Asians (38%) were more likely than were Blacks (22%) to be helped by a husband or partner.[86] This information may be important for the small minority of patients who indicated that discouragement from family (< 1%) and friends (< 1%) was a barrier to ET use.[83]

We should note that although marital status was associated with increased initiation in 1 study,[82] it was not associated with ET adherence among participants receiving a low-income subsidy through Medicare,[22] and not being married was associated with improved adherence (OR = 1.90; $P = .006$) and persistence (OR = 1.74; $P = .031$) among North Carolina Medicaid participants.[60] The authors suggested that this association reflects a different pattern of social support among the North Carolina Medicaid population than among other populations.[60] Variation in findings may reflect not only differences in patient populations but also differences in measures of social support. Marital status has been used as a proxy for social support; however, it may reflect only a fraction of the social support construct.

Community Factors

Community factors may also be associated with ET use. During interviews in a qualitative study, key informants indicated that "communities must be educated about breast cancer to maximize their use of available resources."[77(p412)] Also noted was the need for more diversity in staff and more partnerships with psychosocial services in the health care system. Finally, culturally and linguistically appropriate programs, such as community-based support groups and targeted public health programs, were identified as potential interventions that may improve quality of care for breast cancer patients.[77]

In support of this qualitative work, 1 study found that participating in the North Carolina Breast and Cervical Cancer Control Program was associated with increased odds of initiating ET.[87] This program provides free and low-cost breast cancer screening and follow-up to low-income women. Services are provided at local health departments, community health centers, hospitals, and practices across North Carolina. Thus, increasing access to public health resources may improve ET use. Other health system–level factors, such as hospital size,[60] urban versus rural residence,[87] and census tract–level income,[22] were not significantly related to ET use among low-income populations, suggesting that provider-and patient-level factors may play a greater role in ET use. However, in 1 North Carolina Medicaid study, women who were seen at a small hospital (< 100 beds) had greater odds of using any ET than women who were seen at a larger hospital (> 100 beds; OR = 1.49; $P = .024$).[60] Reasons for this difference were not discussed.

DISCUSSION

Medication initiation, adherence, and persistence remain a challenge for women taking adjuvant ET. Generally, medication adherence decreases as the longevity of a drug regimen increases.[2] Thus, issues surrounding adherence to ET have become even more important because evidence has demonstrated the additional benefit of taking ET for as long as 10 years after hormone receptor–positive breast cancer diagnosis.[88] Patterns of nonadherence mirror those of other long-term oral medications, with only approximately half of women completing ET as prescribed.

Although the evidence is mixed, the vast majority of studies included in this review suggested that ET is less optimally used by minorities and that barriers and facilitators to use also vary by race/ethnicity and SES. Studies examining adherence and persistence across multipayer populations will provide more insight into racial disparities in ET use. Although some barriers to care are relevant and cut across all racial/ethnic and socioeconomic subgroups (e.g., patient-centered communication, community factors), other barriers seem to vary in importance by subgroup and even within subgroups. For example, side effects, less education, and lack of physician recommendation were reported as potential barriers to ET use at different rates across racial/ethnic groups. At a more granular level, variation in ET use existed within racial/ethnic subgroups, such as Latina women with different levels of acculturation.

Results also indicated potential interactions between SES and race. In 1 study, the effect of cost on ET use did not vary by race among women receiving Medicare low-income subsidies; however, this was not true for women without the subsidy.[22] SES has long been recognized as a confounding factor for racial/ethnic disparities.[31] Competing social and economic demands may take priority over medication adherence, resulting in lower adherence among those in lower SES groups. Two of the 4 included Medicaid studies found no association between ET use and race, which contrasts with findings with more socioeconomically diverse populations.

Although race/ethnicity and SES are associated with medication behaviors, the current literature suggests that modifiable targets for improving ET exist. These targets include intrapersonal characteristics (such as side effect management, health beliefs, and costs), interpersonal characteristics (such as provider referral and provider communication), and community factors (such as community-based support groups, education, and resources). The multidimensional mechanisms behind nonadherence to medication remain complex and uncertain; however, this literature review homes in on modifiable barriers to ET use among racial/ethnic minority and low-SES subgroups and suggests that interventions to improve ET adherence should target these patient-specific modifiable barriers. Discussions in broader reviews of medication adherence suggest that the majority of current interventions to improve medication adherence have reported relatively small gains.[1–3] Thus, there remains a need for more innovative, multidimensional, patient-centered, and methodologically sound interventions.[1–3] The results of this literature review indicate that tailoring interventions to racial/ethnic and socioeconomic subgroups may improve ET use.

Looking forward, further disentangling the independent and interactive effects of race/ethnicity and SES on ET use will be important. Drawing a clear conclusion about their effects on ET use remains difficult because the current literature has used heterogeneous study designs, populations, and measures. Longitudinal cohort studies and qualitative work with providers and patients are needed to assess the role of race/ethnicity in ET initiation, adherence, and persistence, as well as to identify unique, multilevel barriers and facilitators across racial/ethnic and low-income groups.

This literature review has several limitations. First, we did not rate the quality of each included article. The quality of included studies varies, thus individual results should be interpreted with caution. Our literature review narrowly focused on racial/ethnic minority and low-SES patient populations in the United States; thus, results may not be applicable to broader breast cancer patient populations. ET is commonly used among women with metastatic breast cancer. We did not examine ET use in this setting; however, to our knowledge no such studies have been conducted. Finally, although we conducted a thorough systematic literature search in 2 large databases, the possibility remains that our review could have missed relevant articles.

To our knowledge, this literature review is the first to examine racial/ethnic and socioeconomic disparities in ET initiation, adherence, and persistence. Although other literature reviews have examined the broad use of ET,[36–48] we have taken a deeper look at studies that examined variations in and barriers to ET use among specific racial/ethnic minority and low-income patient populations. These results raise awareness of the need for (1) more nuanced information on how to overcome barriers to ET use across racial/ethnic and socioeconomic subgroups and (2) development of tailored interventions to improve ET use in targeted subpopulations. By further developing knowledge about barriers to ET use among racial/ethnic and low-SES subgroups, we can build the evidence required to help ameliorate disparities in breast cancer outcomes.

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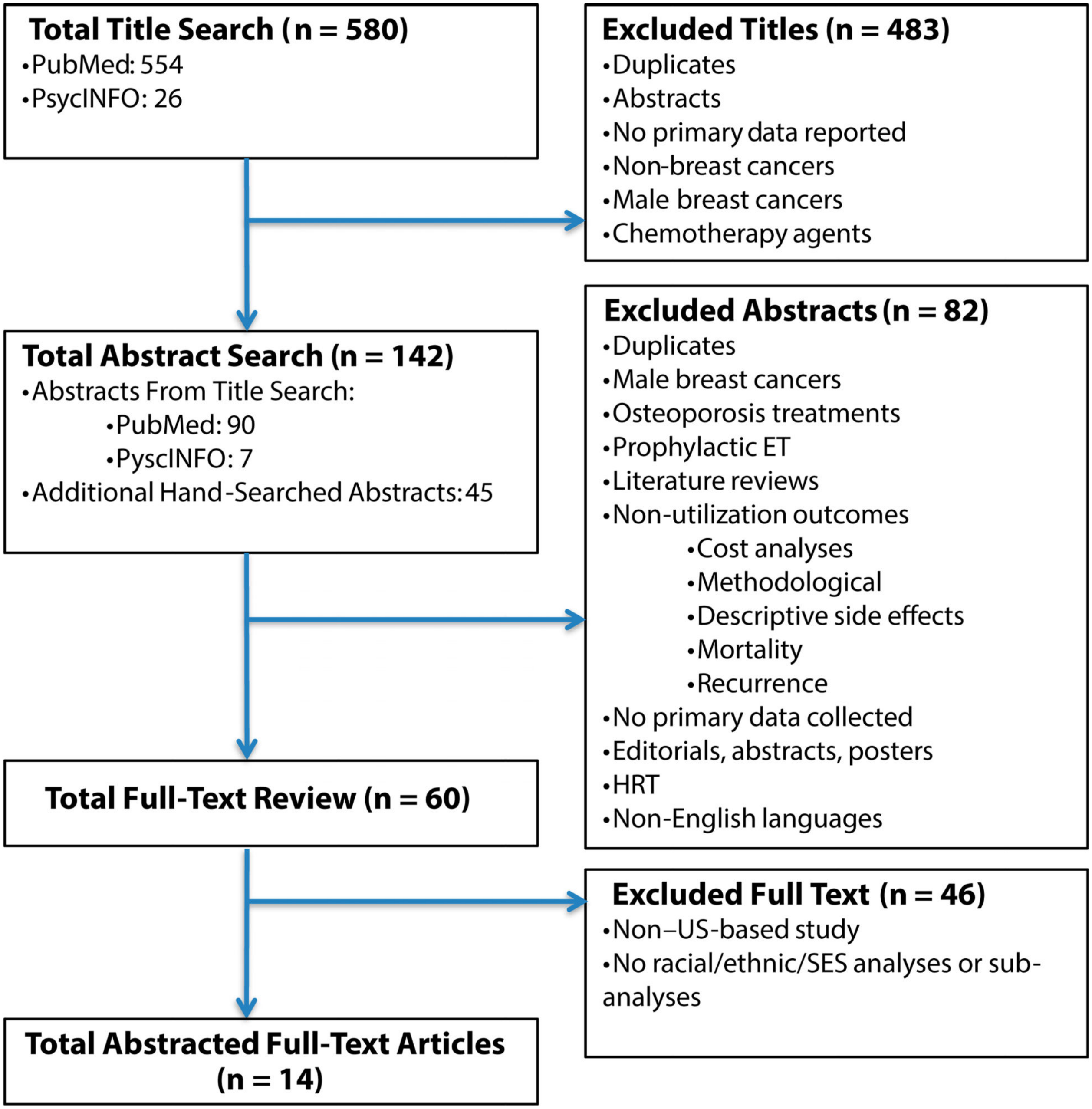

Note. ET = endocrine therapy; HRT = hormone replacement therapy; SES = socioeconomic status.

Figure 1.
Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram depicting the systematic search strategy.
Note. ET = endocrine therapy; HRT = hormone replacement therapy; SES = socioeconomic status.

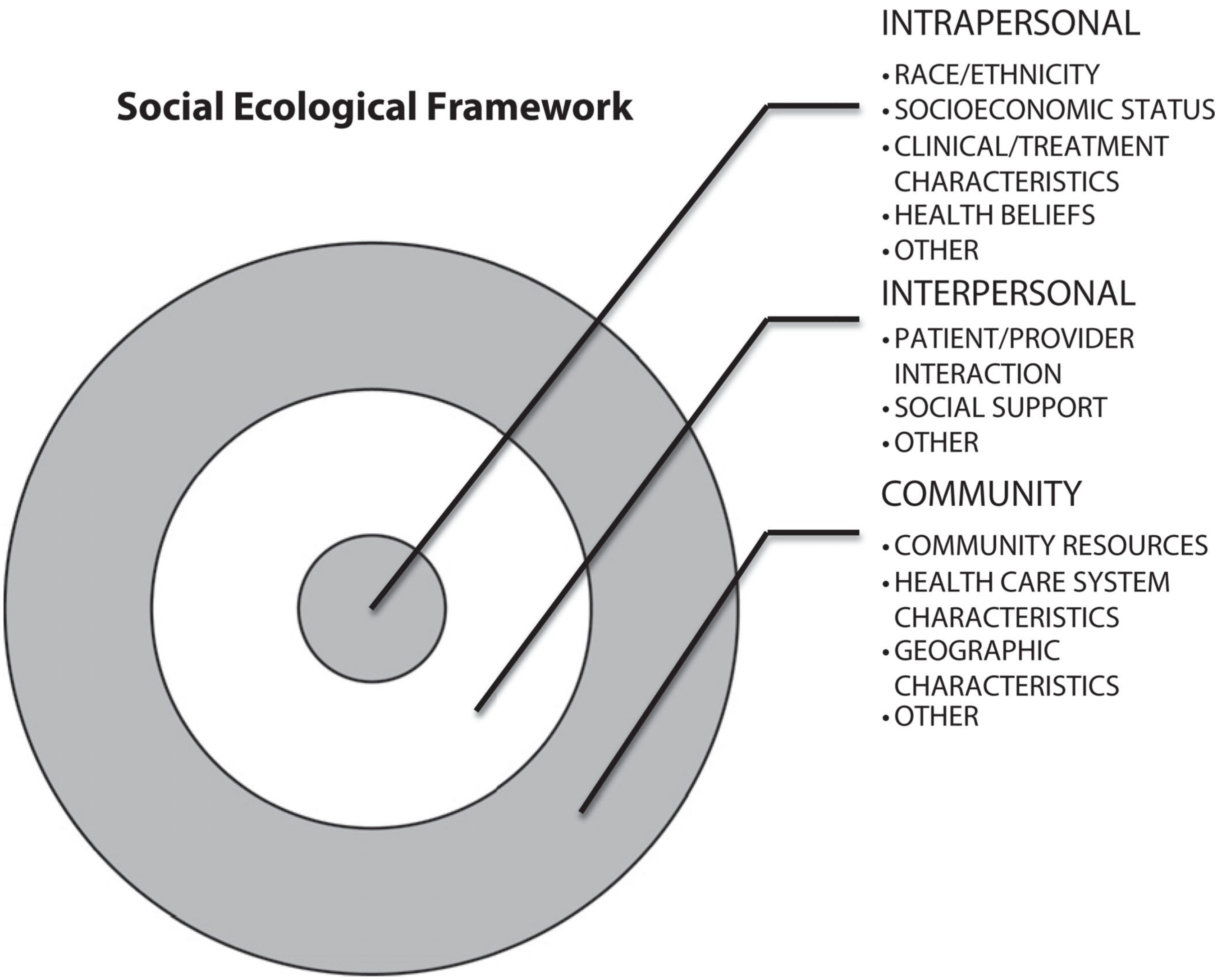

Figure 2.

Social ecological framework guiding data analysis.

TABLE 1

Description of Included Studies

First Author	Mean Age of Participants, Years	Sample, No.	% White	Cancer Stage	Medicaid or Medicare	Data Source	Type of ET	Dependent Variable	Analysis	Racial Comparators	Years of Data Collection	Setting
Ashing-Giwa[77]	NR	Patient, 102; provider, 20	Patient, 12; provider, 20	0–IV	Neither	Qualitative: interviews and focus groups	Breast cancer care (including ET)	NA	Qualitative	African American, Asian American, Latina, Caucasian	NR	UCLA community
Bhatta[78]	58	197	69	I–III	Neither	Survey and medical record review	Tamoxifen, AIs	Adherence, persistence	Multivariable logistic regression	White, Black	NR	University of Chicago Hospital
Bickell[79]	60	677	49	I–II	Neither	Medical record review	Breast cancer care (including ET)	Initiation	Multivariable logistic regression	White, Black, Hispanic, Asian, unknown	1999 and 2000 (diagnoses), 2002–2004 (abstraction)	6 NYC hospitals
Friese[80]	59	743	48	I–III	Neither	Survey and SEER Registry	Tamoxifen, AIs	Initiation, persistence	Multivariable logistic regression	White, Black, Latina	Time of diagnosis, survey 4 y after diagnosis	Multisite: LA and Detroit sites
Kimmick[60]	67	1 491	59	I–III	Medicaid	NC Central Tumor Registry and Medicaid claims	Tamoxifen, AIs	Initiation, adherence, persistence	Multivariate logistic regression	White, other	1998–2002	NC Medicaid
Liu[81]	51	303	34	I–III	Medicaid	Survey	Tamoxifen, AIs	Persistence	Multivariate logistic regression	Less acculturated Latina, more acculturated Latina, and other	2003–2005 enrollment	CA Medicaid
Livaudais[82]	59	13 753	76	I–III	Neither	SEER Registry, KPNC claims, and US Census	Tamoxifen, AIs	Initiation	Multivariable logistic regression	Hispanic, African American, Chinese, Japanese, Filipino, and South Asian vs WNH	1996–2007	Multisite, KPNC
Livaudais[83]	69	3 575	92	I–III	Neither	WHI Extension Survey	Tamoxifen, AIs	Initiation, persistence	Multivariable logistic regression	Hispanic, African American, Asian/Pacific Islander vs WNH	2009–2010	Multisite, parent study (WHI)
Livaudais[84]	Phase 1 = 49; phase 2 = 50	Phase 1 = 731; phase 2 = 654	Phase 1 = 58; phase 2 = NA	I–III	Neither	NCBCF Registry and self-report	Tamoxifen, AIs	Initiation	Multivariable logistic regression	African American, Hispanic, WNH vs Asian American	1995–1998 (phase 1) or 1998–2003 (phase 2)	Multisite, NCBCF Registry
Partridge[19]	75	2 378	83	0–III	Medicaid	NJ cancer registry and Medicaid claims	Tamoxifen	Adherence	Unconditional logistic regression	White, non-White	1991–1995	NJ Medicaid and NJ PAAD program
Reeder-Hayes[85]	NR	2 640	89	I–III	Neither	NC Central Tumor Registry and Claims: ICISS	Tamoxifen, AIs	Initiation	Generalized estimating equations; Cox proportional hazards	White, Black	2004–2009	Multisite: NC Registry
Riley[22]	NR	15 542	81	I–IV	Medicare	SEER Registry and Medicare claims	Tamoxifen, AIs	Adherence	Multivariable logistic regression	WNH, WH, Black, other or unknown	2003–2005 (time of diagnosis), 2006–2007 (time of ET use)	Multisite

First Author	Mean Age of Participants, Years	Sample, No.	% White	Cancer Stage	Medicaid or Medicare	Data Source	Type of ET	Dependent Variable	Analysis	Racial Comparators	Years of Data Collection	Setting
Shelton[86]	NR	1 145	69	I–III	Neither	Survey and medical record review	Breast cancer care (including hormonal therapy)	Treatment decision-making	χ^2 test and analysis of variance	White, Black, Hispanic, Asian, other	2006–2010	Multisite: Detroit, NYC, Northern CA (KPNC)
Wheeler[87]	49	222	47	0–II	Medicaid	NC Central Tumor Registry and Medicaid claims	Tamoxifen, AIs	Initiation	Multivariable logistic regression	White, Black, other	2004–2007	NC Medicaid

Note. AI = aromatase inhibitor; CA = California; ET = endocrine therapy; ICISS = Integrated Cancer Information Surveillance System; KPNC = Kaiser Permanente Northern California; LA = Los Angeles; NA = not applicable; NC = North Carolina; NCBCF = Northern California Breast Cancer Family Registry; NJ = New Jersey; NR = not reported; NYC = New York City; PAAD = Pharmaceutical Assistance to the Aged and Disabled; SEER = Surveillance, Epidemiology, and End Results; UCLA = University of California, Los Angeles; WH = White Hispanic; WHI = Women’s Health Initiative; WNH = White, non-Hispanic.

TABLE 2

Reported Barriers to Care and Recommendations From Included Studies

Barriers and Recommendations	Description
Intrapersonal factors	
Side effects	Side effects were noted as barriers to care.[77,80,83] In particular body image and sexual concerns emerged as common barriers for women across all racial groups during a qualitative analysis.[77] Fear of side effects was reported as a reason to not initiate ET among noninitiators (28.8%) and as a reason to discontinue (25%) among discontinuers. Also, some noninitiators (18.8%) chose not to initiate ET despite provider recommendations.[80]
Cost	Financial burden and job disruption emerged as barriers to care, with participants noting a need for affordable breast cancer care.[77] However, in a survey, cost specific to ET was a barrier among only 5% of patients and insurance was a barrier among only 1% of patients.[83] Another study reported a small number of women who discontinued ET reported lack of coverage by insurance as a reason for discontinuation (7.1%).[80] A small proportion of noninitiators (5%) reported that ET was too expensive.[80] However, a larger proportion of women noted cost as a reason for having discontinued ET (18.8%). Furthermore, < 1% of women were concerned about missing work.[83]
Education	Latina women felt that low education may be a barrier to care.[77]
Other	Patients infrequently listed inconvenience of use (< 1%) as a barrier to care.[83] Some women reported disliking medication (23.2%), being unsure whether it was helping(22.3%), feeling as though they had taken ET long enough (17.9%) and wanting to move on from cancer (16.1%) as reasons for having discontinued ET early.
Interpersonal factors	
Communication	Lack of a provider recommendation was the most commonly cited barrier across racial groups; however, Black women cited it most often.[83] Language was noted as a barrier to communication and breast cancer care.[77] “Doctor said I did not need” (33.8%), “doctor left it up to me” (21.3%), and “doctor never discussed” (7.5%) were reported as reasons for noninitiation among a group of noninitiators.[80] Patients reported discontinuing ET early because a doctor told them to (25%).[80]
Social	Discouragement from family (< 1%) and discouragement from friends (< 1%) were given as barriers to care.[83]
Community factors: recommendations	Recommendations from focus groups in 1 study primarily target a community-level approach so that patients can receive culturally and linguistically appropriate care.[77] Furthermore, educating the community and increasing cultural sensitivity were recommended to improve breast cancer care for a diverse patient population.[77]

Note. ET = endocrine therapy.

TABLE 3

Effect of Race on Endocrine Therapy Use Among Eligible Included Studies

First Author	**Outcome**	**Disparity**	**Data Source**	**Population (% African American)**
Partridge[19]	Adherence	White > non-White	Pharmacy claims	NJ Medicaid and NJ PAAD program (17%[a])
Riley[22]	Adherence	White > African American[b]	Pharmacy claims	Medicare (6%)
Kimmick[60]	Initiation	No significant association	Pharmacy claims	NC Medicaid (41%[a])
	Persistence	No significant association		
	Adherence	No significant association		
Liu[81]	Persistence	Less acculturated Hispanic > White	Self-report	CA Medicaid: CA Breast and Cervical Cancer Treatment Program (6%)
Livaudais[82]	Initiation	NHW > Hispanic, NHW > Chinese	Pharmacy claims	KPNC (6%)
Livaudais[84]	Initiation	Asian > NHW, African American[c]	Self-report	NCBCF (11%)
Livaudais[83]	Initiation, persistence	No significant association	Self-report	WHI study (4%)
Wheeler[87]	Initiation	No significant association	Pharmacy claims	NC Medicaid (53%[a])
Bhatta[78]	Adherence	No significant association	Self-report	University of Chicago Hospital (31.5%)
	Persistence		Self-report and medical record review	
	Compliance			
Reeder-Hayes[85]	Initiation	White > African American	Pharmacy claims	Privately insured (11%)
Friese[80]	Initiation	African American and Latina > White	Self-report	LA County and metropolitan Detroit SEER regions (14.2%)
	Persistence	No significant association		
Bickell[79]	Initiation	White > Black, Hispanic	Medical record review	6 NYC hospitals (21%)

Note. CA = California; LA = Los Angeles; NC = North Carolina; NHW = Non-Hispanic White; NJ = New Jersey; KPNC = Kaiser Permanente of Northern California; NCBCF = Northern California Breast Cancer Family Registry; NYC = New York City; PAAD = Pharmaceutical Assistance to the Aged and Disabled; SEER = Surveillance, Epidemiology, and End Results; WHI = Women’s Health Initiative.

[a] % non-White.

[b] Only among women without the low-income subsidy.

[c] Only among women with suspected hereditary breast cancer.

TABLE 4

Correlates of Endocrine Therapy Initiation, Persistence, and Adherence Among Minority and Low-Income Populations and Subpopulations in Included Studies

Correlate	Initiation	Adherence	Persistence
Age			
Older	Positive,[60,82] NS[87,80]	Negative,[19] NS[60]	Negative,[80] NS[81]
Younger		Negative[19]	
Married	Positive,[82] negative[60]	Negative,[60] NS[22]	Negative,[60] NS[81]
Education			NS[81]
Financial adequacy			NS[81]
Blind or disabled	NS[87]		
Comorbidity	Negative,[82] NS[60,85,87]	Positive,[19] NS[60]	Positive[60,81]
High hierarchical condition category (insurance risk)		Positive,[22] NS[22]	
Preexisting depression	NS[85]		
History of estrogen replacement therapy		NS[19]	
No. of prescription medications	Positive[60]	NS[60]	Positive,[89] NS[60]
Hormone receptor positive status	Positive[60]	NS[60]	NS[60]
Stage	Negative,[85] NS[80,87]	NS,[22] positive[22]	NS[80,81]
Grade 2 (vs 1)	Positive[80,82]		NS[80]
Grade 3 (vs 1)	NS[80,82]		NS[80]
Well differentiated (vs poorly)	Positive[85]		
Moderately differentiated (vs poorly)	Positive[85]		
Unknown differentiation (vs poorly)	NS[85]		
Lobular (vs ductal)	Positive[82]		
Other nonlobular histology (vs ductal)	Negative[82]		
Regional (direct extension or lymph node) vs local	Positive[60,82]	NS[60]	Positive[60]
Regional (direct extension and lymph node) vs local	NS[82]		
Mastectomy (vs BCS and/or no surgery)	Positive,[82] NS[60,87]	Negative,[19] NS[22,60]	NS[60,81]
BCS no radiation (vs BCS with radiation)	Negative[85]		
Mastectomy, no radiation (vs mastectomy with radiation)	NS[85]		
Adjuvant chemotherapy	Negative,[60,85] NS[82,87]	NS[19,60]	NS[60,81]
Radiation	Positive,[60] NS[87]	NS[19,60]	NS[60,81]
Perceived importance of ET		Positive[78]	
Value provider’s opinion		Positive[78]	
Concern about side effects		NS[78]	
Worry about recurrence	Positive[80]		NS[80]
Perceived efficacy in patient-provider interactions			Positive[81]
ET side effects			Negative[81]
Out-of-pocket costs		Negative[22]	
No insurance			Negative[81]

Correlate	Initiation	Adherence	Persistence
Insurance plan type (public employee versus other)	NS[85]	NS[19,22]	
Age at Part D enrollment		NS[22]	
Breast Cancer Cervical Cancer Control Program (vs Medicaid only)	Positive[87]		
Oncology visit within year		Positive[19]	
Primary oncology provider: medical oncology (vs surgeon)	Positive[80]		NS[80]
Patient-centered care			Positive[81]
Discussion about ET			NS[81]
Received enough information about ET	Positive[80]		
Use of other prescriptions (nonbaseline)		NS[19]	
No. of outpatient visits		NS[19]	
Nursing home use		NS[19]	
Days of acute hospitalization in prior y		NS[19]	
Urban	NS[60,87]	NS[22,60]	NS[60]
Small hospital (vs large)	Positive[60]	NS[60]	NS[60]
Zip code income ($30 000–$40 000 vs < $30 000)		Positive,[22] NS[22]	
% county poverty			
Lowest quartile vs high mid	NS[85]		
Lowest quartile vs highest	NS[85]		
Lowest quartile vs low mid	Negative[85]		
No. hospitals with oncology services in county			
Lowest quartile vs high mid	NS[85]		
Lowest quartile vs highest	NS[85]		
Lowest quartile vs low mid	Negative[85]		
Calendar year	Positive,[82] negative,[87] NS[85]	Negative,[22] NS[19,22]	

Note. BCS = Breast-conserving surgery; ET = endocrine therapy; negative = negative association with outcome ($P \leq .05$); NS = nonsignificant association with outcome ($P > .05$); positive = positive association with outcome ($P \leq .05$). Studies that looked at adjuvant breast cancer treatment broadly are not included. For studies that looked at racial/ethnic and socioeconomic subpopulations, only multivariable regression results for racial/ethnic minorities or low-income populations are included in this table.