



Disparities in Time to Treatment for Breast Cancer: Existing Knowledge and Future Directions in the COVID-19 Era

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Abstract

Purpose of Review Despite significant advances in detection and treatment for breast cancer, the breast cancer mortality rate for Black women remains 40% higher than that for White women. Timely work-up and treatment improve outcomes, yet no gold standard exists for which to guide providers.

Recent Findings A large body of literature demonstrates disparities in time to treatment for breast cancer, and most studies show that Black women receive treatment later than their White counterparts. The COVID-19 pandemic has been projected to worsen these disparities, but the extent of this impact remains unknown.

Summary In this review, we describe the available evidence on disparities in time to treatment, potential drivers, and possible mitigation strategies. Future research must address how the COVID-19 pandemic has impacted the timely treatment of breast cancer patients, particularly populations vulnerable to disparate outcomes. Improved access to multidisciplinary breast programs, patient navigation services, and establishment of standards for timely treatment are necessary.

Keywords Disparities · Breast cancer · Cancer screening · Time to treatment

Introduction

Despite advances in screening/early detection and systemic therapy, breast cancer remains a leading cause of cancer death among women and is the most commonly diagnosed malignancy in women after skin cancer [1]. While overall mortality from breast cancer has improved in recent decades, disparities persist and mortality rates are 40% higher among African American compared to White American women [2]. Additionally, African American women are more likely to present at a younger age and with later stage disease; they are also more likely to have biologically aggressive tumors such as high-grade disease and estrogen-receptor-negative tumors [1]. Compounding these biological differences in breast cancer presentation are additional factors such as socioeconomic status and reduced access to high-quality, timely

treatment among Black women. Prolonged time to treatment of newly diagnosed breast cancer has been associated with lower overall and disease-specific survival [3, 4]. However, heterogeneity exists regarding the definition of a treatment delay, as there is no current standard for time to treatment. To date, several studies have characterized racial disparities in time to treatment and provide retrospective data on how this may explain discrepancies in survival [4, 5–10]. In this review, we aim to summarize the current literature regarding disparities in time to treatment for breast cancer and the impact on survival, identify directions for future study considering the COVID-19 pandemic, and propose potential strategies to mitigate these time to treatment disparities.

Time to Treatment Impacts Survival

One of the difficulties in improving disparities in time to treatment is that there are currently no universally established benchmarks defining optimal intervals for initiating treatment following detection of a breast cancer. For example, time to treatment from the first diagnostic imaging study to core needle biopsy and time from the first positive needle biopsy to initial breast cancer surgery are included

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in quality measures developed by the National Consortium of Breast Centers [11]. Additionally, the Commission on Cancer (CoC) includes several measures regarding timely treatment for benchmark performance in CoC-accredited cancer programs [12] (Table 1). Evidence for these recommendations is driven by analyses of large national datasets that demonstrate that longer time to treatment is associated with worse outcomes, including reduced overall and disease-specific survival [3, 13–15]. Streamlining these definitions for providers would strengthen quality improvement efforts.

A large population-based study of SEER-Medicare data comprised of more than 94,000 patients showed that overall survival diminished with progressively increasing intervals of treatment delay (≤ 30 , 31–60, 61–90, 91–120, and 121–180 days) in time to surgery. In an analysis of the National Cancer Database (NCDB), the overall mortality hazard ratio was 1.10 for each increasing time interval [3]. For patients requiring neoadjuvant chemotherapy, a delay of more than 61 days from breast cancer diagnosis to initiation of neoadjuvant chemotherapy was associated with an increased risk of death [13]. Regarding adjuvant chemotherapy, multiple studies demonstrate adverse outcomes with initiation of therapy more than three months after diagnosis [14, 15].

These data suggest that ensuring timely treatment for breast cancer patients is relevant to the goal of optimizing outcomes.

Disparities in Time to Treatment

Disparities in time to treatment for breast cancer have been well documented over the last two decades. Currently, a large body of data exists that is driven predominantly by retrospective studies, ranging from single institutional studies to investigations of large national datasets. Most find that regardless of the first treatment modality, racial and ethnic minorities, particularly Black women, experience prolonged treatment delays compared to White women (Table 2).

Examining time to treatment among early-stage breast cancer patients, Hoppe and colleagues analyzed over 540,000 patients within the National Cancer Database

(NCDB). Black patients were found to have a significantly longer time to first treatment (35.5 days vs. 28.1 days) compared to White patients. This trend continued when stratified by treatment modality: surgery (36.6 days vs. 28.8 days), chemotherapy (88.1 days vs. 75.4 days), radiation (131.3 days vs. 99.1 days), and endocrine therapy (152.1 days vs. 126.5 days). Subset analysis among patients with private insurance found that the disparity remained, although it was reduced by 1.2 days [10].

In another NCDB study, time to surgery, defined as date of biopsy to first surgery, was examined among a cohort of 378,499 patients. Jackson et al. found that the odds of receiving surgery more than 60 days after diagnosis were higher among non-Hispanic Blacks (NHB) (OR 1.77, 95% CI 1.64–1.91) compared to non-Hispanic Whites. Specifically, 30.6% of NHB women had surgery more than 60 days after diagnosis compared to only 18% of White women [16•].

For patients undergoing primary surgical therapy for breast cancer, many factors may impact the interval from diagnosis to surgery such as genetic testing, consultation with a plastic surgeon for consideration of all surgical options such as contralateral prophylactic mastectomy (CPM) and reconstruction, and obtaining multiple oncology treatment opinions [3]. Recent work has found that racial and ethnic minorities are in fact less likely to undergo CPM and less likely to have genetic testing which would potentially reduce the odds of surgical delay for this patient population [17, 18]. However, most studies have nonetheless found that Black women tend to experience longer time to surgery than their White counterparts [5, 10, 16•, 19–23].

The role that other socioeconomic factors play in the treatment delays has been well studied, particularly the impact of insurance status. Analyzing patients from Phase 3 of the Carolina Breast Cancer Study, Reeder-Hayes et al. found that women with the longest treatment durations were more likely to be Black, younger, have a lower income, be uninsured or have Medicaid, be less educated, and have a higher stage at diagnosis [24]. Another study of 420,792 breast cancer patients from the NCDB undergoing primary surgical therapy found that as time to surgery increased, the percentage of Medicaid and uninsured patients also increased [8]. Importantly, other work has shown that higher

Table 1 Commission on Cancer (CoC) quality measures in time to treatment for breast cancer

Commission on Cancer (CoC) quality measures in time to treatment for breast cancer

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- Radiation therapy is administered within 1 year of diagnosis for women under age 70 receiving breast conservation surgery for breast cancer
 - Combination chemotherapy is recommended or administered within 4 months (120 days) of diagnosis for women under age 70 with AJCC T1cN0M or stage IB–III hormone receptor-negative breast cancer
 - Tamoxifen or third-generation aromatase inhibitor is recommended or administered within 1 year of diagnosis for women with AJCC T1cN0M0 or stage IB–III hormone receptor-positive breast cancer
 - Radiation therapy is recommended or administered following any mastectomy within 1 year of diagnosis for women with ≥ 4 positive regional lymph nodes
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Table 2 Recent studies evaluating disparities in time to treatment for breast cancer

Study	Design	Setting and number of subjects	Main findings
Babatunde (2021)	Retrospective cohort	South Carolina Central Cancer Registry (SCCCR) and Office of Revenue and Fiscal Affairs (RFA), 2002–2010, <i>n</i> = 2155	<ul style="list-style-type: none"> Black women received surgery, chemotherapy, and radiotherapy later than White counterparts Unadjusted mean time to surgery from diagnosis was longer for Blacks
Benefield (2021)	Population-based study with in-home interview	Carolina Breast Cancer Study Phase III, 2008–2013, <i>n</i> = 437	<ul style="list-style-type: none"> After adjusting for stage, Black women with hormone receptor-positive/HER2- high-grade tumors were more likely to experience a treatment delay
Bleicher (2017)	Retrospective cohort	National Cancer Database, 2004–2015, <i>n</i> = 622,793	<ul style="list-style-type: none"> After adjusting for all other variables, factors that nearly or more than doubled odds of having > 90 days between diagnosis and surgery included Black race and Hispanic ethnicity
Bustami (2014)	Retrospective cohort study	NYU and Morristown Medical Center tumor registry, 2007–2011, <i>n</i> = 3071	<ul style="list-style-type: none"> Longest median time to surgery observed for African American patients and longer absolute difference between African American compared to Whites with difference less pronounced for Asian/other compared to White
Champion (2020)	Retrospective cohort	National Cancer Database, 2004–2015, <i>n</i> = 903,008	<ul style="list-style-type: none"> After adjustment, Hispanic White women had longer time to surgery compared to non-Hispanic White women, regardless of treatment sequence No significant racial differences in time to surgery among Hispanic patients
Doe (2020)	Retrospective cohort	Henry Ford Health System, 2015–2017, <i>n</i> = 541	<ul style="list-style-type: none"> Mean time to treatment was significantly longer for Blacks than Whites both before and after implementation of multidisciplinary approach (MDC) Before MDC, significantly more White patients were treated ≤ 60 days than Black and significantly more Black patients were treated > 60 days but this difference no longer appeared after MDC
Eaglehouse (2019)	Retrospective cohort	Department of Defense Central Cancer Registry and Military Health System Data Repository, 1998–2008, <i>n</i> = 4887	<ul style="list-style-type: none"> In multivariable models, NHB women had longer time to surgery than NHW women Regarding survival, addition of time to surgery to multivariable model did not substantially attenuate the HR estimates compared with adjusted model—NHB had higher risk for all-cause death compared to NHW women
Foy (2018)	Retrospective cohort	James Cancer Hospital, 2005–2014, <i>n</i> = 4593	<ul style="list-style-type: none"> Mean number of days between diagnosis and treatment was significantly greater for Black women Proportion of Black women with more than 90 days between diagnosis and treatment onset was significantly greater than White women
George (2015)	Retrospective cohort	NJ State Cancer Registry, 2005–2010, <i>n</i> = 575	<ul style="list-style-type: none"> Median time to surgery was 29 days for White vs. 32 days for Black with 92% of White compared to 80% of Black patients receiving surgery within 2 months of diagnosis Black patients more likely to experience surgical delay more than 3 months In models adjusted for situational barriers, Black patients at increased risk for both diagnostic and surgical delay compared to Whites

Table 2 (continued)

Study	Design	Setting and number of subjects	Main findings
Halpern (2016)	Retrospective cohort study	Medicaid data, 2006–2008, $n = 7452$	<ul style="list-style-type: none"> Black Medicaid beneficiaries were more likely to experience delays for breast-conserving surgery and outpatient and inpatient mastectomy
Hoppe (2019)	Retrospective cohort	National Cancer Database, 2004–2014, $n = 546,351$	<ul style="list-style-type: none"> Black women had significantly longer times to first treatment, time to surgery, chemotherapy, radiation, and endocrine therapy than White women Despite private insurance, Black women still had longer time to surgery than White patients
Jackson (2021)	Retrospective cohort	National Cancer Database, 2010–2016, $n = 378,499$	<ul style="list-style-type: none"> Median time from diagnosis to first surgery was longer for Black women than White 30.6% of Black women had surgery > 60 days from biopsy compared to 18.0% White On multivariable logistic regression, Black race associated with increased odds of surgery > 60 days from diagnosis
Khanna (2017)	Retrospective cohort	Boston Medical Center, 2004–2014, $n = 1130$	<ul style="list-style-type: none"> Black women had longer time to treatment compared to all other race groups and significance primarily driven by comparison of Black vs. White On multivariate model with race/ethnicity, marital status, stage, and first treatment delivered, race/ethnicity was the only independent predictor of time to treatment
Khorana (2019)	Retrospective cohort	National Cancer Database, 2004–2013, $n = 1,368,024$	<ul style="list-style-type: none"> On multivariable analysis, race was one of the several predictors of delay Black race was associated with increased time to initiation compared to White Increased time to initiation was associated with worsened survival in stage I and II breast cancer
Lamb (2018)	Retrospective cohort	Methodist University Hospital, 2002–2012, $n = 3072$	<ul style="list-style-type: none"> Black women with stage 0, I, II, and III breast cancer all had significantly longer median time to surgery than White women
Polverini (2016)	Retrospective cohort	National Cancer Database, 2004–2012, $n = 420,792$	<ul style="list-style-type: none"> As time to surgery increased, the percentage of Medicaid and uninsured patients and patients of Black or Hispanic race increased Overall, only time to surgery > 12 weeks was associated with significantly shorter survival When stratified by stage, stage I patients treated at 8 to < 12 weeks and > 12 weeks as well as stage II patients treated > 12 weeks had decreased overall survival compared with patients treated within 4 weeks

Table 2 (continued)

Study	Design	Setting and number of subjects	Main findings
Reeder-Hayes (2019)	Retrospective cohort	Carolina Breast Cancer Study, unknown timeline, <i>n</i> = 2659	<p>Women with delayed treatment initiation were significantly more likely to be Black</p> <ul style="list-style-type: none"> • Black women more frequently experience delayed treatment • Even in fully adjusted models, Black women had almost twice the frequency of delayed initiation compared to White women • After adjustment for age, receptor status, grade, and tumor size, a nonsignificant trend association with recurrence risk was suggested for patients with delayed initiation

Medicaid reimbursements for breast conserving surgery are associated with a decreased time from diagnosis to surgery [25]. These studies suggest that the etiology of these disparities is multifactorial and that insurance status clearly plays an important role.

Potential Mitigation Strategies

Potential strategies to mitigate disparities in time to treatment for breast cancer include a multidisciplinary approach to breast cancer care and utilization of patient navigators.

Recent work by Doe et al. sought to examine whether a multidisciplinary approach to breast cancer care may improve disparities in time to treatment. In their analysis of 541 patients, mean time to treatment was significantly longer for Blacks than Whites among patients both before and after implementation of the multidisciplinary care program (MDC). Although the gap in time to treatment between races was shortened in the MDC group from 18.7 days to 8.5 days, the improvement did not achieve statistical significance [26]. These data suggest that a multidisciplinary approach to breast cancer treatment may be one potential method to reduce disparities but additional confirmatory studies are needed.

Other data have shown that with the use of patient navigation services, time from initial presentation to definitive treatment can be reduced. For example, in their analysis of patients at an urban safety net hospital, Haideri et al. found that 67% of women in the pre-navigation group received treatment within 60 days of presentation vs. 75% in the navigator group [27].

While minority patients have historically been under-represented in National Cancer Institute (NCI)-designated cancer centers, one study elucidates how among certain communities comprised of predominantly minority patients, disparities may be reduced. For example, Parsons et al. retrospectively reviewed patients treated at an NCI-designated cancer center where 50% of the population identifies as Hispanic. On multivariate Cox proportional hazards modeling adjusting for age, cancer and treatment characteristics, and sociodemographic factors, no difference in time to treatment was found between Hispanic versus non-Hispanic White patients [28]. This finding underscores the importance of improving access to care at NCI-designated cancer centers particularly among communities where at least 50% of the population identifies as either Hispanic, Black, or other.

Disparities also appear to be less pronounced among patients treated within the U.S. military healthcare system. Outcomes of 6577 patients from the Department of Defense (DoD) central tumor registry demonstrate more equal access to treatment. Specifically, wait time from diagnosis to treatment was significantly shorter for Black women.

Additionally, Black women have improved survival when treated at a DoD facility compared to within the general population. These findings are likely explained by the fact that military personnel have unique characteristics and similarities in education, lifestyle, and socioeconomic status that is more consistent among race groups. This includes equal wage and housing policies that may contribute to less inequity compared to that seen within the general population. This work is further evidence that disparities are driven by more than just race, but also social determinants of health [29]. Furthermore, U.S. military healthcare system may serve as a model for providing more equitable care.

Impact of the COVID-19 Pandemic on Time to Treatment

The COVID-19 pandemic has been the catalyst for a tremendous amount of research in understanding and addressing healthcare disparities in the United States. This has been largely driven by the disproportionate impact of the COVID-19 mortality on racial and ethnic minorities which mirrors disparities seen with cancer. For example, in recent data from the Kaiser Family Foundation, Black, Hispanic, and American Indian/Alaska Native people are at least twice as likely to die from COVID-19 as their White counterparts. These disparities are also seen with respect to hospitalization rates [30].

Beginning in the spring of 2020 in the Northeast, widespread shelter-in-place mandates were enacted to curb the spread of COVID-19. Simultaneously, large healthcare systems underwent a major reorganization to allocate resources toward pandemic management. These measures included diversion of resources and personnel and suspension of routine healthcare including cancer screenings. At this time, surgeons were faced with a necessary surgical pause, to conserve personal protective equipment, and in some institutions transform operating rooms toward caring for COVID-19 patients [31, 32].

In response to this, the American College of Surgeons developed a set of guidelines for the triage and prioritization of surgery relative to illness severity and time sensitivity [33]. Additionally, the American Society of Breast Surgeons, the National Accreditation Program for Breast Centers, the Commission on Cancer, and the National Comprehensive Cancer Network assembled a COVID-19 Pandemic Breast Cancer Consortium to establish guidelines for the treatment of breast cancer patients during this unprecedented time [34]. Treatment recommendations were based on various features including clinical stage, biologic and phenotype characteristics, and patient-related factors.

As a result, many breast cancer patients who would have been eligible for immediate surgery were now having their

surgery postponed. While these guidelines were well intentioned, they may have inadvertently exacerbated disparities in time to treatment for surgery for Black patients [35•]. For example, previous studies have quantified the absolute difference in median time to surgery for Black versus White patients undergoing primary surgery. The majority demonstrate that Black patients consistently have surgery later than their White counterparts [5, 10, 16•, 19, 21–23].

Thus far, the impact of the COVID-19 surgical pause on outcomes for breast cancer patients remains unknown. Few studies have sought to quantify patient-reported delays in treatment and have identified patient factors that increase the odds of a delay. For example, one study of breast medical oncology patients from February 1, 2020, to April 30, 2020, who were scheduled for outpatient appointments found that 42.6% of patients had a COVID-19-related delay and/or change in treatment plan. The median COVID-19-related delay in systemic therapy was 24.5 days, and the median COVID-19-related delay for surgery and radiation was 47 and 55 days, respectively. On univariate analysis, Black/African American, Asian, and Other race groups were more likely to experience a COVID-19-related delay and/or change compared to White patients; however, on multivariate modeling, race and ethnicity were not associated with a delay [36•]. Another survey of breast cancer survivors in the United States found that race had no significant effect on patient-reported delays in care [37].

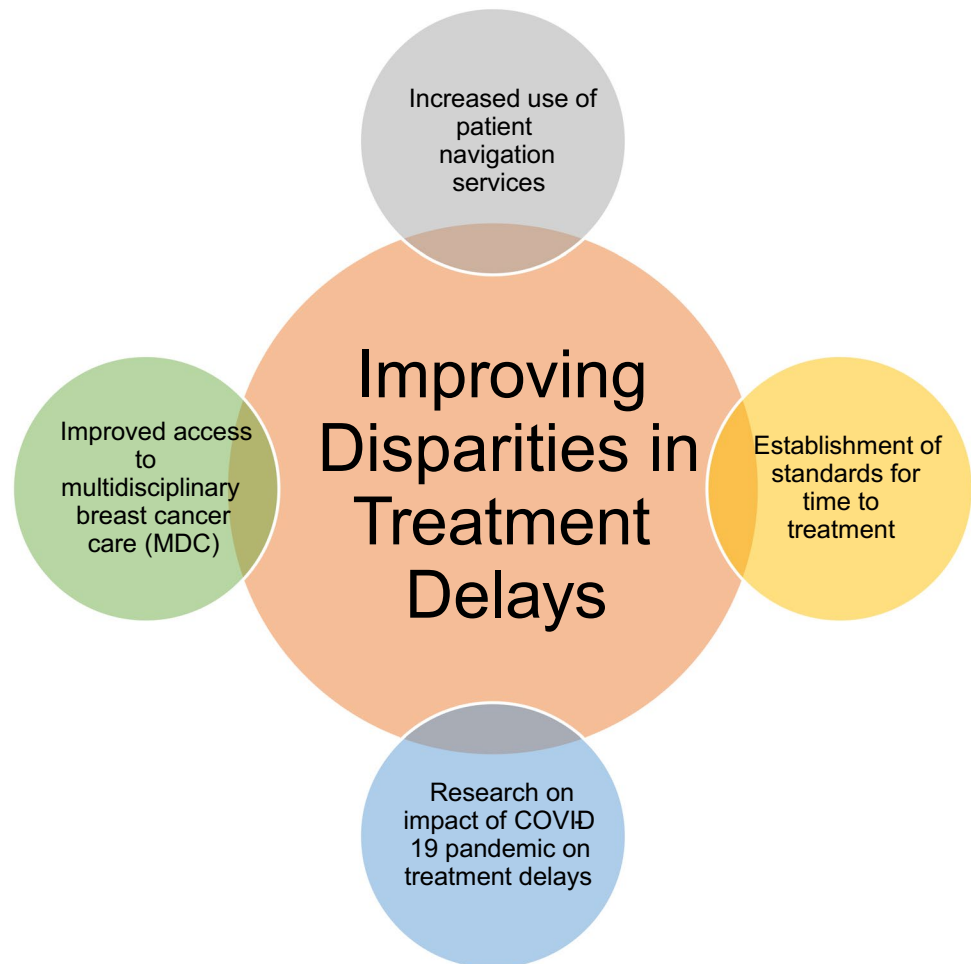
Future Directions

Future work is needed to characterize the impact of these widespread surgical delays, especially among vulnerable populations. Specifically, studies are needed that characterize time from diagnosis to surgery for breast cancer patients. Studies must be designed to account for social determinants of health such as financial stress, education, travel time to a healthcare facility, and geographical features specific to the pandemic, such as local lockdowns and suspensions of elective surgery.

While a large body of data exists documenting disparities in time to treatment for breast cancer, a paucity of data exists for mitigation strategies. Designing targeted interventions for more equitable breast cancer care is complex and should include the following (Fig. 1):

- Increased implementation of multidisciplinary breast programs at hospitals with a large volume of breast cancer patients
 - o Multidisciplinary breast cancer programs should be designed to provide comprehensive but efficient breast cancer care. Enabling patients to be seen by

Fig. 1 Strategies for improving disparities in treatment delays in the COVID-19 era



multiple disciplines on a single day can help overcome barriers to timely treatment by minimizing the number of visits. Additionally, coordination between disciplines such as surgery, medical oncology, radiation oncology, plastic surgery, and genetic counseling at a single site can streamline care for patients and improve communication about individualized treatment plans.

- Increased funding for patient navigation services, particularly among hospitals treating a large population of medically underserved patients
 - o Patient navigation services have been shown to improve outcomes and reduce treatment intervals for patients requiring complex cancer care [38]. Since the expanded use of telehealth services since the COVID-19 pandemic, expansion of navigation services to include telehealth visits will be prudent to increase access [39]. However, considering the digital divide, this will require expanded resources
- Establishment of standards for time to treatment to enhance awareness among providers
 - o More visibility on how time to treatment is an essential element of cancer care that improves outcomes is needed, particularly among providers caring for a large proportion of racial minorities and Medicaid or underinsured patients. By establishing standards for acceptable treatment intervals from presentation to diagnosis, diagnosis to treatment, and delivery of adjuvant therapies, providers will have metrics to adhere to, similar to the monitoring of adverse events.

to improve broadband internet services and education to familiarize patients with use of electronic communication methods. For example, orientation to the methods of communication available through the electronic medical record can empower patients to obtain enhanced follow-up and coordination of care.

Conclusions

In conclusion, disparities in time to treatment for breast cancer have been well documented. While most studies have found significant differences in the interval from diagnosis to treatment for racial and ethnic minorities and Medicaid or uninsured patients, more work is needed to investigate the impact that the COVID-19 pandemic has had on the diagnosis and treatment of breast cancer patients, particularly among vulnerable populations. Mitigating differences in treatment delays is complex but should include more widespread availability of multidisciplinary breast programs and patient navigators, as recent data have indicated their potential to improve disparities.

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Declarations

Ethics Approval and Consent to Participate This article does not contain any studies with human or animal subjects performed by any of the authors.

Conflict of Interest The authors declare no competing interests.

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