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Breast Cancer Disparities at home and abroad: A Review of the Challenges and Opportunities for System-Level Change

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Abstract

Sizeable disparities exist in breast cancer outcomes, both between Black and White patients in the United States, and between patients in the US and other high-income countries compared to low- and middle-income countries (LMICs). In both settings, health system factors are key drivers of disparities. In the US, Black women are more likely to die of breast cancer than Whites, and have poorer outcomes even among patients with similar stage and tumor subtype. Over-representation of higher-risk “triple negative” breast cancers contributes to breast cancer mortality in Black women; however, the greatest survival disparities occur within the good-prognosis hormone-receptor positive (HR+) subtypes. Disparities in access to treatment within the complex US health system may be responsible for a substantial portion of these differences in survival. In LMICs, breast cancer mortality rates are substantially higher than in the US, while incidence continues to rise. This mortality burden is largely attributable to health system factors, including late-stage presentation at diagnosis and lack of availability of systemic therapy. This article will review the existing evidence for how health-system factors in the United States contribute to breast cancer disparities, discuss methods for studying the relationship of health system factors to racial disparities, and provide examples of health system interventions that show promise for mitigating breast cancer disparities. We will then review evidence of global breast cancer disparities in low and middle income countries, the treatment factors that contribute to these disparities, and actions being taken to combat breast cancer disparities around the world.

Keywords

Breast Cancer; Disparities; Access to Care; Early Detection; Resource-Stratified Guidelines

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Introduction: Variation in Breast Cancer Outcomes at Home and Around the Globe

At first glance, the issues of breast cancer disparities in the United States and around the world appear to be quite distinct. In the US, a complex health care system offers widespread breast cancer screening and multidisciplinary breast cancer care including surgery, radiation, chemotherapy and targeted therapies. When appropriately delivered, this combination of screening and treatment has been highly effective in reducing mortality over time. In contrast, in low and middle income countries (LMICs), screening and multi-modality treatment are not widely accessible or affordable, with correspondingly higher mortality rates. Thus, when viewed through a global lens, breast cancer disparities are a complex series of comparisons: between more and less advantaged patients within each setting, and between the more favorable range of outcomes in high-income countries compared to the worsened spectrum in LMICs. In this review, we discuss how health system factors in both settings impact breast cancer disparities. In the US, we consider how the complexities of the health care system create disparities in access to care, at individual points on the cancer care continuum and cumulatively, that drive differences in outcome, focusing on the Black-White disparity. In the global context, we consider how gaps in the health care systems impact overall outcomes in LMICs compared to high income countries (HICs), as well as variation in outcomes for patients with better or worse access to care within LMICs. In both contexts, we discuss the promise of interventions at the health system level to improve outcomes for disadvantaged patients with breast cancer.

Disparities in the U.S

Epidemiology of Breast Cancer Race Disparities in the U.S

It is well-recognized that Black women in the United States are more likely to die of their disease than Whites, a survival gap that has persisted for more than three decades even as overall mortality rates have improved by 36%.⁽¹⁾ In 2012, Black women were 42% more likely to die of breast cancer than non-Hispanic White women, with a breast cancer death rate of 31 per 100,000 among Blacks compared to 22 per 100,000 among Whites.⁽²⁾ Meanwhile, breast cancer incidence among Black women continues to rise and has recently converged with the stable incidence rate of non-Hispanic White women, with incidence rates of 128/100,000 for Whites and 124/100,000 for Blacks in 2008–2012. This trend appears to be driven by increases in ER+ breast cancers (Fig 1a).⁽²⁾

Several recognized biological and clinical difference contribute to the breast cancer mortality gap, including higher incidence of hormone receptor (HR) and HER2 receptor-negative or “triple negative” tumor subtype in young Black women with correspondingly lower incidence of HR+/HER2– cancers (Figure 1a),^(1,3) more advanced stage at presentation, and higher grade and other adverse pathologic features in Black women with hormone receptor-positive tumor types.^(4,5) As discussed elsewhere in this issue by Desmedt and colleagues, considerable genomic variability exists among HR+/HER2– cancers, as well as other clinical subtypes, with regard to both pre-treatment mutational

status and acquired mutations associated with treatment resistance.(6) With the plethora of recent sequencing data, it is argued that sequencing further primary breast tumors is unlikely to discover new, common mutational signatures.(7) However, we posit that further characterization of racial differences in within-subtype biology, made possible by sequencing of tumors from large minority-enriched cohorts such as the Carolina Breast Cancer Study, may yield novel information regarding the biologic underpinnings of racial disparities.(8) Once tumor biology is accounted for, however, the presence of disparities within similar stage and subtype cancers, the unusual prominence of disparities in the highly treatable HR+/HER2- subtype relative to others, and the widening of the racial disparity in mortality over time (Figure 1) also suggest an influence of post-diagnosis factors on differences in outcome.(9) (10) This history and pattern of breast cancer disparity exemplifies the fundamental cause theory, which posits that disparities in health outcomes are related to differential access to and utilization of a complex variety of resources, and thus will persist despite treatment advances and be widest in groups where the most effective treatments exist.(11) It is possible that if novel, effective and expensive therapies emerge for triple negative breast cancer, such as the immunotherapy approaches discussed elsewhere in this issue,(12) disparities in the mortality of triple negative disease will paradoxically widen even as overall outcomes improve, if we do not solve the underlying problem of racial differences in access to cancer care.

The Health System and Breast Cancer Disparities

If we accept that differential access to healthcare resources is a key contributor to breast cancer disparities in the US and around the world, we must understand not only person-level but provider, institution and health system-level drivers of inequities in breast cancer outcomes in order to bring about change. Racial disparities in treatment exist across the cancer care continuum from diagnosis through surgery, chemotherapy, radiation and targeted therapies, are known to impact survival, and have been extensively described elsewhere. (13,14) Figure 2 illustrates how observed treatment disparities in the US add to biologic and stage differences to compound disparities in outcome.

Disparities in US Breast Cancer Diagnosis, Surgery and Adjuvant Therapy

At the entry point of the cancer care continuum, differences in access to diagnostic testing and surgical care may impact outcomes. For the most part, these disparities relate to delayed care, limited ability to pay for care, or inability to complete treatment. Uninsured women are more likely to have delays in resolution of abnormal mammographic findings,(15) and Black women in Medicaid or Medicare are more likely to experience delays in surgical treatment than Whites. Further, surgical delays are more common in states with less generous Medicaid reimbursement for breast surgery and more restrictive re-enrollment policies. (16,17) Black race and insurance type have been noted to be independent predictors of delays in surgical treatment in studies where both factors are considered.(18,19) However, among uniformly insured women, delays in surgery are more common among Blacks after controlling for clinical factors.(20) Thus, access to care may be particularly problematic for publically insured minority women, but racial disparities in surgical timeliness persist despite access to insurance.

The quality of surgical therapy also differs by race, and these differences are linked to the institutions where minority patients seek care. We and others have noted slower adoption and lower rates of sentinel lymph node biopsy, an innovative morbidity-sparing surgical procedure, among eligible Black women compared to Whites,(21,22) and these differences are partially explained by the concentration of White patients within National Cancer Institute (NCI)-designated comprehensive cancer centers, hospitals with high breast cancer volume, greater affiliation with research cooperative groups and the American College of Surgeons Oncology Group (ACOSOG), and the NCI's Comprehensive Community Oncology Program (CCOP).(23,24) Breast reconstruction is also less utilized by minority women, which appears to be related to lower access to plastic surgeons.(25) Interestingly, one large study showed that Black women were less actively involved in choosing their surgeon or hospital for breast surgery.(26)

Similar disparities are seen in radiation therapy. In two national studies, racial disparities in receipt and timeliness of adjuvant radiation were largely explained by differences in the distance to radiation care and the type of facility where patients received surgery.(27,28) Another study found that in California, racial disparities in radiation were found only in the most urban regions, and low socio-economic status was an independent risk factor.(29) A third study found that among low-income women, Blacks remained less likely than Whites to receive radiation.(30) Together, these studies suggest that racial disparities in radiation treatment differ based on where patients live, and that both race and poverty affect access to treatment.

Disparities in chemotherapy have been more difficult to pinpoint, with some studies showing Black women no less likely than Whites to receive chemotherapy for clinically similar disease.(31) However, multiple challenges exist in how chemotherapy is delivered. Black and Hispanic patients are more likely to have delays in initiating chemotherapy, which are associated with decrements in survival in multiple studies.(14,32,33) Black patients more often receive reduced-intensity adjuvant regimens and under-dosing of chemotherapy, particularly with respect to inappropriate "capping" of doses for overweight and obese patients.(34,35) Freedman and colleagues offer a more comprehensive discussion regarding the impacts of obesity, which is more common in Black breast cancer patients, on breast cancer treatment and outcomes elsewhere in this issue.(36) Regarding targeted therapies, Black women are less likely to receive trastuzumab and are more likely to receive non-standard chemotherapy in combination with trastuzumab within the Medicare program (37,38) and less likely to complete a full course of adjuvant trastuzumab even within National Comprehensive Cancer Network (NCCN) hospitals,(39) suggesting that insurance and site of care are not necessarily protective in the setting of very expensive treatments and those of long duration. Black women are less likely to initiate endocrine therapy than Whites, (40) and more likely to have difficulty with adherence.(41–43) Although not specific to Black women, multiple studies suggest that policy factors such as co-payment amount, the availability of generic alternatives, and Medicare low-income subsidies enhance adherence to endocrine therapy.(44–46)

Methods for Observational Study of Health System Contributors to Disparities

The Institute of Medicine (IOM) has defined disparities as “the difference in treatment or access not justified by the differences in health status or preferences of the groups.”.(47,48) In practical terms, the IOM framework has been interpreted to mean that researchers should not adjust for factors such as education or poverty as separate covariates in models of racial disparities, because inequity in these factors is part of the social construct of race, and models that treat them as separate may give a distorted picture of the experience of minority patients. In other words, unequal treatment offered to clinically similar patients of different races constitutes a racial disparity, even if the basis of said unequal treatment was a socioeconomic factor such as lack of ability to pay for care. However, other researchers present models that examine the “residual direct effect” of race, or the remaining independent association between race and an outcome after adjustment for a wider variety of potential confounders including factors such as income and education.(49) Unadjusted differences between racial groups may also be informative and descriptive, as for instance when we examine the percentage of Black and White patients treated in a certain hospital who receive mastectomy. All three approaches may be valuable, but the investigator should consider the purpose of the research. Where the intent is to generate hypotheses about an unmeasured or unknown characteristic of a given racial group that might explain worse survival outcomes, such as biologically aggressive disease, a model that adjusts for all measurable confounders including clinical and socioeconomic factors may help support or refute the hypothesis of an as-yet-unmeasured factor in the disparity (the residual direct effect of race). However, if the purpose is to point out an area in which a racial group is receiving sub-standard care, and for which an intervention may improve delivery of appropriate care, a model that adjusts only for clinical need and treatment appropriateness (IOM model) will likely give a more interpretable picture of the extent of the disparity. Further, if the purpose is to understand the treatment experience of patients at a given point of care, descriptive estimates of treatment differences by race, without adjusting for other factors, may give an early indicator of whether there is cause for concern for a disparity, and are straightforward for most audiences to understand.

System-Level Actions to Reduce US Breast Cancer Disparities

Interventions at the level of individual institutions, health systems or insurance payers are an attractive avenue to narrow disparities for several reasons. They can reach a large number of patients, can be aimed at sites or geographic areas serving disproportionately minority patients, or where disparities are known to be largest. They may rely to some extent on tested strategies for organizational change and adoption of innovations. Finally, they may be attractive to funders and policy-makers when framed as improvements to quality of care, which can benefit patients broadly, but will be expected to accrue more benefit to patients currently receiving sub-standard care, which usually includes vulnerable populations. In their landmark “Unequal Treatment” report, the Institute of Medicine highlighted this need for interventions focused on the health services drivers of disparities.(47) Unfortunately, more than a decade later, research in this area of cancer care delivery is still under-developed. Examples of successful health-system interventions are highlighted in the following paragraphs.

Access to mammography and timely surgical care after mammography can reduce disparities by removing access barriers that contribute to advanced stage at diagnosis. The Centers for Disease Control Breast and Cervical Cancer Early Detection Program (BCCEDP) is a national program offering free or low cost screening to uninsured women, as well as Medicaid waivers and case management for women with abnormal screening results. Evaluations of this program have demonstrated that 90% of enrollees with abnormal results completed diagnostic workup and initiated treatment within 30 days of their abnormal finding.(50) There is also some evidence of decreases in breast cancer mortality related to uptake of BCCEDP screening.(51) Although not yet evaluated, Medicaid expansion and other provisions of the Affordable Care Act that lowered uninsured rates may also act to close disparities in access to breast screening and surgical treatment. This hypothesis is indirectly supported by data that ACA policies disproportionately increased insurance rates among lower-income and non-white patients.(52) However, the narrow care networks of ACA plans may paradoxically limit access to high quality cancer care; a recent study found that only 41% of ACA networks included an NCI-designated comprehensive cancer center. (53)

Patient navigation is an established intervention that may disproportionately benefit minority patients by mitigating differences in health literacy, access to resources, and self-advocacy. Navigators improve timeliness of diagnostic breast cancer care in vulnerable populations. (54) The Patient Care Connect Program, which provides lay navigation in rural and under-resourced community cancer centers in the network of the University of Alabama at Birmingham (UAB), shows promise as a cost-effective intervention in minority and low patients of lower socioeconomic status to enhance access and possibly increase enrollment to clinical trials, but requires intensive training and program support to be successful.(55–58) Navigation has been associated with high patient satisfaction, particularly among minority and elderly patients,(59) but more work on how to implement navigation in vulnerable populations and low resource settings is needed. At the provider and practice level, programs that engage practices in collaborative quality improvement work, such as the American Society of Clinical Oncology’s (QOPI) program and the MUSIC (Michigan Urological Surgical Improvement Collaborative) program for urology providers in Blue Cross Blue Shield’s Michigan network, hold promise to engage providers, identify high-value targets for quality improvement and promote adoption of guideline-concordant care by providers.(60–62) To date, no such program has been tested in breast cancer specifically, or as a direct intervention on treatment disparities. Payer-level interventions may also be vehicles to raise care to desired standards or to reach out directly to patients at risk of sub-optimal outcomes. Within integrated health systems, oncology clinical care pathways have been demonstrated to lower ER and hospital utilization and cost during breast cancer treatment;(63) they may also may offer a way to mitigate treatment disparities, but this application has not been evaluated.

Audit and feedback interventions offer potential to improve cancer care delivery to minority patients by using automated functions, such as the electronic health record (EHR), to alert providers or researchers when gaps in care occur, and putting systems in place to correct gaps. One such intervention in safety-net hospital sites in New York consists of a registry that interacts with EHRs across institutions to ensure that handoffs from surgery to oncology

providers occur seamlessly. Many technical barriers to implementation and competing priorities have been noted in this low-resource setting.(64) A similar intervention, the Accountability for Cancer Care Through Undoing Racism and Equity (ACCURE) study, is underway to improve delivery of adjuvant breast and lung cancer care in North Carolina.(65) Neither project has reported long term results at this time.

Disparities around the Globe

Epidemiology of Breast Cancer as a Global Epidemic

Breast cancer is the most common cause of cancer deaths among women worldwide, representing 25–35% of all female cancer cases.(66) Breast cancer incidence rates are higher in more developed than less developed regions, with 2012 incidence rates ranging from 18.9 cases/100,000 in Eastern Africa compared to 166.9 cases/100,000 in Western Europe. However, breast cancer incidence is increasing most rapidly in LMICs, which are poorly equipped to deal with this burden and are disproportionately affected by the rising incidence and mortality. Breast cancer fatality rates are inversely correlated with per capita gross domestic product (GDP).(67,68) Once considered primarily a disease of women in HICs, over half (52%) of new breast cancer cases and 62% of deaths occur in LMICs.(69) In 2012, breast cancer incidence in the U.S. and Canada combined accounted for only 15% of new breast cancer cases worldwide. In contrast, countries in Asia, Latin America and Africa, which include the majority of LMICs around the world, accounted for 54% of new cases. (68) The disproportionate number of young lives lost to breast cancer is especially concerning; among the 94,000 women ages 15–49 years who died of breast cancer around the world in 2010, 68,000 (72%) were in LMICs.(70) The impressive progress made in HICs to improve breast cancer outcomes has not been mirrored in LMICs. Breast cancer mortality rates in the U.S. and Europe have dropped nearly 2% each year since 1990.(71,72) In HICs, implementation of breast cancer early detection programs (including, but not limited to, population-based mammographic screening) together with locoregional treatment (management of the breast and axillary nodes using surgery and radiotherapy) (73–76) and systemic treatments (pharmacologic therapy that reduces the risk of metastatic spread) (77–80) has resulted in impressive reductions in national breast cancer mortality in HICs.(81–84) By contrast, breast cancer incidence rates have historically been low in LMICs, but these rates are rising disproportionately at the same time that mortality rates are continuing to rise or remain high. The aging of the current global population means that nearly 50 percent more women will develop and die from breast cancer in 2020 than in 2002.(85)

There are many parallels between the domestic breast cancer disparities issues and global breast cancer, especially in comparing underserved communities in the U.S. with populations from LMICs. However, the global breast cancer questions have to consider a broader set of questions that relate to cancer treatment access overall. In much of the world, countries are just beginning to consider making cancer treatment available at a population level. Thus the most critical research questions have some fundamental differences comparing the U.S. and global communities. In the U.S., we view cancer early detection, diagnosis and treatment as a standard component of healthcare delivery and therefore focus on biological questions related to incidence and treatment. In LMICs by contrast, cancer

treatment is often considered beyond what is feasible for healthcare delivery outside of private healthcare facilities treating the minority with adequate financial means to pay independently for care, making the most important questions related to access and resource-appropriate treatments with therapies already proven to be effective in HICs. In Table 1, we compare and contrast key contributors to racial disparities in the US and LMICs, along with examples of system-level interventions that may be effective for each.

Breast Cancer Early Detection – A Prerequisite for Improving Global Breast Cancer Outcomes

The case for improved breast cancer early detection, i.e., making diagnoses at an earlier phase of malignant progression, to improve breast cancer survival is supported by evidence from randomized controlled trials (RCTs) and meta-analyses, which demonstrate better prognosis with incrementally smaller tumors.(86,87) A study examining breast cancers diagnosed between 1975–1999 reported that stage migration – as assessed by a reduction in tumor size in the period – accounted for a significant proportion of the survival benefit during that time in the U.S.(88) While screening mammography has been shown to be effective at reducing breast cancer mortality,(89,90) clinical breast examination (CBE) has been shown to effectively downstage breast cancer in LMICs where women are commonly diagnosed with advanced stage cancer at first presentation.(91,92) The 25-year update of the Canadian National Breast Screening Study was widely publicized for finding no survival benefit for women who underwent screening mammography.(93) Largely overlooked, however, were the highly successful early detection rates achieved in the study’s control group receiving clinical evaluation without mammographic screening, where the median invasive tumor size at diagnosis approximated 2cm for the first 10 years of the study, which is significantly better than LMICs like India where 75% of patients present with locally advanced (stage III) or metastatic (stage IV) cancer. The highly favorable early detection outcomes of the Canadian trial control group were achieved through breast health education combined with annual CBE but without mammographic screening, suggest that the study’s control group methodology could be a model for early detection program development. These findings indicate that countries unable to afford or implement mammographic screening should begin with the development of breast cancer awareness and CBE programs as a foundation for establishing breast cancer early detection.(94)

Systemic Adjuvant Therapy – An Essential Element for Improving Breast Cancer Survival

Early detection and adjuvant systemic therapy are synergistic and mutually dependent for improving breast cancer outcomes, since early detection only works if it can be followed by prompt, effective therapy.(95) Mathematical modeling suggests that between 28% and 65% of breast cancer mortality reduction can be attributed to early detection; the balance is due to pharmacotherapy with endocrine therapy, cytotoxic chemotherapy and targeted biologic treatments.(77,79,80,96,97) Unfortunately, many LMICs have limited resources to allocate to early breast-cancer detection, as well as cultural and social barriers, resulting in late diagnosis, which is more difficult to treat effectively, and is associated with increased morbidity and mortality.(98) Multiple barriers to breast healthcare exist in LMICs including lack of resources, inequitable distribution of services in urban vs. rural areas, and poverty. Total expenditure on health per capita (US\$) in 2013 in counties classified by the World

Bank as low income averaged US\$36, compared to \$277 in middle-income countries, and \$4,687 in HICs.(99) Despite the increase in breast cancer incidence and the concomitant increase in breast-cancer related mortality, cancer is often a low priority in many LMICs, with spending on all cancers averaging 5% of the total expenditure on health.(100) In the past, the primary focus of healthcare dollars was for infectious diseases. However, rising rates of mortality related to the major noncommunicable diseases (NCD) led the United Nations to hold a high level General meeting in September 2011, heightening the awareness of member states to focus on the importance of leading non-communicable disease killers including cancer, heart disease, diabetes, and chronic respiratory disease.(101)

At the present time, access to effective treatment is limited or unavailable in many or most LMICs. A recent report reviewing national essential medicines lists (NEMs) from LMICs found significant variation in available treatments for different types of early breast cancer: over 80% of the countries in the American hemisphere included all therapy components for all types of early breast cancer (except for HER2-overexpressing tumors). By comparison, over 40% of the countries in the Eastern Mediterranean and African regions did not have all treatment components for any subtype, and guideline-recommended treatments were less frequently included in the NEMs of low-income than in middle income countries.(102) Even when included in NEMs, actual availability of and access to many anti-cancer therapies can fall far short in many countries. As a result, cancer early detection and treatment disparities are reflected in worsened survival rates for women in LMICs versus HICs: five-year survival following breast cancer diagnosis is greater than 80% in the United States compared to only 32% in in sub-Saharan Africa.(98,103) Effective solutions are thus urgently needed at the global level to improve breast cancer outcomes and make measureable improvements in women's health and well-being. Tools that have proven effective in the U.S., such as patient navigation, could play a valuable role in improving patient coordination in LMICs. There may also be opportunities for collective bargaining to achieve drug access at affordable rates in LMICs.

Call to Action to Reduce Global Breast Cancer Disparities

In 2014, a call for action to reduce disparities in breast cancer outcomes around the world by the American Cancer Society, Susan G. Komen for the Cure® and the Union for International Cancer Control (UICC), led to the formation of the Breast Cancer Initiative 2.5 (www.bci25.org), co-organized by the Breast Health Global Initiative (BHGI) and WE-CAN. BCI2.5 is a global campaign to unite the global breast cancer community behind a common goal to make breast health a global health priority and to reduce disparities in breast cancer outcomes for 2.5 million women by 2025. BCI2.5 explores innovative ways to implement affordable, appropriate, acceptable and feasible evidence-based strategies. A key element of this initiative is identifying, documenting and fostering dissemination of innovative approaches to the delivery of breast healthcare developed in low-resource settings.(104) This demands a collaborative effort that draws on the collective expertise and resources of individuals and institutions engaged in breast cancer care.(105) Future directions will hinge on identifying individualized approaches based upon building functional systems that provide effective early detection, diagnosis and treatment approaches based upon the implementation of existing resources.(106)

Conclusion

The issue of breast cancer disparities can be seen from many perspectives, domestically and globally. We have demonstrated that in both high-resource settings such as the United States, as well as the resource-constrained settings of LMICs, the outcome of breast cancer is often determined not only by its inherent biological and clinical characteristics, but by modifiable treatment factors highly influenced by access to care within a given health system. Across these diverse settings, a common thread is the need for innovative, flexible methods of delivering cancer care that make the best use of resources and eliminate barriers to optimal care for the most vulnerable patients. A true cancer care continuum links resources from early detection through timely and effective treatment in a robust chain leading to the best possible outcome for each individual patient. Only through strong health systems can we see the amazing innovations of breast cancer research in the 21st century reach their full potential as we reach the right patients at the right time with the right treatment.

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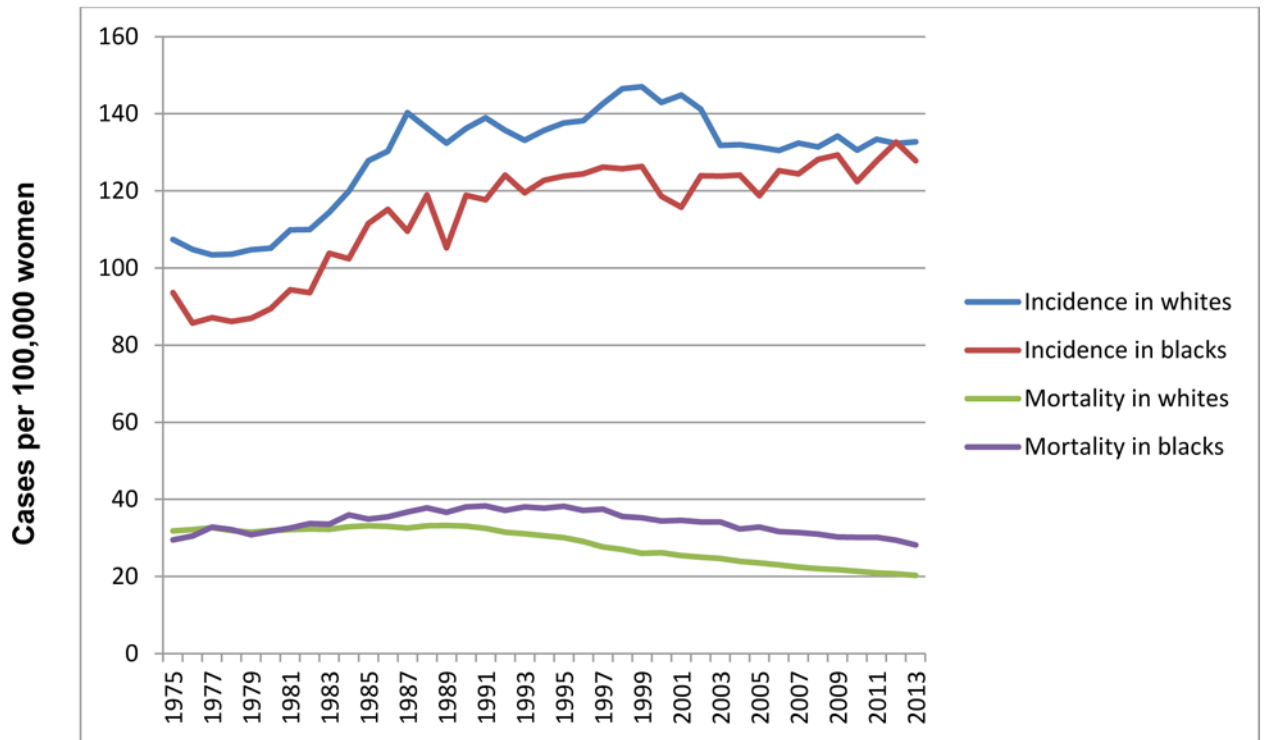
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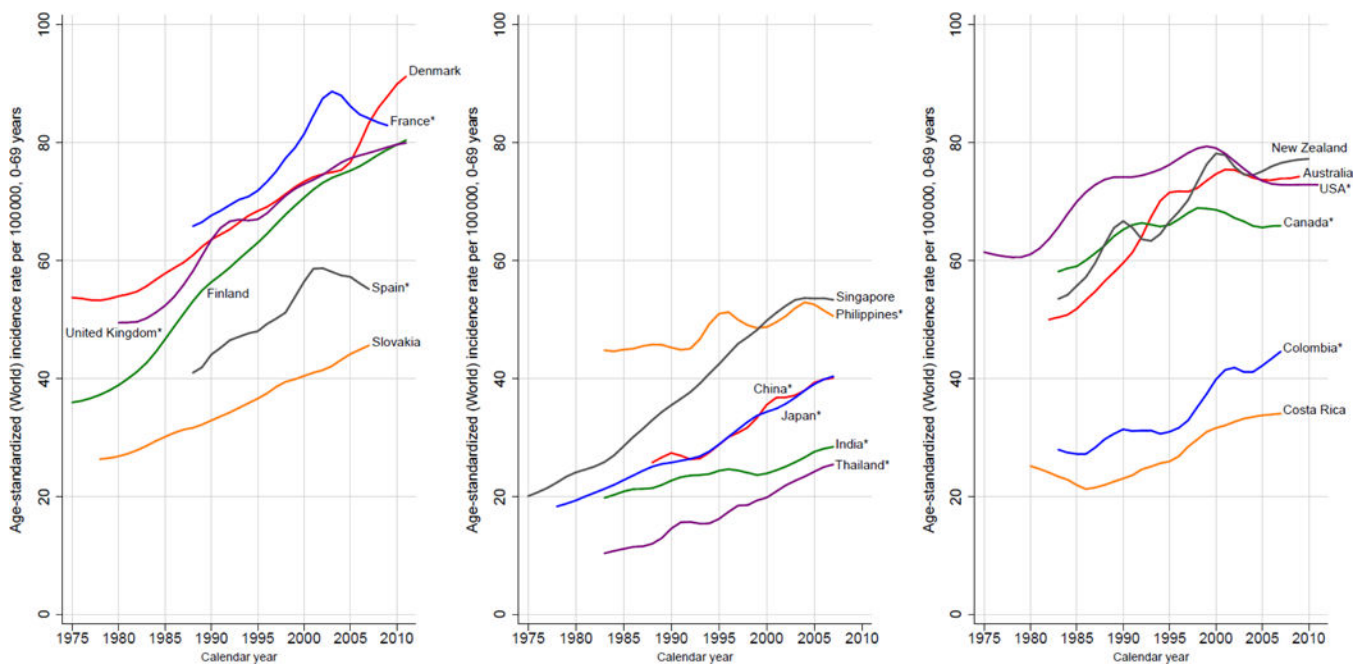
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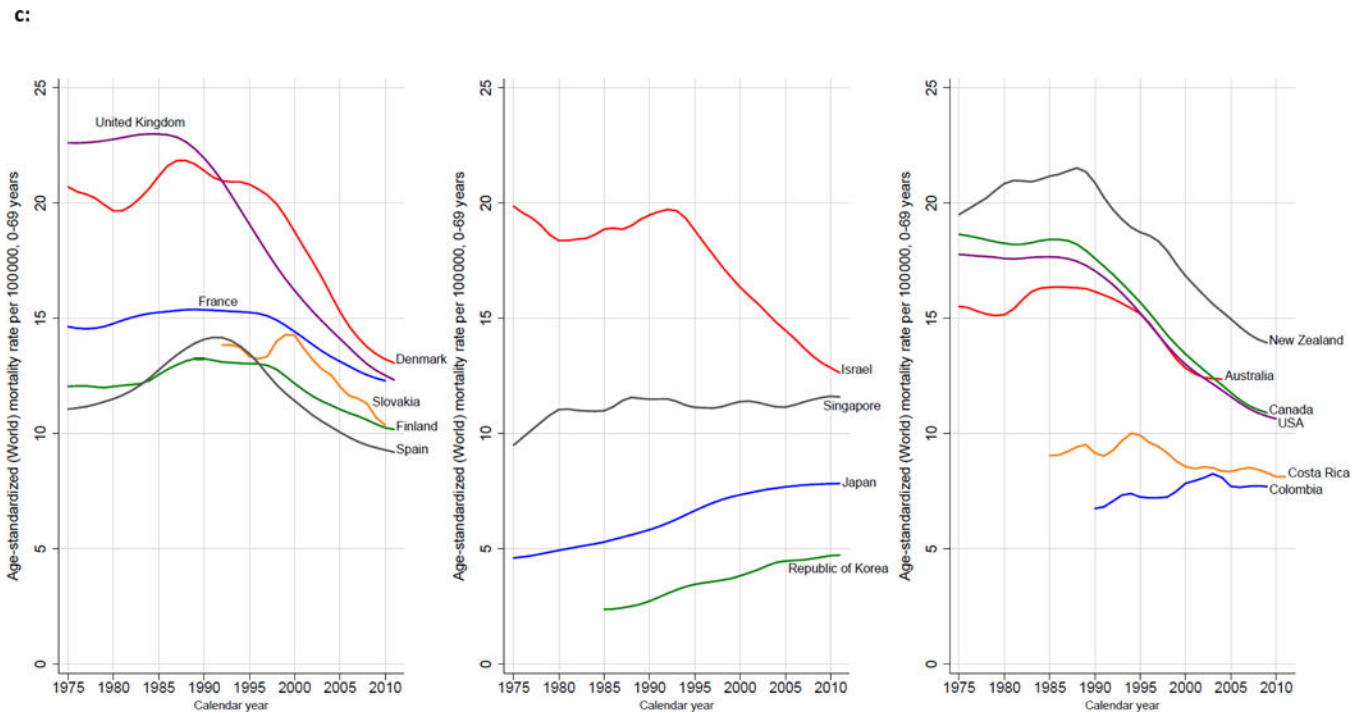


Figure 1.

a: Trends in age-adjusted incidence and mortality of breast cancer in US black and white women, 1975–2013 (data from Surveillance Epidemiology and End Results (SEER) 9 Sites)

b: Trends in Age-Standardized Breast Cancer Incidence, Selected Countries, 1975–2010.

Source: Ferlay and others 2013; WHO Mortality Database (http://www.who.int/healthinfo/statistics/mortality_rawdata/en/index.html), previously published.(107)

c: Trends in Age-Standardized Breast Cancer Mortality, Selected Countries, 1975–2010.

Source: Ferlay and others 2013; WHO Mortality Database (http://www.who.int/healthinfo/statistics/mortality_rawdata/en/index.html), previously published.(107)

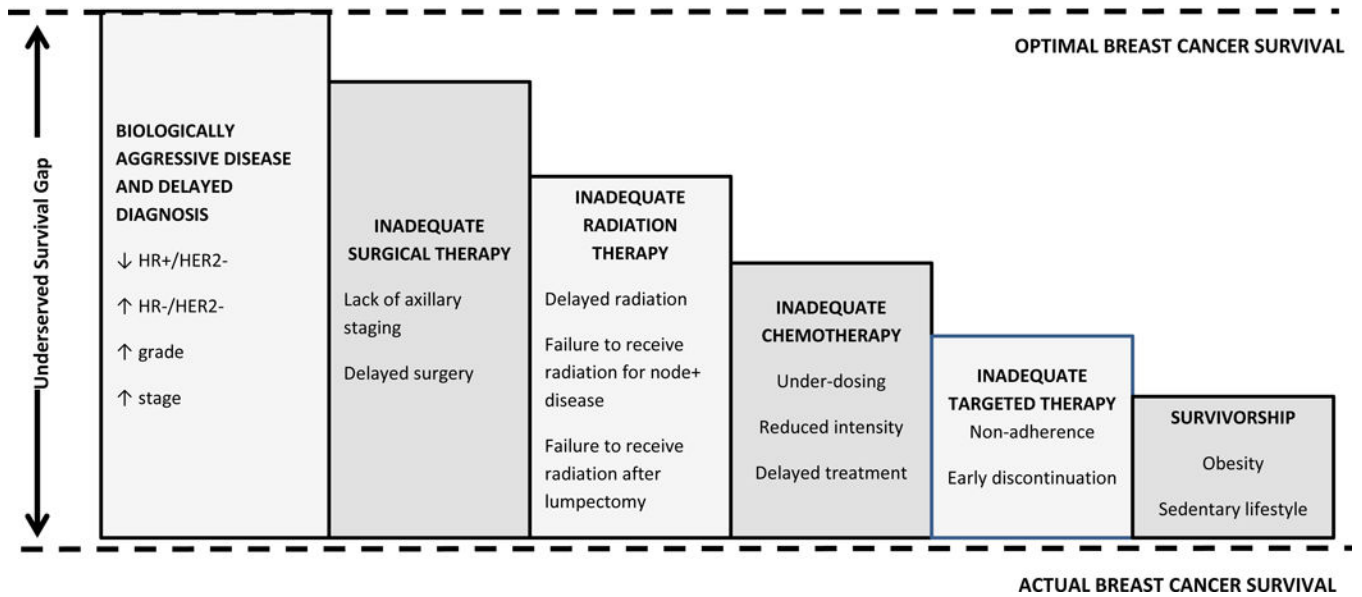


Figure 2. Contributors to US and global outcome disparities in breast cancer across the cancer care continuum. In addition to lack of any treatment (e.g. lack of radiation, lack of chemotherapy), specific treatment gaps are listed in each bar.

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Table 1

Summary of cancer care delivery gaps and possible system-level interventions in the US and low and middle income countries (LMICs)

Care Gap	United States	LMIC	US System Interventions	LMIC System Interventions
Advanced stage at diagnosis	Yes	Yes	Free screening programs Medicaid expansion Increased insurance access	Breast health awareness education and improved early diagnosis strategies
Delayed or Inadequate surgery	Yes	Yes	Insurance access Medicaid policy change Patient navigation QI programs EHR alerts	Address timely access to cancer surgery without requiring patients to pay privately out of pocket
Delayed or No radiation	Yes	Yes	Patient navigation Audit and Feedback QI programs EHR alerts	Determine if radiation therapy is available in country and then properly triage patients for timely treatment
Lack of chemo therapy/ biologics	No	Yes	–	Assess access to drugs on WHO's Essential Medicine List and improve availability at decreased cost through collective bargaining
Chemo under-dosing or non-standard agents; early discontinuation	Yes	Yes	Audit and Feedback Clinical Pathways QI Programs	Assess proper drug utilization and delivery in existing systems and evaluate quality control
Lack of endocrine therapy	Yes	Yes	Pharmacy system alerts Patient navigation Co-pay assistance	Establish estrogen-receptor testing availability and secure tamoxifen and generic aromatase inhibitor access for properly selected patients