

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 United States and other high-income countries compared with low- and middle-income countries (LMIC). In both settings, health system factors are key drivers of disparities. In the United States, 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. Overrepresentation 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 U.S. 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 United States, whereas 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 LMICs, the treatment factors that contribute to these disparities, and actions being taken to combat breast cancer disparities around the world. *Clin Cancer Res*; 23(11); 2655–64. ©2017 AACR.

See all articles in this CCR Focus section, "Breast Cancer Research: From Base Pairs to Populations."

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 United States, a complex health care system offers widespread breast cancer screening and multidisciplinary breast cancer care including surgery, radiotherapy, 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 (LMIC), 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 with the worsened spectrum in LMICs. In this review, we discuss how health system factors in both settings affect breast cancer disparities. In the United States, 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 affect overall outcomes in LMICs compared with high-income countries (HIC), 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 United States

Epidemiology of breast cancer race disparities in the United States

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 with 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 to 2012. This trend appears to be driven by increases in estrogen receptor-positive (ER⁺) breast cancers (Fig. 1; ref. 2).

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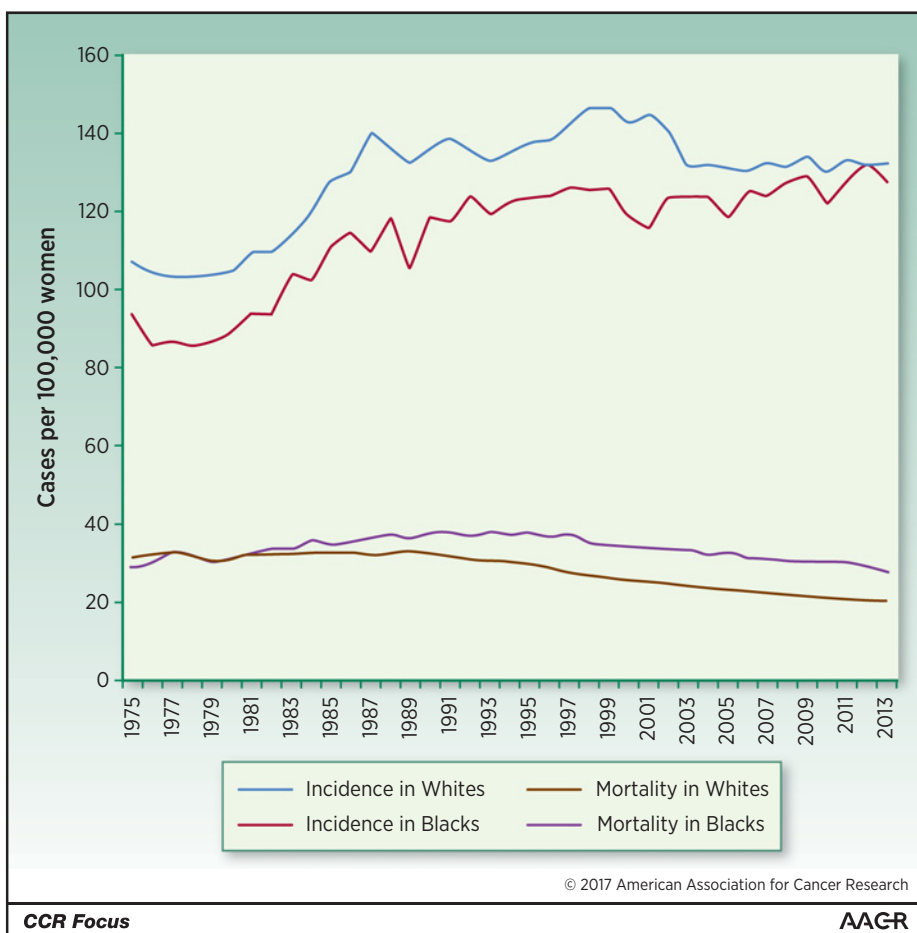


Figure 1. Trends in age-adjusted incidence and mortality of breast cancer in U.S. Black and White women, 1975–2013 [data from Surveillance, Epidemiology, and End Results (SEER) 9 sites].

Several recognized biological and clinical differences contribute to the breast cancer mortality gap, including higher incidence of hormone receptor (HR)⁻ and HER2 receptor-negative (HER⁻) or "triple-negative" tumor subtype in young Black women, with correspondingly lower incidence of HR-positive (HR⁺)/HER2⁻ cancers (Fig. 1; refs. 1, 3), more advanced stage at presentation, and higher grade and other adverse pathologic features in Black women with HR⁺ tumor types (4, 5). As discussed elsewhere in this *CCR Focus* by Yates and Desmedt, considerable genomic variability exists among HR⁺/HER2⁻ cancers, as well as other clinical subtypes, with regard to both pretreatment 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 biological 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 (Figs. 1 and 2) also suggest an influence of postdiagnosis 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 *CCR Focus* (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 health care resources is a key contributor to breast cancer disparities in the United States 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, radiotherapy, and targeted therapies; are known to affect survival; and have been extensively described elsewhere (13, 14). Figure 3 illustrates how observed treatment disparities in the United States add to biological and stage differences to compound disparities in outcome.

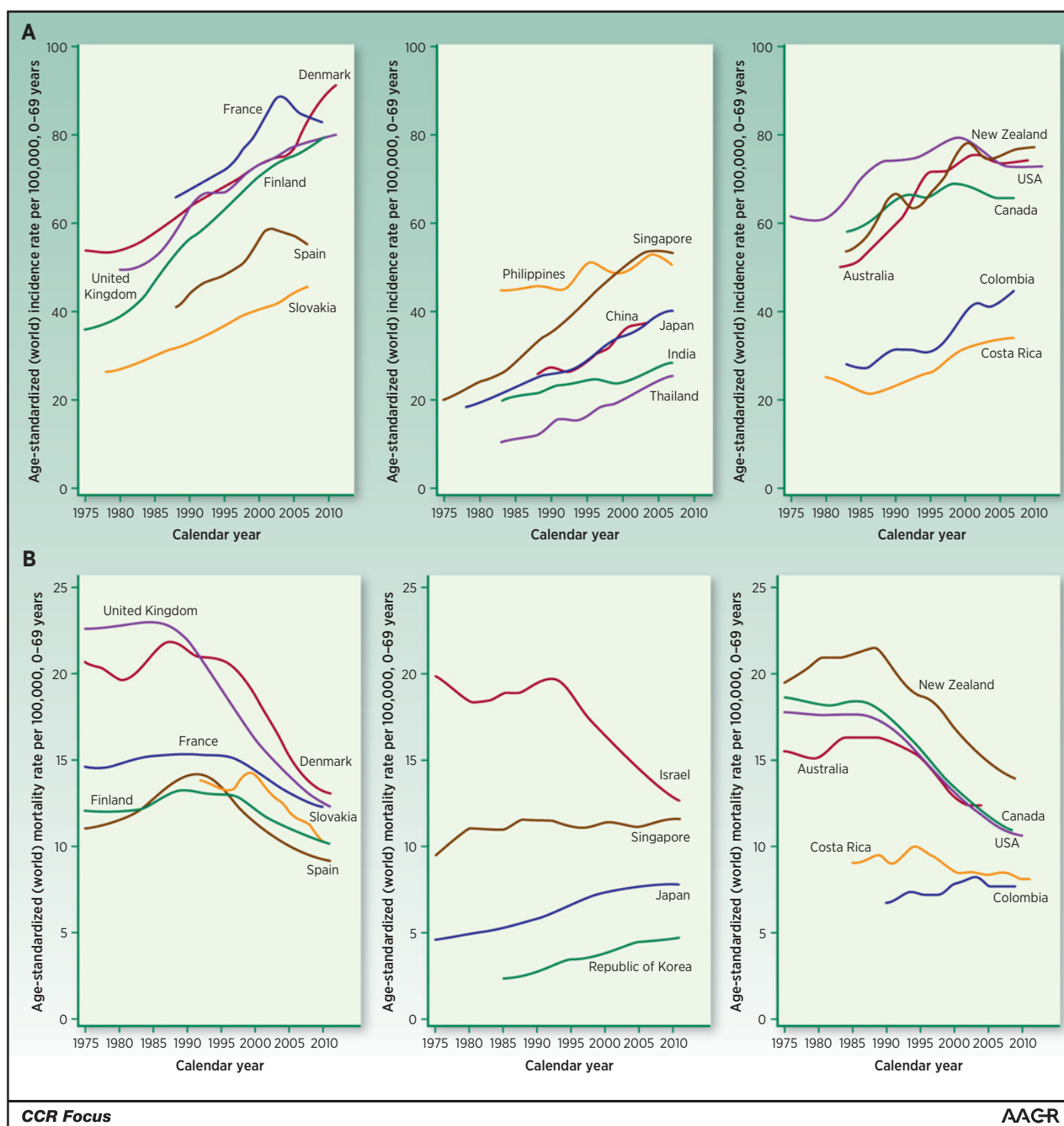


Figure 2.

A, Trends in age-standardized breast cancer incidence, selected countries, 1975-2010. **B**, Trends in age-standardized breast cancer mortality, selected countries, 1975-2010. Reprinted with permission from Anderson et al. (84); WHO Mortality Database (http://www.who.int/healthinfo/statistics/mortality_rawdata/en/index.html).

Disparities in U.S. 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 affect 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

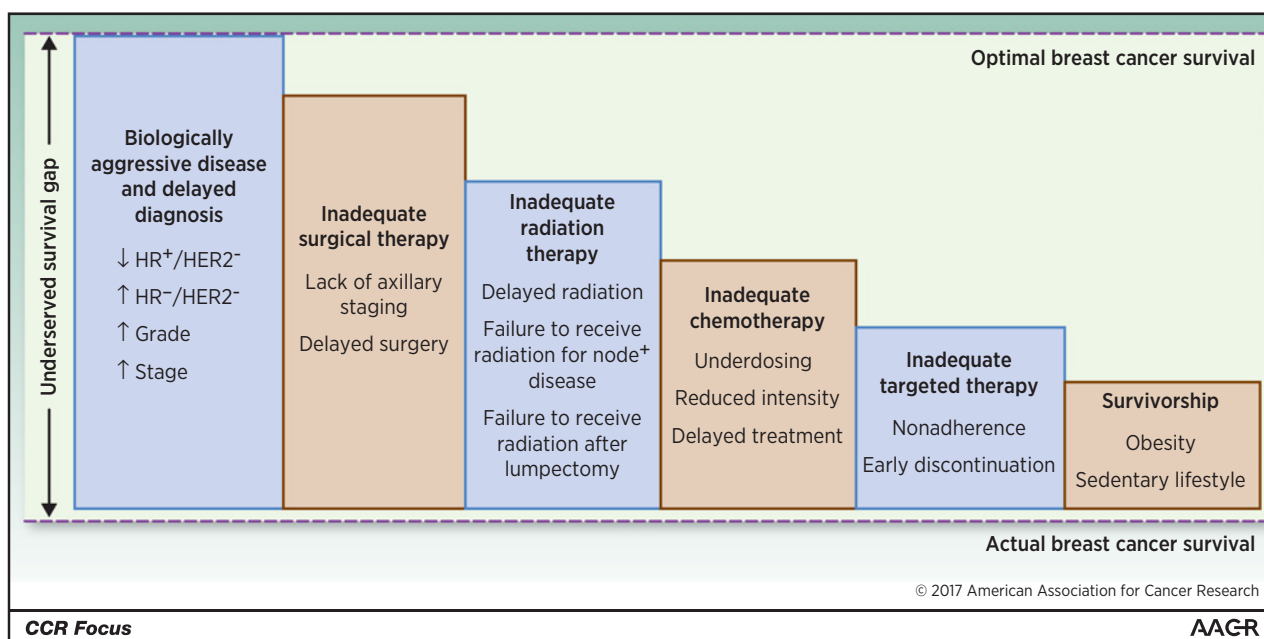


Figure 3.

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

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 with Whites (21, 22), and these differences are partially explained by the concentration of White patients within 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, and the NCI's Community Oncology Research Program (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 radiotherapy. 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 socioeconomic 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 underdosing of chemotherapy, particularly with respect to inappropriate "capping" of doses for overweight and obese patients (34, 35). Freedman and Partridge 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 *CCR Focus* (36). Regarding targeted therapies, Black women are less likely to receive trastuzumab and are more likely to receive nonstandard 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 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 substandard 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 a cause for concern for a disparity and are straightforward for most audiences to understand.

System-level actions to reduce U.S. 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 and 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 policymakers 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 substandard care, which usually includes vulnerable populations. In their landmark "Unequal Treatment" report, the IOM 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 and Prevention National Breast and Cervical Cancer Early Detection Program (NBCCEDP) 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 NBCCEDP screening (51). Although not yet evaluated, Medicaid expansion and other provisions of the Affordable Care Act (ACA) 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 Quality Oncology Practice Initiative (QOPI) program and the Michigan Urological Surgery 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 suboptimal outcomes. Within integrated health systems, oncology clinical care pathways have been demonstrated to lower emergency room and hospital utilization and cost during breast cancer treatment (63); they may also 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 study, is underway to improve delivery of adjuvant breast and lung cancer care in North Carolina (NCT01954641). 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% to 30% of all female cancer cases (65). Breast cancer incidence rates are higher in more developed than less developed regions, with 2012 incidence rates ranging nearly 4-fold across the world regions, with rates ranging from 27 cases/100,000 in Middle Africa and Eastern Asia to 92 cases/100,000 in Northern America. 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 (66, 67). Once considered primarily a disease of women in HICs, over half (52%) of new breast cancer cases and 62% of deaths occur in LMICs (68). In 2012, breast cancer incidence in the United States 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 (67). The disproportionate number of young lives lost to breast cancer is especially concerning; among the 94,000 women ages 15 to 49 years who died of breast cancer around the world in 2010, 68,000 (72%) were in LMICs (69). The impressive progress made in HICs to

improve breast cancer outcomes has not been mirrored in LMICs. Breast cancer mortality rates in the United States and Europe have dropped nearly 2% each year since 1990 (70, 71). 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; refs. 72–75) and systemic treatments (pharmacologic therapy that reduces the risk of metastatic spread; refs. 76–79) has resulted in impressive reductions in national breast cancer mortality in HICs (80–83). 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% more women will develop and die from breast cancer in 2020 than in 2002 (84).

There are many parallels between the domestic breast cancer disparities issues and global breast cancer, especially in comparing underserved communities in the United States 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 United States, we view cancer early detection, diagnosis, and treatment as a standard component of health care 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 health care delivery outside of private health care 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 with racial disparities in the United States and LMICs, along with examples of system-level interventions that may be effective for each.

Table 1. Summary of cancer care delivery gaps and possible system-level interventions in the United States and LMICs

Care gap	United States	LMIC	U.S. 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 radiotherapy is available in country and then properly triage patients for timely treatment
Lack of chemotherapy/biologics	No	Yes	—	Assess access to drugs on the WHO Model List of Essential Medicines and improve availability at decreased cost through collective bargaining
Chemo underdosing or nonstandard 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 ER testing availability and secure tamoxifen and generic aromatase inhibitor access for properly selected patients

Abbreviations: QI, quality improvement; WHO, World Health Organization.

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 and meta-analyses, which demonstrate better prognosis with incrementally smaller tumors (85, 86). A study examining breast cancers diagnosed between 1975 and 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 United States (87). Although screening mammography has been shown to be effective at reducing breast cancer mortality (88, 89), 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 (90, 91). 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 (92). 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 2 cm for the first 10 years of the study, which is significantly better than LMICs such as 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 and 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 (93).

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 (94). 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 (76, 78, 79, 95, 96). 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 (97). Multiple barriers to breast health care exist in LMICs, including lack of resources, inequitable distribution of services in urban versus rural areas, and poverty. Total expenditure on health per capita (US\$) in 2014 in countries classified by the World Bank as low income averaged US\$37 compared with \$290 in middle-income countries and \$5,251 in HICs (98). 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

(99). In the past, the primary focus of health care dollars was for infectious diseases. However, rising rates of mortality related to the major noncommunicable diseases led the United Nations to hold a high-level General Assembly meeting in September 2011, heightening the awareness of member states to focus on the importance of leading noncommunicable disease killers including cancer, heart disease, diabetes, and chronic respiratory disease (100).

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 (NEML) 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 NEMLs of low-income than in middle-income countries (101). Even when included in NEMLs, actual availability of and access to many anticancer 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: 5-year survival following breast cancer diagnosis is greater than 80% in the United States compared with only 32% in sub-Saharan Africa (97, 102). Effective solutions are, thus, urgently needed at the global level to improve breast cancer outcomes and make measurable improvements in women's health and well-being. Tools that have proven effective in the United States, 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, led to the formation of the Breast Cancer Initiative 2.5 (www.bci25.org), co-organized by the Breast Health Global Initiative 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 health care developed in low-resource settings (103). This demands a collaborative effort that draws on the collective expertise and resources of individuals and institutions engaged in breast cancer care (104). 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 (105).

Conclusions

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, and the resource-constrained settings of LMICs, the outcome of breast cancer is often determined not only by its inherent biological and clinical characteristics but also 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.

References

- Howlader N, Altekruse SF, Li CI, Chen VW, Clarke CA, Ries LA, et al. US incidence of breast cancer subtypes defined by joint hormone receptor and HER2 status. *J Natl Cancer Inst* 2014;106. pii: dju055.
- DeSantis CE, Fedewa SA, Goding Sauer A, Kramer JL, Smith RA, Jemal A. Breast cancer statistics, 2015: convergence of incidence rates between black and white women. *CA Cancer J Clin* 2016;66:31–42.
- Carey LA, Perou CM, Livasy CA, Dressler LG, Cowan D, Conway K, et al. Race, breast cancer subtypes, and survival in the Carolina Breast Cancer Study. *JAMA* 2006;295:2492–502.
- Chen VW, Correa P, Kurman RJ, Wu XC, Eley JW, Austin D, et al. Histological characteristics of breast carcinoma in blacks and whites. *Cancer Epidemiol Biomarkers Prev* 1994;3:127–35.
- Porter PL, Lund MJ, Lin MG, Yuan X, Liff JM, Flagg EW, et al. Racial differences in the expression of cell cycle-regulatory proteins in breast carcinoma. *Cancer* 2004;100:2533–42.
- Yates LR, Desmedt C. Translational genomics: practical applications of the genomic revolution in breast cancer. *Clin Can Res* 2017;23:2630–9.
- Nik-Zainal S, Morganella S. Mutational signatures in breast cancer: the problem at the DNA level. *Clin Can Res* 2017;23:2617–29.
- Troester MA, Sun X, Allot EH, Gerads J, Cohen SM, Tse CH, et al. Racial differences in PAM50 subtypes in the Carolina Breast Cancer Study. *J Natl Cancer Inst*. In press.
- Curtis E, Quale C, Haggstrom D, Smith-Bindman R. Racial and ethnic differences in breast cancer survival: how much is explained by screening, tumor severity, biology, treatment, comorbidities, and demographics? *Cancer* 2008;112:171–80.
- O'Brien KM, Cole SR, Tse CK, Perou CM, Carey LA, Foulkes WD, et al. Intrinsic breast tumor subtypes, race, and long-term survival in the Carolina Breast Cancer Study. *Clin Cancer Res* 2010;16:6100–10.
- Phelan JC, Link BG, Tehranifar P. Social conditions as fundamental causes of health inequalities: theory, evidence, and policy implications. *J Health Soc Behav* 2010;51 Suppl:S28–40.
- Vonderheide RH, Domchek SM, Clark AS. Immunotherapy for breast cancer: what are we missing? *Clin Can Res* 2017;23:2640–6.
- Wheeler SB, Reeder-Hayes KE, Carey LA. Disparities in breast cancer treatment and outcomes: biological, social, and health system determinants and opportunities for research. *Oncologist* 2013;18:986–93.
- Hershman D, McBride R, Jacobson JS, Lamerato L, Roberts K, Grann VR, et al. Racial disparities in treatment and survival among women with early-stage breast cancer. *J Clin Oncol* 2005;23:6639–46.
- Durham DD, Robinson WR, Lee SS, Wheeler SB, Reeder-Hayes KE, Bowling JM, et al. Insurance-based differences in time to diagnostic follow-up after positive screening mammography. *Cancer Epidemiol Biomarkers Prev* 2016;25:1474–82.
- Halpern MT, Schrag D. Effects of state-level medicaid policies and patient characteristics on time to breast cancer surgery among Medicaid beneficiaries. *Breast Cancer Res Treat* 2016;158:573–81.

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- George P, Chandwani S, Gabel M, Ambrosone CB, Rhoads G, Bandera EV, et al. Diagnosis and surgical delays in African American and white women with early-stage breast cancer. *J Women's Health* 2015;24:209–17.
- Polverini AC, Nelson RA, Marcinkowski E, Jones VC, Lai L, Mortimer JE, et al. Time to treatment: measuring quality breast cancer care. *Ann Surg Oncol* 2016;23:3392–402.
- Smith EC, Ziogas A, Anton-Culver H. Delay in surgical treatment and survival after breast cancer diagnosis in young women by race/ethnicity. *JAMA Surg* 2013;148:516–23.
- Sheppard VB, Oppong BA, Hampton R, Snead F, Horton S, Hirpa F, et al. Disparities in breast cancer surgery delay: the lingering effect of race. *Ann Surg Oncol* 2015;22:2902–11.
- Reeder-Hayes KE, Bainbridge J, Meyer AM, Amos KD, Weiner BJ, Godley PA, et al. Race and age disparities in receipt of sentinel lymph node biopsy for early-stage breast cancer. *Breast Cancer Res Treat* 2011;128:863–71.
- Black DM, Jiang J, Kuerer HM, Buchholz TA, Smith BD. Racial disparities in adoption of axillary sentinel lymph node biopsy and lymphedema risk in women with breast cancer. *JAMA Surg* 2014;149:788–96.
- Carpenter WR, Reeder-Hayes K, Bainbridge J, Meyer AM, Amos KD, Weiner BJ, et al. The role of organizational affiliations and research networks in the diffusion of breast cancer treatment innovation. *Med Care* 2011;49:172–9.
- Meyer AM, Reeder-Hayes KE, Liu H, Wheeler SB, Penn D, Weiner BJ, et al. Differential receipt of sentinel lymph node biopsy within practice-based research networks. *Med Care* 2013;51:812–8.
- Alderman AK, Hawley ST, Janz NK, Mujahid MS, Morrow M, Hamilton AS, et al. Racial and ethnic disparities in the use of postmastectomy breast reconstruction: results from a population-based study. *J Clin Oncol* 2009;27:5325–30.
- Freedman RA, Kouri EM, West DW, Keating NL. Racial/ethnic differences in patients' selection of surgeons and hospitals for breast cancer surgery. *JAMA Oncol* 2015;1:222–30.
- Wheeler SB, Carpenter WR, Peppercorn J, Schenck AP, Weinberger M, Biddle AK. Structural/organizational characteristics of health services partly explain racial variation in timeliness of radiation therapy among elderly breast cancer patients. *Breast Cancer Res Treat* 2012;133:333–45.
- Keating NL, Kouri E, He Y, Weeks JC, Winer EP. Racial differences in definitive breast cancer therapy in older women: are they explained by the hospitals where patients undergo surgery? *Med Care* 2009;47:765–73.
- Parise CA, Bauer KR, Caggiano V. Disparities in receipt of adjuvant radiation therapy after breast-conserving surgery among the cancer-reporting regions of California. *Cancer* 2012;118:2516–24.
- Royak-Schaler R, Pelsler C, Langenberg P, Hayes J, Gardner L, Nesbitt K, et al. Characteristics associated with the initiation of radiation therapy after breast-conserving surgery among African American and white women diagnosed with early-stage breast cancer in Maryland, 2000–2006. *Ann Epidemiol* 2012;22:28–36.
- Griggs JJ, Hawley ST, Graff JJ, Hamilton AS, Jagsi R, Janz NK, et al. Factors associated with receipt of breast cancer adjuvant chemotherapy in a diverse population-based sample. *J Clin Oncol* 2012;30:3058–64.

32. Chavez-MacGregor M, Clarke CA, Lichtensztajn DY, Giordano SH. Delayed initiation of adjuvant chemotherapy among patients with breast cancer. *JAMA Oncol* 2016;2:322-9.
33. Nurgalieva ZZ, Franzini L, Morgan RO, Vernon SW, Liu CC, Du XL. Impact of timing of adjuvant chemotherapy initiation and completion after surgery on racial disparities in survival among women with breast cancer. *Med Oncol* 2013;30:419.
34. Griggs JJ, Sorbero ME, Stark AT, Heining SE, Dick AW. Racial disparity in the dose and dose intensity of breast cancer adjuvant chemotherapy. *Breast Cancer Res Treat* 2003;81:21-31.
35. Griggs JJ, Culakova E, Sorbero ME, Poniewierski MS, Wolff DA, Crawford J, et al. Social and racial differences in selection of breast cancer adjuvant chemotherapy regimens. *J Clin Oncol* 2007;25:2522-7.
36. Freedman RA, Partridge AH. Emerging data and current challenges for young, old, obese, or male patients with breast cancer. *Clin Can Res* 2017;23:2647-54.
37. Freedman RA, Vaz-Luis I, Barry WT, Lii H, Lin NU, Winer EP, et al. Patterns of chemotherapy, toxicity, and short-term outcomes for older women receiving adjuvant trastuzumab-based therapy. *Breast Cancer Res Treat* 2014;145:491-501.
38. Reeder-Hayes K, Peacock Hinton S, Meng K, Carey LA, Dusetzina SB. Disparities in use of human epidermal growth hormone receptor 2-targeted therapy for early-stage breast cancer. *J Clin Oncol* 2016;34:2003-9.
39. Freedman RA, Hughes ME, Ottesen RA, Weeks JC, He Y, Wong YN, et al. Use of adjuvant trastuzumab in women with human epidermal growth factor receptor 2 (HER2)-positive breast cancer by race/ethnicity and education within the National Comprehensive Cancer Network. *Cancer* 2013;119:839-46.
40. Reeder-Hayes K, Meyer A-M, Dusetzina S, Liu H, Wheeler SB. Racial disparities in initiation of endocrine therapy for early-stage breast cancer. *J Clin Oncol* 31, 2013 (suppl; abstr 6572).
41. Hershman DL, Kushi LH, Shao T, Buono D, Kershenbaum A, Tsai WY, et al. Early discontinuation and nonadherence to adjuvant hormonal therapy in a cohort of 8,769 early-stage breast cancer patients. *J Clin Oncol* 2010;28:4120-8.
42. Partridge AH, Wang PS, Winer EP, Avorn J. Nonadherence to adjuvant tamoxifen therapy in women with primary breast cancer. *J Clin Oncol* 2003;21:602-6.
43. Roberts MC, Wheeler SB, Reeder-Hayes K. Racial/ethnic and socioeconomic disparities in endocrine therapy adherence in breast cancer: a systematic review. *Am J Public Health* 2015;105 Suppl 3:e4-e15.
44. Hershman DL, Tsui J, Meyer J, Glied S, Hillyer GC, Wright JD, et al. The change from brand-name to generic aromatase inhibitors and hormone therapy adherence for early-stage breast cancer. *J Natl Cancer Inst* 2014;106. pii: dju319.
45. Neugut AI, Subar M, Wilde ET, Stratton S, Brouse CH, Hillyer GC, et al. Association between prescription co-payment amount and compliance with adjuvant hormonal therapy in women with early-stage breast cancer. *J Clin Oncol* 2011;29:2534-42.
46. Neuner JM, Kamaraju S, Charlson JA, Wozniak EM, Smith EC, Biggers A, et al. The introduction of generic aromatase inhibitors and treatment adherence among Medicare D enrollees. *J Natl Cancer Inst* 2015;107.
47. Institute of Medicine (US) Committee on Understanding and Eliminating Racial and Ethnic Disparities in Health Care; Smedley BD, Stith AY, Nelson AR, editors. *Unequal treatment: confronting racial and ethnic disparities in health care*. Washington (DC): National Academies Press (US); 2003.
48. McGuire TG, Alegria M, Cook BL, Wells KB, Zaslavsky AM. Implementing the institute of medicine definition of disparities: an application to mental health care. *Health Serv Res* 2006;41:1979-2005.
49. Cook BL, McGuire TG, Zaslavsky AM. Measuring racial/ethnic disparities in health care: methods and practical issues. *Health Serv Res* 2012;47(3 Pt 2):1232-54.
50. Miller JW, Hanson V, Johnson GD, Royalty JE, Richardson LC. From cancer screening to treatment: service delivery and referral in the National Breast and Cervical Cancer Early Detection Program. *Cancer* 2014;120 Suppl 16:2549-56.
51. Howard DH, Ekwueme DU, Gardner JG, Tangka FK, Li C, Miller JW. The impact of a national program to provide free mammograms to low-income, uninsured women on breast cancer mortality rates. *Cancer* 2010;116:4456-62.
52. Courtemanche C, Marton J, Ukert B, Yelowitz A, Zapata D. Early impacts of the affordable care act on health insurance coverage in medicaid expansion and non-expansion states. *J Policy Anal Manage* 2017;36:178-210.
53. Kehl KL, Liao KP, Krause TM, Giordano SH. Access to accredited cancer hospitals within federal exchange plans under the affordable care act. *J Clin Oncol* 2017;35:645-51.
54. Battaglia TA, Darnell JS, Ko N, Snyder F, Paskett ED, Wells KJ, et al. The impact of patient navigation on the delivery of diagnostic breast cancer care in the National Patient Navigation Research Program: a prospective meta-analysis. *Breast Cancer Res Treat* 2016;158:523-34.
55. Rocque GB, Partridge EE, Pisu M, Martin MY, Demark-Wahnefried W, Acemgil A, et al. The patient care connect program: transforming health care through lay navigation. *J Oncol Pract* 2016;12:e633-42.
56. Meade CD, Wells KJ, Arevalo M, Calcagno ER, Rivera M, Sarmiento Y, et al. Lay navigator model for impacting cancer health disparities. *J Cancer Educ* 2014;29:449-57.
57. Steinberg ML, Fremont A, Khan DC, Huang D, Knapp H, Karaman D, et al. Lay patient navigator program implementation for equal access to cancer care and clinical trials: essential steps and initial challenges. *Cancer* 2006;107:2669-77.
58. Rocque GB, Pisu M, Jackson BE, Kvale EA, Demark-Wahnefried W, Martin MY, et al. Resource use and Medicare costs during lay navigation for geriatric patients with cancer. *JAMA Oncol* 2017 Jan 26. [Epub ahead of print].
59. Jean-Pierre P, Cheng Y, Wells KJ, Freund KM, Snyder FR, Fiscella K, et al. Satisfaction with cancer care among underserved racial-ethnic minorities and lower-income patients receiving patient navigation. *Cancer* 2016;122:1060-7.
60. Myers SN, Ghani KR, Dunn RL, Lane BR, Schervish EW, Gao Y, et al. Notable outcomes and trackable events after surgery: evaluating an uncomplicated recovery after radical prostatectomy. *J Urol* 2016;196:399-404.
61. Hurlay P, Dhir A, Gao Y, Drabik B, Lim K, Curry J, et al. A statewide intervention improves appropriate imaging in localized prostate cancer. *J Urol* 2017;197:1222-8.
62. Dangi-Garimella S. QOPI, the ASCO initiative, improves compliance and promotes quality of patient care. *Am J Manag Care* 2014;20(5 Spec No.):E1.
63. Hoverman JR, Klein I, Harrison DW, Hayes JE, Garey JS, Harrell R, et al. Opening the black box: the impact of an oncology management program consisting of level I pathways and an outbound nurse call system. *J Oncol Pract* 2014;10:63-7.
64. McAlearney AS, Murray K, Sieck C, Lin JJ, Bellacera B, Bickell NA. The challenge of improving breast cancer care coordination in safety-net hospitals: barriers, facilitators, and opportunities. *Med Care* 2016;54:147-54.
65. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, et al. 2013 GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11. Lyon (France): International Agency for Research on Cancer; 2017 [cited 2017 May 12]. Available from: <http://globocan.iarc.fr>.
66. Greenlee RT, Murray T, Bolden S, Wingo PA. Cancer statistics, 2000. *CA Cancer J Clin* 2000;50:7-33.
67. DeSantis CE, Bray F, Ferlay J, Lortet-Tieulent J, Anderson BO, Jemal A. International variation in female breast cancer incidence and mortality rates. *Cancer Epidemiol Biomarkers Prev* 2015;24:1495-506.
68. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. *CA Cancer J Clin* 2015;65:87-108.
69. Forouzanfar MH, Foreman KJ, Delossantos AM, Lozano R, Lopez AD, Murray CJ, et al. Breast and cervical cancer in 187 countries between 1980 and 2010: a systematic analysis. *Lancet* 2011;378:1461-84.
70. Siegel R, Ma J, Zou Z, Jemal A. Cancer statistics, 2014. *CA Cancer J Clin* 2014;64:9-29.
71. Kalager M, Zelen M, Langmark F, Adami HO. Effect of screening mammography on breast-cancer mortality in Norway. *N Engl J Med* 2010;363:1203-10.

72. Fisher B, Anderson S, Bryant J, Margolese RG, Deutsch M, Fisher ER, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med* 2002;347:1233–41.
73. Veronesi U, Cascinelli N, Mariani L, Greco M, Saccozzi R, Luini A, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med* 2002;347:1227–32.
74. Early Breast Cancer Trialists' Collaborative G, Darby S, McGale P, Correa C, Taylor C, Arriagada R, et al. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomised trials. *Lancet* 2011;378:1707–16.
75. Early Breast Cancer Trialists' Collaborative G, McGale P, Taylor C, Correa C, Cutter D, Duane F, et al. Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials. *Lancet* 2014;383:2127–35.
76. Early Breast Cancer Trialists' Collaborative G, Davies C, Godwin J, Gray R, Clarke M, Cutter D, et al. Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials. *Lancet* 2011;378:771–84.
77. Tamoxifen for early breast cancer: an overview of the randomised trials. Early Breast Cancer Trialists' Collaborative Group [see comments]. *Lancet* 1998;351:1451–67.
78. Early Breast Cancer Trialists' Collaborative Group (EBCTCG), Dowsett M, Forbes JF, Bradley R, Ingle J, Aihara T, et al. Aromatase inhibitors versus tamoxifen in early breast cancer: patient-level meta-analysis of the randomised trials. *Lancet* 2015;386:1341–52.
79. Early Breast Cancer Trialists' Collaborative Group (EBCTCG), Peto R, Davies C, Godwin J, Gray R, Pan HC, et al. Comparisons between different polychemotherapy regimens for early breast cancer: meta-analyses of long-term outcome among 100,000 women in 123 randomised trials. *Lancet* 2012;379:432–44.
80. Weir HK, Thun MJ, Hankey BF, Ries LA, Howe HL, Wingo PA, et al. Annual report to the nation on the status of cancer, 1975–2000, featuring the uses of surveillance data for cancer prevention and control. *J Natl Cancer Inst* 2003;95:1276–99.
81. Broeders M, Moss S, Nystrom L, Njor S, Jonsson H, Paap E, et al. The impact of mammographic screening on breast cancer mortality in Europe: a review of observational studies. *J Med Screen* 2012;19 Suppl 1:14–25.
82. Njor S, Nystrom L, Moss S, Paci E, Broeders M, Segnan N, et al. Breast cancer mortality in mammographic screening in Europe: a review of incidence-based mortality studies. *J Med Screen* 2012;19 Suppl 1:33–41.
83. Paci E, Broeders M, Hofvind S, Puliti D, Duffy SW. European breast cancer service screening outcomes: a first balance sheet of the benefits and harms. *Cancer Epidemiol Biomarkers Prev* 2014;23:1159–63.
84. Anderson BO, Lipscomb J, Murillo RH, Thomas DB. Breast cancer. In: Gelband H, Jha P, Sankaranarayanan R, Horton S, editors. *Cancer: disease control priorities*. 3rd ed. Vol. 3. Washington (DC): The World Bank; 2015. p. 45–68.
85. Smith RA, Caleffi M, Albert US, Chen TH, Duffy SW, Franceschi D, et al. Breast cancer in limited-resource countries: early detection and access to care. *Breast J* 2006;12 Suppl 1:S16–26.
86. McPhail S, Johnson S, Greenberg D, Peake M, Rous B. Stage at diagnosis and early mortality from cancer in England. *Br J Cancer* 2015;112 Suppl 1: S108–15.
87. Elkin EB, Hudis C, Begg CB, Schrag D. The effect of changes in tumor size on breast carcinoma survival in the U.S.: 1975–1999. *Cancer* 2005;104: 1149–57.
88. Independent UKPoBCS. The benefits and harms of breast cancer screening: an independent review. *Lancet* 2012;380:1778–86.
89. Lauby-Secretan B, Scoccianti C, Loomis D, Benbrahim-Tallaa L, Bouvard V, Bianchini F, et al. Breast-cancer screening—viewpoint of the IARC Working Group. *N Engl J Med* 2015;372:2353–8.
90. Mitra I, Mishra GA, Singh S, Aranke S, Notani P, Badwe R, et al. A cluster randomized, controlled trial of breast and cervix cancer screening in Mumbai, India: methodology and interim results after three rounds of screening. *Int J Cancer* 2010;126:976–84.
91. Sankaranarayanan R, Ramadas K, Thara S, Muwonge R, Prabhakar J, Augustine P, et al. Clinical breast examination: preliminary results from a cluster randomized controlled trial in India. *J Natl Cancer Inst* 2011;103:1476–80.
92. Miller AB, Wall C, Baines CJ, Sun P, To T, Narod SA. Twenty five year follow-up for breast cancer incidence and mortality of the Canadian National Breast Screening Study: randomised screening trial. *Bmj* 2014;348:g366.
93. Rajaraman P, Anderson BO, Basu P, Belinson JL, Cruz AD, Dhillon PK, et al. Recommendations for screening and early detection of common cancers in India. *Lancet Oncol* 2015;16:e352–61.
94. Guide to cancer early diagnosis. Geneva (Switzerland): World Health Organization; 2017 [cited 2017 May 9]. Available from: http://www.who.int/cancer/publications/cancer_early_diagnosis/en/.
95. Berry DA, Cronin KA, Plevritis SK, Fryback DG, Clarke L, Zelen M, et al. Effect of screening and adjuvant therapy on mortality from breast cancer. *N Engl J Med* 2005;353:1784–92.
96. Slamon DJ, Eirmann W, Robert NJ, Giermek J, Martin M, Jasiowka M, et al. Ten year follow-up of BCIRG-006 comparing doxorubicin plus cyclophosphamide followed by docetaxel (AC→T) with doxorubicin plus cyclophosphamide followed by docetaxel and trastuzumab (AC→TH) with docetaxel, carboplatin and trastuzumab (TCH) in HER2+ early breast cancer [abstract]. In: Proceedings of the 38th Annual San Antonio Breast Cancer Symposium; 2015 Dec 8–12; San Antonio, TX. San Antonio (TX): SABCS. Abstract nr S5-04.
97. Coleman MP, Quaresma M, Berrino F, Lutz JM, De Angelis R, Capocaccia R, et al. Cancer survival in five continents: a worldwide population-based study (CONCORD). *Lancet Oncol* 2008;9:730–56.
98. The World Bank. Health expenditure per capita (current US\$). Washington (DC): The World Bank; 2017 [cited 2017 May 5]. Available from: <http://data.worldbank.org/indicator/SH.XPD.PCAP?view=chart>.
99. Farmer P, Frenk J, Knaul FM, Shulman LN, Alleyne G, Armstrong L, et al. Expansion of cancer care and control in countries of low and middle income: a call to action. *Lancet* 2010;376:1186–93.
100. United Nations General Assembly. Political declaration of the high-level meeting of the general assembly on the prevention and control of non-communicable diseases (A/RES/66/2). New York: United Nations; 2011.
101. Bazargani YT, de Boer A, Schellens JH, Leufkens HG, Mantel-Teeuwisse AK. Essential medicines for breast cancer in low and middle income countries. *BMC Cancer* 2015;15:591.
102. Price AJ, Ndom P, Atenguena E, Mambou Nouemssi JP, Ryder RW. Cancer care challenges in developing countries. *Cancer* 2012;118:3627–35.
103. Anderson BO, Ilbawi AM, El Saghir NS. Breast cancer in low and middle income countries (LMICs): a shifting tide in global health. *Breast J* 2015;21:111–8.
104. Ilbawi AM, Anderson BO. Global cancer consortiums: moving from consensus to practice. *Ann Surg Oncol* 2015;22:719–27.
105. Anderson BO, Duggan C. Resource-stratified guidelines for cancer management: correction and commentary. *J Global Oncol* 2016;0: JGO006213.

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