Do Lifestyle or Social Factors Explain Ethnic/Racial Inequalities in Breast Cancer Survival?

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Despite numerous studies documenting ethnic inequalities in breast cancer survival between minority and majority ethnic groups worldwide, reasons for these inequalities remain unclear. The authors performed a systematic review of published literature to identify studies that investigated the explanatory power of smoking, alcohol consumption, body mass index (BMI), and socioeconomic position (SEP) on ethnic inequalities in breast cancer survival. Sixteen studies were included in the review. From 5 studies, the authors found that differences in breast cancer survival between ethnic groups may be in part explained by BMI, but there was little evidence to implicate smoking or alcohol consumption as explanatory factors of this inequality. From 12 studies, the authors found that SEP explains part of the ethnic inequality in all-cause survival but that it was not evident for breast-cancer-specific survival. SEP explains more of the disparities among African-American versus white women in the United States compared with other ethnic comparisons. Furthermore, given social patterning of BMI and other lifestyle habits, it is possible that results for SEP and BMI are measuring the same effect. In this review, the authors make suggestions regarding the role of epidemiology in facilitating further research to better inform the development of effective policies to address ethnic differences in survival.

breast neoplasms; ethnic groups; healthcare disparities; health status disparities; meta-analysis; review; socioeconomic factors; survival analysis

Abbreviations: BMI, body mass index; CI, confidence interval; HR, hazard ratio; SEP, socioeconomic position.

INTRODUCTION

Ethnicity and race are complex constructs whose definitions vary from country to country. The constructs can include shared history, cultural affiliation and practice, language, religion, lifestyle, and sometimes biology (1, 2). In this review, we use the word ethnicity to cover race and/or ethnicity. Because of different definitions of ethnicity, we would not necessarily expect to see the same ethnic differences in survival in different countries. However, lower breast cancer survival has consistently been found not only in African-American compared with white American women (3–5) but also between other racial/ethnic groups in the United States (4, 6, 7) and between indigenous and other groups in New Zealand (8, 9) and Australia (10), whereas South Asian women in the United Kingdom appear to have a better survival profile than white women (11, 12).

Many possible reasons for these disparities have been suggested, which can be grouped into the following broad categories: 1) structural barriers/system factors, 2) physician/clinical factors, and 3) patient factors (13–15). Within the first 2 categories are factors such as access to health care and screening, receipt of optimum treatment, and grade/disease stage at diagnosis. However, there is little empirical evidence regarding the role that patient factors play in explaining ethnic inequalities in breast cancer survival. We need to pinpoint the causes of ethnic differences in survival to create effective policies to address them. Policy options would be very different depending on whether ethnic differences are due to socioeconomic factors, lifestyle, treatment, or access to care.

Some work has sought to separate socioeconomic status from other influences on ethnic differences in survival. Newman et al. reviewed literature to investigate whether ethnic inequalities exist after accounting for socioeconomic position (SEP) in 2002 (16) and updated their findings in 2006 (17). The 2006 review included 20 studies that estimated survival for African-American and white American people...
breast cancer patients. Newman et al.’s pooled analysis found African-American ethnicity to be an independent predictor of worse overall survival, showing a 28% excess risk of death after adjustment for SEP measures (hazard ratio (HR) = 1.28, 95% confidence interval (CI): 1.18, 1.38). Disease-specific results were based on 8 pooled studies that looked specifically at death from breast cancer and, while smaller, were also found to be statistically significant (HR = 1.19, 95% CI: 1.09, 1.30).

While an increasing amount of data are available on the effect that personal risk factors (e.g., smoking (18–23), alcohol consumption (24–28), weight (19, 29–35)) have on survival, there is a paucity of evidence comparing the effect of those risk factors on differences in survival between ethnicities. Several authors have postulated that these factors could explain some or all of the observed ethnic inequalities in breast cancer survival (36–42).

In an effort to identify possible means by which we can address survival disparities, our main interest was to investigate modifiable lifestyle risk factors in majority and minority populations and to determine the magnitude of that part of the inequality attributable to individual risk factors. However, because many studies look at SEP, we also decided to include that risk factor in the review; despite it not being easily amenable to modification, it is highly relevant given that the lifestyle factors in which we are interested are socially patterned. The previously reported meta-analysis (17) was restricted to only one ethnic comparison within one country, whereas the current review is more extensive and international, and it investigates other ethnic minority populations as well. The aim of this review is to summarize the evidence regarding whether lifestyle factors (smoking, alcohol consumption, BMI, or SEP) explain some or all of the ethnic inequalities in breast cancer survival, and, where possible, to quantify this inequality.

MATERIALS AND METHODS

Search methodology

We conducted a systematic search of published English-language studies indexed in MEDLINE (National Library of Medicine, Bethesda, Maryland) from 1966 to June 2008. We devised a search strategy based on both text and Medical Subject Headings (MeSH) terms to identify papers that investigated reasons for breast cancer survival in at least 2 ethnic groups. The search terms used are given in the Appendix. The titles resulting from this search were reviewed independently by each author. When either author thought the paper could be relevant, it was included. The abstracts of included papers were then independently examined by the same 2 authors. The full text of the paper was obtained if the abstract mentioned 1) breast cancer survival, 2) ethnicity, and 3) at least one risk factor (smoking, alcohol consumption, BMI, or SEP). Disagreements were resolved by consensus. Hand searches were conducted of the bibliographies of review papers identified by the search, as well as relevant papers identified, and these papers were subjected to the same relevance criteria as those used during the initial search process. In addition, a search of EMBASE (1980 to July 2008) (Elsevier B. V., Amsterdam, the Netherlands) was performed with broader search terms than those used in the MEDLINE search (ethnicity or race) and breast and cancer and survival) by one reviewer (M. J.) but did not result in identification of any further relevant papers.

Inclusion and exclusion criteria

Studies were included if they reported on breast cancer survival, defined as at least one of the following: overall survival, excess mortality, disease-free survival, or mortality in a cohort of breast cancer patients. Studies that reported breast cancer mortality in a healthy cohort (i.e., not in a cohort of patients with breast cancer) were excluded because this endpoint is a combination of incidence and survival. When the same study was reported on in more than one publication, we included the data from the more recent publication. Studies were included if they either 1) presented data for at least 2 racial/ethnic groups or 2) reported data for a minority racial/ethnic group and compared them with similar published data from another other racial/ethnic group in the same country.

We realized from the first search that there would be very few studies investigating the effects of smoking, alcohol consumption, and BMI; therefore, 2 different approaches were used:

1. Narrative synthesis that was applied to studies investigating BMI, smoking, and/or alcohol use. The small number of studies examining these factors in relation to ethnic differences in breast cancer survival precluded use of statistical methods of synthesis.

2. Meta-analysis of studies from which it was possible to extract the effect of the ethnic inequality attributable to SEP. The following inclusion criteria were applied to only those studies that reported the effect of SEP on ethnic inequalities in breast cancer survival. Only those studies that reported results from which we could extract the effect of SEP on inequalities in breast cancer survival were eligible for inclusion. Data could be extracted if 2 comparable models were presented, comparing survival in one ethnic group with that in another, with the 2 models differing only in terms of inclusion of one or more SEP parameter(s). Methods to extract crude survival for the purposes of meta-analyses have been described (43). We used these methods, where possible, with the exception for studies that presented only crude survival data in graphic form, because of the difficulties in extracting data from such studies (43). Studies in which noncomparable estimates for crude and adjusted survival measures, such as crude relative survival followed by adjusted hazard ratios, were not eligible for inclusion.

Data extraction

A pro forma was developed to ensure consistent and accurate data extraction from included papers. Bibliographic information, study setting and source of patients, age range of patients, years of diagnosis and length of follow-up, ethnicity information (including number of patients in each
ethnic group), outcome of interest, crude and adjusted hazard ratios, adjustment parameters, exposure variable measurement, and whether the study was conducted in an equal access health care system were all recorded. Data were extracted to the exact number of decimal places, as reported in the original papers.

**Pooling of results**

Because only a few studies investigated the effect of BMI, smoking, or alcohol consumption in explaining ethnic inequalities in breast cancer survival, these studies were combined by using a narrative synthesis. The studies investigating the role that SEP plays in determining ethnic inequalities in breast cancer survival were combined by using a DerSimonian and Laird (44) random-effects meta-analysis. Separate models were run for each of 3 outcome measures: 1) overall survival, 2) breast-cancer-specific survival, and 3) excess mortality (a multivariable extension of relative survival). For each outcome, hazard ratios comparing the outcome between a minority and the majority ethnic group were obtained from the individual studies. For each outcome, separate pooled estimates were estimated for 1) the crude (or age-adjusted) effect of ethnicity on outcome; 2) the effect of ethnicity after additionally adjusting for clinical factors, but not SEP; and 3) the effect of ethnicity after adjusting for clinical factors and SEP. Interstudy heterogeneity was quantified by using the Q statistic.

To investigate the magnitude of the effect of SEP on ethnic inequalities in survival, we estimated for each study the percentage change in the minority versus majority survival disparity as follows: \((HR_{model1} - HR_{model2}) \times 100/(HR_{model1} - 1)\), where model 2 is an estimate of survival disparity adjusted for age, clinical factors, and SEP; and model 1 is the same as model 2 but without SEP. For papers in which a model 1 was not presented, the 2 models used for this analysis were a crude model and an SEP-adjusted model. In all instances, because of our inclusion criteria, the models compared differed by only one or more SEP parameter(s).

A linear regression model was used to estimate the effect of the following variables on change in ethnic inequality following adjustment for SEP: 1) whether the comparison was between African-American and white women in the United States, because these comparisons formed the bulk of the evidence, or between other ethnic groups; 2) whether they were set in the context of an equal-access health care system; and 3) decade of publication. Each of these models was run by using all available comparisons because some publications made comparisons between several pairs of ethnic groups. The standard errors of this regression were adjusted for this clustering effect.

To assess whether the results could have been affected by publication bias, we used funnel plots and Egger's regression asymmetry test (45). All analyses were performed by using Stata Statistical Software, version 10.0 (StataCorp, College Station, Texas).

**RESULTS**

Sixteen papers were included in this review (Figure 1). The majority of these papers investigated the effect of SEP on breast cancer survival, primarily using census-derived SEP measures.
Smoking, alcohol consumption, and BMI

The studies that investigated modifiable risk factors are described in Table 1, and the results are presented in Table 2. Only 2 studies could be identified in which the effects of smoking and alcohol consumption on ethnic inequalities in survival were considered. In one (46), 698 African-American women with breast cancer were compared with 5,879 white women. All women were treated in a US Department of Defense equal-access health care system. The crude effect of race on all-cause mortality was a 40% higher risk for African-American women. This effect was unchanged by the simultaneous effect of adjusting for several factors, including clinical factors, smoking, and alcohol consumption.

In the Black/White Cancer Survival Study (47), the 2-fold excess risk of both all-cause and breast-cancer-specific survival for black compared with white women in the United States was not altered following simultaneous adjustment for comorbidities, smoking, and BMI. In a relatively small study (\(n = 325\)), BMI was found to explain a small proportion of the black/white breast cancer survival inequalities in women with stage III cancer (48). Tammemagi et al. (49) investigated whether low BMI could explain ethnic inequalities in breast cancer mortality and non-breast cancer mortality. The effect of controlling for low BMI left the hazard ratio essentially unchanged. One final study, which followed up women diagnosed with breast cancer in the Women's Health Initiative, found that after adjusting for age, stage of disease, BMI, and whether the women was in the clinical or observational arm of the study, a significant increased risk of death still remained for African-American compared with white women (50).

Taken together, these studies suggest, with a very limited evidence base, that it is unlikely that either smoking or alcohol consumption can explain ethnic inequalities in breast cancer survival. It is possible that BMI may play some role in explaining these inequalities, but further research evidence is required. From our review, there do not appear to be any studies that have investigated whether these lifestyle factors could explain inequalities in breast cancer survival between groups other than African-American and white American women.

Socioeconomic position

The studies that investigated SEP are described in Table 3. The results are presented in Table 4.

**Excess mortality.** Only one study used excess mortality modeling (12) to investigate ethnic inequalities in survival. In this study, women were assigned to South Asian ethnicity by a computerized algorithm. South Asian women were less likely than non–South Asian women to die during the follow-up period (crude excess mortality rate ratio = 0.82, 95% CI: 0.72, 0.94). Adjusting for a census-derived measure of deprivation strengthened this association (rate ratio = 0.77, 95% CI: 0.67, 0.87).

**All-cause mortality.** Eight studies (9 comparisons) (6, 11, 47, 51–55) investigated ethnic inequalities in all-cause mortality in cohorts of women with breast cancer. Of the 9 comparisons, 7 compared African-American with white women.
Table 2.

Results From Studies Investigating the Effect of Health Behaviors (Smoking, Alcohol Consumption, BMI) on Ethnic Inequalities in Breast Cancer Survival

<table>
<thead>
<tr>
<th>First Author</th>
<th>Publication Year</th>
<th>Outcome</th>
<th>Model 1 Parameters</th>
<th>Model 2 Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cranes (48)</td>
<td>1990</td>
<td>All-cause mortality</td>
<td>1.61 (95% CI: 1.02, 2.53)</td>
<td>1.44 (95% CI: 0.82, 2.52)</td>
</tr>
<tr>
<td>Tammemagi (49)</td>
<td>2005</td>
<td>Non-breast cancer mortality</td>
<td>1.27 (95% CI: 1.00, 1.63)</td>
<td>1.48 (95% CI: 0.83, 2.66)</td>
</tr>
<tr>
<td>Eley (47)</td>
<td>1994</td>
<td>Breast cancer mortality</td>
<td>2.10 (95% CI: 1.08, 2.00)</td>
<td>1.49 (95% CI: 1.07, 2.07)</td>
</tr>
<tr>
<td>Chlebowski (50)</td>
<td>2005</td>
<td>All-cause mortality</td>
<td>2.00 (95% CI: 1.57, 2.57)</td>
<td>2.00 (95% CI: 1.57, 2.57)</td>
</tr>
<tr>
<td>Wojcik (46)</td>
<td>1998</td>
<td>All-cause mortality</td>
<td>1.41 (95% CI: 1.17, 1.70)</td>
<td>1.41 (95% CI: 1.17, 1.70)</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index; CI, confidence interval; HR, hazard ratio.

- This paper did not report a crude hazard ratio of ethnicity on mortality but noted that the cumulative mortality was 21/242 for black women and 191/3,455 for white women. The crude effect given is therefore a risk ratio, not a hazard ratio.

In the United States, one compared other (non-African-American) with white women in the United States, and one compared South Asian with non–South Asian women in the United Kingdom. Seven studies contributed to the overall crude analyses. The pooled hazard ratio showed that women in the minority ethnic groups were more likely to die during follow-up (HR = 1.42, 95% CI: 1.19, 1.68) (Figure 2A). However, there was significant heterogeneity between studies (P < 0.001). Exclusion of the one study that showed a considerable difference in its results, with better survival in the ethnic minority population (11), slightly strengthened the pooled hazard ratio but did not remove the interstudy heterogeneity. Six studies (7 comparisons) adjusted for factors other than SEP (6, 47, 51–53, 55). The pooled hazard ratio was reduced to 1.31 (95% CI: 1.05, 1.62) (Figure 2B). Further adjusting for SEP reduced the hazard ratio to 1.15 (95% CI: 0.95, 1.41) (Figure 2C).

Breast cancer mortality. Five studies (10 comparisons) (4–6, 47, 56) investigated ethnic inequalities in breast cancer mortality in cohorts of women with breast cancer, all based in the United States. Of the 10 comparisons, 5 compared African-American, 2 compared Hispanic, 2 compared Asian/Pacific Islander, and 1 compared non-African-American women with white women. Five studies (9 comparisons) contributed to the overall crude analyses. The pooled hazard ratio showed that women in the minority ethnic groups were more likely to die during follow-up (HR = 1.38, 95% CI: 1.16, 1.64) (Figure 3A). However, there was significant heterogeneity between studies (P < 0.001). Exclusion of the one comparison that showed considerably different results, with better survival in the ethnic minority (Asian/Pacific Islander vs. white American) population (4), slightly strengthened the pooled hazard ratio but did not remove the interstudy heterogeneity. All but one comparison (56) provided results adjusted for factors other than SEP. The pooled hazard ratio was substantially reduced to 1.08 (95% CI: 0.93, 1.25) (Figure 3B), indicating that almost all of the ethnic inequalities were due to adjustment variables (primarily clinical factors) other than SEP. Further adjusting for SEP reduced the hazard ratio to 1.05 (95% CI: 0.92, 1.20) (Figure 3C).

The usefulness of the funnel and regression asymmetry plots in determining the possibility of publication bias was limited by the small numbers of studies included. Given this limitation, there was no evidence of publication bias for either outcome based on the fully adjusted models (P = 0.81 for breast cancer mortality and P = 0.14 for all-cause mortality) (plots not shown).

Overall, these results indicate that SEP may explain approximately half of the inequality in breast cancer survival (all causes) between ethnic groups but that SEP is not an important determinant of inequalities in breast-cancer-specific survival once clinical factors such as grade and stage have been accounted for.

The percentage change in the minority versus majority survival disparity following SEP adjustment ranged from −100% (i.e., a doubling of the strength of effect) to 80% (i.e., adjusting for SEP explained 80% of the disparities), with a median of 16.7% and an interquartile range of −2.6% to 44.9%. It was clear that the impact of SEP adjustment was...
more pronounced in studies of all-cause mortality (median, 34.6%; interquartile range, 10.9% to 57.1%) than in studies of breast cancer mortality (median, 16.3%; interquartile range, −2.6% to 21.4%). In all comparisons of African-American and white women in the United States, adjustment for SEP resulted in an attenuation of the hazard ratio, whereas in comparisons of other ethnicities, adjustment tended to have small or negligible effects. For all-cause mortality, the impact was 45% versus −17% (i.e., a strengthening of effect following SEP adjustment); for breast cancer mortality, the impact was 20% versus −3%.

Furthermore, it appeared that the impact of adjusting for SEP on ethnic inequalities was weaker in studies in which there was more equal access to health care, defined as studies based in the United Kingdom, or in a US health maintenance organization or Department of Defense setting. For all-cause mortality, the impact was 40% versus −12%; for breast cancer mortality, it was 18% versus 3%. There was also a suggestion that those papers published in earlier years, compared with those published in later years, were more likely to demonstrate that SEP had a greater impact on explaining ethnic inequalities. For all-cause mortality, the impact was 40% prior to the year 2000 compared with −12% in later studies; for breast cancer mortality, it was 29% versus 8%. It is important to note that these differences are not weighted by the size of the study (as would be the case in meta-regression).

**DISCUSSION**

In this systematic review, we found that SEP explains part of the ethnic inequality in survival from all causes but that this finding was not evident for breast-cancer-specific survival. SEP explains more of the disparities for African-American versus white women in the United States compared with other ethnic comparisons. The role of SEP appears to be smaller in more recently published papers. We also found that the differences in breast cancer survival between ethnic groups may in part be explained by BMI, but there is little evidence to implicate smoking or alcohol consumption as explanatory factors for this inequality. Furthermore, given social patterning of BMI and other lifestyle habits, it is possible that our results for SEP and BMI are measuring the same effect.

To our knowledge, this review is the first to try to quantify the effect of specific lifestyle factors on ethnic differences in survival. Our study was strengthened by the carefully conducted review process, which attempted to minimize bias and error at all stages. A further strength is the inclusion of various ethnic groups, treated in a range of health care systems. Given that evidence of a genetic basis for inequalities in breast cancer survival is minimal, as discussed below, there may be lessons to be learned from comparisons of survival between majority and minority ethnic populations.

Our findings were limited by the insufficient detail reported in many of the published studies. It is very common for studies to adjust for many factors simultaneously, which does not enable investigation of which specific factors could be important determinants of ethnic inequalities in survival. Furthermore, several papers had to be excluded because the results were not reported in such a way that the effect of a variable could be quantified for extraction. We did not search the “gray literature,” such as technical reports and unpublished work, nor did we attempt to contact authors to request that data be presented in a different manner. Therefore, we cannot rule out the possibility of selection or publication bias in the review, although there was no evidence of the latter from the statistical tests that we performed.

In attempting to quantify the effect of the contribution of variables to ethnic inequalities in survival, it is important that these variables be measured accurately. Most studies investigating the effect of excess weight have used BMI; however, this variable is unlikely to be sufficient and may not be the most pertinent measure of overweight. BMI and waist/hip ratio affect all-cause and breast-cancer-specific mortality independently (29) and to a similar degree (19), although this effect may be restricted to younger women. Almost all the studies included in the review used an ecological measure of SEP based on area of residence and census information. This method assumes socioeconomic homogeneity within residential areas. Such measures underestimate socioeconomic disparities in breast cancer survival in the United Kingdom by up to 25% (57). In the United States, US Census-derived, area-based SEP measures at census tract poverty levels, rather than those made at block group or ZIP code level, have been advocated as the most useful measure of SEP at a small-area level (58). Ideally, individual-based measures of SEP would be used; for example, car access and housing tenure have been identified in the United Kingdom as more sensitive measures of deprivation than area-based measures (59). Furthermore, Nazroo (60) has argued that traditional socioeconomic groupings are not useful in investigating the impact of SEP on ethnic inequalities, since, within socioeconomic ethnic groups, ethnic minorities are likely to be the most deprived (in terms of income, housing tenure, employment, etc.).

In population-based studies of cancer survival, as many of the included studies were, it has been argued that the preferred statistical method of analysis is relative survival (61), with complementary excess mortality modeling. This method compares the survival experience of a group of patients with cancer with that of the general population and does not require cause-of-death information. Only one of the included studies used this method (12), but to adequately adjust for background mortality, it is preferable that ethnic-specific life tables be used; however, these tables are not available in the United Kingdom. In cohort studies, when excess mortality modeling is not appropriate, it is important to distinguish cause of death. Inequalities in all-cause mortality will be larger than those in breast cancer mortality because of the strong effect of socially patterned variables such as BMI and smoking on non–breast cancer deaths. A follow-up of over 233,000 women with breast cancer found that ethnic inequalities in mortality from breast cancer were of a magnitude similar to the inequalities in mortality from 4 obesity-related outcomes (62).

The source of the ethnicity data used was not reported in the bulk of the papers that we reviewed. Cancer ethnicity data are abstracted from medical records, and the patient
<table>
<thead>
<tr>
<th>First Author (Reference No.)</th>
<th>Publication Year</th>
<th>Source of Patients</th>
<th>Years of Diagnosis</th>
<th>Setting</th>
<th>Follow-up</th>
<th>Source of Ethnicity Data</th>
<th>Ethnicity 1</th>
<th>Ethnicity 2</th>
<th>No. of Patients</th>
<th>SEP Measure</th>
<th>Managed Care/Equal Access System?</th>
</tr>
</thead>
<tbody>
<tr>
<td>dos Santos Silva (12)</td>
<td>2003</td>
<td>Cancer Registry</td>
<td>1986–1993</td>
<td>Southeast England, United Kingdom</td>
<td>December 31, 1997</td>
<td>Assigned on the basis of name South Asian Non–South Asian</td>
<td>1,037</td>
<td>50,201</td>
<td></td>
<td>Census (Carstairs’s index)</td>
<td>Yes (United Kingdom)</td>
</tr>
<tr>
<td>Perkins (51)</td>
<td>1996</td>
<td>One Cancer Centre</td>
<td>Treated in 1958–1987</td>
<td>Texas</td>
<td>5 years (range, 0.1–416 months)</td>
<td>Patient self-report Black White</td>
<td>801</td>
<td>2,581</td>
<td></td>
<td>Insurance pay code</td>
<td>No</td>
</tr>
<tr>
<td>Bassett (52)</td>
<td>1986</td>
<td>Western Washington Cancer Surveillance System</td>
<td>1973–1983</td>
<td>Washington</td>
<td>To December 1983 (667 black woman-years and 3,156 white woman-years)</td>
<td>Not stated Black White</td>
<td>251</td>
<td>1,255</td>
<td></td>
<td>Race-specific census block group social class indicators (several)</td>
<td>No</td>
</tr>
<tr>
<td>Ansell (53)</td>
<td>1993</td>
<td>Hospital/ university cancer registry</td>
<td>1973–1985</td>
<td>Chicago, Illinois</td>
<td>8.3 years mean/&lt;13 years</td>
<td>Not stated Black White</td>
<td>887</td>
<td>265</td>
<td></td>
<td>Race-specific (where available) census tract information on income, education, employment, and poverty status</td>
<td>No</td>
</tr>
<tr>
<td>O’Malley (5)</td>
<td>2003</td>
<td>Greater San Francisco Bay Area Cancer Registry (part of SEER)</td>
<td>1988–1992</td>
<td>California</td>
<td>Up to July 2001</td>
<td>Medical records Black Hispanic Asian/Pacific Islander White</td>
<td>940</td>
<td>10,414</td>
<td></td>
<td>Race-specific measures for census block on income, education, poverty, and employment</td>
<td>No</td>
</tr>
<tr>
<td>Velikova (11)</td>
<td>2004</td>
<td>Yorkshire Cancer Registry</td>
<td>1986–1994</td>
<td>England, United Kingdom</td>
<td>January 1, 1999</td>
<td>Nam Penchan algorithm, place of birth, name South Asian Non–South Asian</td>
<td>120</td>
<td>16,759</td>
<td></td>
<td>Carstairs’s index</td>
<td>Yes (United Kingdom)</td>
</tr>
<tr>
<td>Franzini (54)</td>
<td>1997</td>
<td>The University of Texas M. D. Anderson Cancer Center</td>
<td>1987–1991</td>
<td>Texas</td>
<td>To September 1992; mean, 30 months</td>
<td>Not stated Black White</td>
<td>163</td>
<td>964</td>
<td></td>
<td>Ability to pay for treatment based on actual household income adjusted for no. of dependents and insurance coverage</td>
<td>No</td>
</tr>
<tr>
<td>El-Tamer (56)</td>
<td>1999</td>
<td>Cancer registry (2 breast cancer centers)</td>
<td>1982–1995</td>
<td>United States</td>
<td>Median, 36 months</td>
<td>Self-identification African American Caucasian</td>
<td>1,297</td>
<td>448</td>
<td></td>
<td>Median income based on ZIP code</td>
<td>No</td>
</tr>
</tbody>
</table>
may have self-identified this information; however, it may also have just been assigned based on the assumption of a health professional. Consequently, the accuracy of ethnicity recording in registries is likely to differ by ethnic group.

Specifically, high rates of misclassification have been reported for Hispanic, Asian, and Pacific Island ethnicities in the United States (63–66). Despite these limitations, collection of ethnicity data in many countries outside the United States is less well advanced. In the United Kingdom, ethnicity data have not, until very recently, been mandatory in National Health Service data sets and are not available in the United Kingdom’s cancer registries. For this reason, computerized algorithms have been used to assign South Asian ethnicity to individuals based on their names (11, 12). Despite relatively high sensitivity and specificity, there are limitations to this method. Furthermore, no similar method is available to identify black Caribbean and black African women, who form a significant proportion of the nonwhite population in the United Kingdom.

Many US studies relied on Surveillance, Epidemiology, and End Results data, which are not representative of the minority populations in terms of ethnicity or SEP (63). This selection bias introduced by using these data is reflected in the higher relative survival noted in the Surveillance, Epidemiology, and End Results areas compared with those 11 US states that contributed to the CONCORD program (67) and emphasizes the importance of nationwide cancer survival analyses. In a study of predominantly low-socioeconomic, uninsured, uneducated, rural women, no difference in overall survival or survival by stage was found between African-American and white women diagnosed with breast cancer throughout the 1990s (68). This finding suggests that, in the absence of privilege, ethnic inequalities in survival are no longer apparent, adding further weight to the argument that socially patterned differences drive these inequalities.

A suggestion frequently made regarding ethnic inequalities in health is that there may be an underlying genetic basis for these inequalities. Although there is a lack of major systematic genetic differences between ethnic groups, there are extensive differences in lifestyle, suggesting that health disparities are most likely driven by environmental factors (1, 2). In relation to breast cancer survival, although differences in certain allele frequencies have been related to prognosis, we are not aware of any studies demonstrating that these differences could explain ethnic inequalities in survival. On the contrary, numerous studies point to equally plausible, and more coherent, alternative explanations for the observed inequalities. The majority of this evidence relates to Asian women. Comparisons within one ethnic group cannot be explained by differences in genetic makeup. Chuang et al. (69) found that Chinese women born in the United States had better survival than Chinese women born in East Asia (HR = 1.22, 95% CI: 1.06, 1.40). Similarly, changes in survival across generations among immigrant women are an indicator of the importance of environmental and cultural factors. Pineda et al. (70) demonstrated such changes for Chinese and Japanese, although not for Filipino, women. These variations were almost fully explained by demographic and stage- and treatment-related factors.

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<tbody>
<tr>
<td>African American</td>
<td>1,971</td>
<td>30-49y</td>
<td>United States</td>
<td>To December 2002</td>
<td>Not stated</td>
<td>Black/White</td>
<td>2,479</td>
<td>White</td>
<td>1,086</td>
<td>612</td>
<td>Not stated</td>
<td>Black/White</td>
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<tr>
<td>Hispanic</td>
<td>1,086</td>
<td>30-49y</td>
<td>United States</td>
<td>To December 2002</td>
<td>Not stated</td>
<td>Black/White</td>
<td>2,479</td>
<td>White</td>
<td>1,086</td>
<td>612</td>
<td>Not stated</td>
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<td>Other</td>
<td>2,574</td>
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<td>To December 2002</td>
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<td>Black/White</td>
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<td>White</td>
<td>1,086</td>
<td>612</td>
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<td>Black/White</td>
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<td>Total cases</td>
<td>6,131</td>
<td>30-49y</td>
<td>United States</td>
<td>To December 2002</td>
<td>Not stated</td>
<td>Black/White</td>
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<td>White</td>
<td>1,086</td>
<td>612</td>
<td>Not stated</td>
<td>Black/White</td>
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</table>

Abbreviations: SEER, Surveillance, Epidemiology, and End Results; SEP, socioeconomic position.
<table>
<thead>
<tr>
<th>First Author (Reference No.)</th>
<th>Publication Year</th>
<th>Outcome</th>
<th>Crude Model</th>
<th>Model 1</th>
<th>Model 1 Parameters</th>
<th>Model 2</th>
<th>Model 2 Parameters</th>
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<td>dos Santos Silva (12)</td>
<td>2003</td>
<td>Excess mortality rate ratio</td>
<td>0.82 0.72, 0.94</td>
<td>1.35 1.21, 1.51</td>
<td>Stage</td>
<td>0.77 0.67, 0.87</td>
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<td>Perkins (51)</td>
<td>1996</td>
<td>All-cause mortality (5 years)</td>
<td>1.63 1.47, 1.82</td>
<td>1.35 1.21, 1.51</td>
<td>Age, stage, clinical factors</td>
<td>1.15 1.03, 1.29</td>
<td>Model 1 plus pay code</td>
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<td>1986</td>
<td>All-cause mortality</td>
<td>1.31 1.03, 1.67</td>
<td>1.35 1.05, 1.72</td>
<td>Age, stage, histology</td>
<td>1.10 0.83, 1.46</td>
<td>Model 1 plus social class (poverty, education, and households on public assistance)</td>
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<td>Ansell (53)</td>
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<td>1.20 1.00, 1.41</td>
<td>1.26 1.02, 1.57</td>
<td>Age, stage</td>
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<td>O’Malley (5)</td>
<td>2003</td>
<td>Death from breast cancer</td>
<td>1.81 1.59, 2.07</td>
<td>1.28 1.12, 1.46</td>
<td>Age, stage, clinical factors</td>
<td>1.22 1.05, 1.38</td>
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<td>2003</td>
<td>Death from breast cancer</td>
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<td>1.05 0.92, 1.20</td>
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<td>2003</td>
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<td>0.96 0.83, 1.11</td>
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<td>0.68 0.50, 0.91</td>
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<td>1.54 1.06, 2.23</td>
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<td>El-Tamer (56)</td>
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<td>1.27 1.05, 1.55</td>
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<td>1.16 0.95, 1.42</td>
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<td>Du (6)</td>
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<td>All-cause mortality</td>
<td>1.35 1.27, 1.45</td>
<td>1.07 0.99, 1.15</td>
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<td>1.21 1.01, 1.46</td>
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<td>1.542 1.365, 1.741</td>
<td>1.542 1.365, 1.741</td>
<td>Age</td>
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<td>1.10 1.00, 1.22</td>
<td>Age, stage, grade, estrogen receptor status, tumor characteristics, SEER site, screening status, treatment, comorbidities</td>
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<td>Breast cancer mortality</td>
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<td>Eley (47)</td>
<td>1994</td>
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<td>2.1 1.6, 2.8</td>
<td>2.2 1.7, 2.9</td>
<td>Age, location</td>
<td>2.0 1.5, 2.7</td>
<td>Model 1 plus marital status, education, poverty index, usual source of care</td>
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<td></td>
<td>1994</td>
<td>All-cause mortality</td>
<td>2.2 1.7, 2.7</td>
<td>2.2 1.7, 2.9</td>
<td></td>
<td>2.0 1.6, 2.6</td>
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Abbreviations: CI, confidence interval; HR, hazard ratio; SEER, Surveillance, Epidemiology, and End Results; SES, socioeconomic status.
Figure 2. Association between ethnicity (minority vs. majority ethnic groups) and all-cause mortality among women with breast cancer. A) Crude association; B) association adjusted for model 1 parameters (refer to Table 4); C) association further adjusted for socioeconomic position (refer to model 2 parameters in Table 4). The size of each square is proportional to the precision of the estimate and hence to the weight contributed by the individual study to the meta-analysis. AA, African American; CI, confidence interval; SA, South Asian; W, White.
Figure 3. Association between ethnicity (minority vs. majority ethnic groups) and breast cancer survival. A) Crude association; B) association adjusted for model 1 parameters (refer to Table 4); C) association further adjusted for socioeconomic position (refer to model 2 parameters in Table 4). The size of each square is proportional to the precision of the estimate and hence to the weight contributed by the individual study to the meta-analysis. AA, African American; API, Asian/Pacific Islander; CI, confidence interval; Hisp, Hispanic; SA, South Asian; W, White.
Some environmental exposures that are culturally related are likely to persist across generations. Furthermore, living as a first-generation immigrant in a country poses its own challenges, and linguistic and cultural barriers in access to care are likely to be important (69). The evidence above is supplemented by observations of changes over time in survival inequalities between ethnic groups. Jatoi et al. (71) documented widening inequality in all-cause mortality following breast cancer between black women and white women in the United States. This effect was driven by the most recently diagnosed cohort of women (1995–1999).

Such changes are more plausibly explained by improvements in the health system being better tailored to a dominant ethnic group. Finally, the importance of SEP and BMI in explaining inequalities, as shown in this review, adds to the evidence that genetic differences between ethnic groups are unlikely to be important determinants of inequalities.

Evidence is accumulating that women of different ethnicities experience disproportionate risks of various breast cancer subtypes. For example, we have shown that, in New Zealand, Māori and Pacific women are more likely than non-Māori/non-Pacific women to have human epidermal growth factor receptor-2–positive breast cancer (72). Māori women are less likely and Pacific women more likely than non-Māori/non-Pacific women to have a negative estrogen receptor and progesterone receptor status. In the United States, Hispanic women are more likely to have estrogen receptor and progesterone receptor negative breast cancer compared with non-Hispanic white women (73), and black women are more likely than white women to have triple-negative breast cancer (74). When Chinese women were compared with white American women, no differences in estrogen receptor or progesterone receptor status were found (69). Because receptor-negative breast cancer is not amenable to hormonal therapy, these ethnic differences could explain some of the inequalities in survival. However, even among women with triple-negative breast cancer, 5-year relative survival was lowest in the non-Hispanic black group (74). The presence of differential subtypes of disease could be due to differential risk factors, and breast cancer epidemiologists should refine their outcomes to account for these differences.

Our final analysis showed that adjusting the breast cancer survival inequalities for measures of SEP had a greater impact in studies of African-American versus white women compared with other ethnic comparisons. This finding is partly due to the higher crude inequality in survival between African-American and white women (Figure 3A), so there was more inequality to “explain” through adjustment. However, it is probably also partly due to the higher proportion of African Americans (compared with other ethnic minorities) living in poverty (25% vs. 8%) (75) and the probable higher level of resulting socioeconomic homogeneity in the census groups used to assign SEP in the studies included in this review. The effect of adjusting ethnic inequalities in health for SEP is strongly affected by the choice of SEP measure, and health inequalities between different ethnic groups respond in different ways to this adjustment (76). Therefore, the aggregation of different ethnic groups, as seen in several of the included studies (e.g., the grouping “Asian/Pacific Islander” in the United States and “South Asian” in the United Kingdom) could be masking the real effect that various individual-level measures of SEP would have on ethnic inequalities in survival.

Despite several of the studies included in our review, and others that did not meet our inclusion criteria (10, 77), being set in “equal access” health care systems, ethnic inequalities in breast cancer outcomes were still evident. However, it is important to point out that, in these contexts, “equal access” means “equal cost” or “no cost at the point of access,” which does not necessarily mean that all ethnic or socioeconomic groups will perceive the access equally, or indeed utilize the health service equally according to need. Underserved/minority ethnic groups may have had previous negative experiences within health systems, causing mistrust. For example, we demonstrated that, in New Zealand, Māori are more than twice as likely as European New Zealanders to have experienced unfair treatment by a health professional because of their ethnicity (78). Since health systems are generally run by and tailored to the majority population, the system can be difficult to navigate and may be culturally inappropriate for patients from minority ethnic groups.

Differential access to treatment is likely to play an important role in ethnic survival disparities, especially in light of continuing treatment advances. Some evidence exists that clinicians’ perceptions about patients, and their diagnostic and treatment decisions, are affected by patients’ ethnicity and SEP (79). In the United States, even when those of the same socioeconomic and health insurance status are compared, African Americans are less likely to receive optimum or curative treatment for cancer (80). A study of the follow-up of abnormal mammogram results in the United States found that being of African-American ethnicity was an independent predictor of inadequate follow-up (81). An American review found evidence of ethnic disparities among those who received definitive primary therapy, conservative therapy, and adjuvant therapy that were not explained by clinical variations (14). Even after adjusting for multivariable factors including stage and comorbidity, Bickell et al. (82) found that women from minority populations (African American and Hispanic) with early-stage breast cancer were twice as likely to experience underuse of necessary adjuvant treatments (HR = 2.0, 95% CI: 1.3, 3.1). This figure was slightly higher than the risk of not receiving appropriate therapies for women without insurance (HR = 1.9, 95% CI: 0.9, 4.0). These results together indicate that at least part of the ethnic inequalities in breast cancer survival is attributable to unequal care.

Differential exposure to risk factors and unequal access to and through a health care pathway can be considered manifestations of racism (83), pervading not only the health system but also society itself. A third manifestation in Krieger et al.’s (83) proposed framework is economic/social deprivation itself, which, as we have shown, is related to all-cause mortality among women with breast cancer. The importance of the macrosocial determinants of inequity and their impact on health have been discussed by Nazroo (84). It is easy to see that living as an ethnic minority woman in a society in which the health system is dominated by a different cultural framework could lead to less easy access.
into and through the health system, resulting in suboptimal care and outcomes. However, identifying points along the pathway that are amenable to immediate change is the challenge for public health and allied professionals. As noted in the recent World Health Organization report, Closing the Gap in a Generation (85), ensuring health equity is the responsibility of the highest level of government, which must be addressed through coherent, cross-policy agendas.

In addition to such high-level action, there is a substantial role for epidemiology in the concerted action to eliminate inequalities in cancer survival. Specifically, we suggest that bivariate as well as multivariable results be presented in a transparent way (e.g., refer to Curtis et al. (4)), with specific factors or groups of factors entered sequentially into models. This method will allow researchers investigating ethnic inequalities in cancer survival to use evidence-based approaches to identify how, and at what point on the care pathway, we can focus interventions specifically to reduce inequalities.

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Author affiliations: Centre for Public Health Research, Massey University, Wellington, New Zealand (Fiona McKenzie); and Department of Social Medicine, University of Bristol, Bristol, United Kingdom (Mona Jeffreys).

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Conflict of interest: none declared.

REFERENCES


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**APPENDIX**

**Search Terms**

- (mortality OR (prognosis) OR (cohort studies) OR (follow-up studies) OR (survival analysis) OR (disease-free survival) OR (survival rate) OR (“survival”) OR (“overall survival”))
- AND ((breast neoplasms) OR (“breast cancer”) OR (“breast carcinoma”) OR (“malignant breast tumor”) OR (“mammary cancer”))
- AND ((ethnic groups) OR (“ethnic minority”) OR (“ethnicity”) OR (“race”) OR (racial stocks))
- AND (((“alcohol consumption”) OR (alcohol drinking) OR (smoking) OR (obesity) OR (body weight) OR (body mass index) OR (“BMI”) OR (social class) OR (education) OR (income) OR (“SES”) OR (Socioeconomic factors) OR (poverty) OR (“deprivation”)))
- AND ((Humans[Mesh]) AND (English[lang]))