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SOCIAL, PROGNOSTIC, AND THERAPEUTIC FACTORS ASSOCIATED WITH CANCER SURVIVAL: A POPULATION-BASED STUDY IN METROPOLITAN DETROIT, MICHIGAN

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Previously, we studied the effect of socioeconomic status (SES) on cancer survival among adults of Toronto, Ontario and Detroit, Michigan.[1] Detroiters' survival was significantly worse among people from lower SES areas for 12 of 15 relatively common types of cancer. In contrast, no such SES-survival associations were found for 12 of 15 cancer types in Toronto Between-country analysis, which compared cases arising from Toronto and Detroit's low-income areas, revealed a significant Toronto survival advantage for 13 of 15 most prevalent cancers. Other studies demonstrated that such Canadian advantage was maintained even with a conservative comparison of Toronto's poor with Detroit's near poor,[2] as well as in other Canada-U.S. comparative locales.[3–5] Furthermore, SES acted as an effect modifier, that is, significant country-by-SES interactions were observed. Canadian survival advantages were observed only among the ecologically defined poor (residents of low-income neighborhoods). The present study aims to advance understanding of the factors associated with such disadvantaged survival among people with cancer in the United States.

Nine of 10 U.S. studies on cancer survival during the past 10 years have found a significant disadvantage with low SES.[1,3,6] Survival among those of relatively high SES was found to be 49 percent greater than that of their lower status counterparts. A similar SES-cancer survival association, although of attenuated magnitude (13 percent differential), has also been observed in other developed continental European and Nordic countries, as well as Australia.[7–10] Interestingly, the aggregate SES-cancer survival differential among Canadian cohorts has been found to be only 3 percent.[1–5,11,12] Health care systems differences, such as the greater representation of universally accessible single-payer systems in Nordic and other European countries, and Canada, may parsimoniously account for the greatly diminished SES-cancer survival associations found in these countries compared with the United States. Studies of race and cancer survival have provided further evidence for an SES-survival association in the United States.[13–16] Cumulative cancer survival among blacks was found to be approximately 43 percent less than that of whites, but this difference

diminished to only 8 percent in studies that provided any adjustment for socioeconomic factors or health care access.[17]

This analytic picture seems straightforward, but its valid policy interpretation is complicated by a number of other known relationships. For example, in the United States, such social factors as SES and race are both highly associated with cancer prognostic and treatment factors,[18–25] which themselves are highly associated with cancer survival in the United States and other countries.[26–28] Moreover, the associations of social factors with tumor biology in the United States[29–32] and the associations of social factors with prognosis and treatment in other countries, including Canada,[33–36] have all been observed to be extremely small or nonsignificant. Separately, each of these meta-estimates seems to be most consistent with a systemic, rather than an individual biological-behavioral, account. This study aims to measure the relative weight of all these factors—social, biological, standard prognostic, and therapeutic—in predicting cancer survival among a well-defined U.S. population.

Method

Cancer cases from the population of metropolitan Detroit, Michigan (3.9 million in 1990; Wayne, Oakland, and Macomb counties) were ascertained by the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) program.[37–39] Primary, malignant, adult (25 years of age or older), microscopically confirmed cases among the most common cancer sites with relatively good prognoses (five-year survival 50 percent or greater for any SES group) were included in the analysis: breast (ICD-9 code 174), prostate (185), colon (153), rectum (154), bladder (188), kidney (189), corpus uteri (182), cervix uteri (180), and oral (141–9).[40] These cancers, which account for 57 percent of all incident cases in metropolitan Detroit, may reasonably be expected to be most affected by health systems access and treatment differences. The study cohort was constrained by the following: 1984 was the first year in which SEER coded nearly all cases by residence, and the date of last follow-up was December 31, 1995. The cohort for five-year survival analysis was based on 58,023 incident cases between 1984 and 1990.

Cancer cases were joined by census tracts at the time of their diagnosis to socioeconomic data collected by the 1990 population census. The federally established, consumer price index–based and household size–adjusted, poverty criterion was then used to divide the cohort into relative socioeconomic areas:[37] high-income (2 percent of households below poverty, median annual household income of $51,500) and middle-income (7 percent poor, median income of $35,700) versus low-income (36 percent poor, median income of $17,800) areas. All of the other study variables were collected by SEER and assessed at the level of individuals: race (white or black), stage (localized or regional/distant), cancer-directed surgery and radiation therapy (none or some), vital status (alive or dead), and underlying cause of death. Other racial strata were excluded because there was insufficient statistical power to assess effects among them adequately. Multivariate analyses of five-year cancer survival were accomplished with proportion hazards regression models that considered deaths from causes other than cancer as censored observations at the time of death.[41,42] Of the cases dead at follow-up (47 percent), 78 percent died as a direct result of cancer. The model's proportional hazards assumption appears to have been met as no study

factors produced a significant differential survival effect (no factor-by-year of diagnosis interaction was significant).

Results

A series of increasingly complex proportional hazards models are displayed in Table 1. The simplest model, which regressed cancer survival only on race, found them to be highly associated among both women and men (respective black hazard ratios [HRs] of 1.65 and 1.69; Model 1). Next, models that regressed cancer survival only on social characteristics found that SES was also highly associated with five-year survival among women and men (respective low-income HRs of 1.62 and 1.49; Model 2). After income status adjustment, race made an additional contribution to the risk of dying among women (HR = 1.46), but not men. Next, a model built on prognostic and treatment factors along with SES and race, which essentially sorted for the most treatable cancers in its first step, found extraordinarily large effects of stage among both women and men (HRs of 12.23 and 8.63; Model 3). It then entered the combined treatment factors of surgery and radiation therapy among women and men (HRs of 3.16 and 1.79). The nonreceipt of stage-appropriate cancer-directed treatments was associated with respective two- to threefold greater risks of death within five years among male and female cancer patients.

Discussion

This study found that SES, race, stage of disease at diagnosis, and the experience of any surgical or radiation therapy were all significantly predictive of five-year survival among a cohort of patients with relatively screenable and treatable types of cancers. Across multivariate models, adjusted hazard ratios—which are interpretable as the relative risk of dying from cancer among the poor (ranged from 1.28 to 1.62), black women (1.31 to 1.46), those with more advanced disease (8.63 to 12.23), and those who did not receive cancer-directed treatments (1.79 to 3.16)—were not only statistically significant but also practically indicative of quite large effects. Black people were also observed to be nearly five times more likely to live in relatively poor neighborhoods where advanced disease at diagnosis and its nontreatment are more prevalent. These findings are consistent with the multiple disadvantaged statuses of people of color on such risk indicators as duration and severity of impoverishment, and being under- or uninsured. They are also consistent with the possibility of residual confounding resultant from only rather gross ecological adjustment for SES. It is well known that within many poor U.S. strata, black people are much poorer, on average, than are white people. Within this study's low-income areas, for example, the typical African American household had an annual income of $15,100 in 1990, while the typical white household had an income of $23,300. It certainly seems probable that the observed residual race-survival hazard is more likely a function of unadjusted socioeconomic and other contextual factors, rather than an effect of race per se. This study's findings seem to implicate health care systemic factors such as access to primary and cancer care; therefore, policy interventions that provide for more equitable initial access to the health care system, as well as similar access to the most appropriate treatments once diagnosed, may be expected to have large beneficial public health effects.

Methodological issues

Using dichotomous stage and treatment variables, which were conveniently available through the SEER program, as proxies for more complex ones (access and treatment protocols), we observed strong associations with cancer survival. Future research in this field ought to build more complex models that can provide more of an explanation for health and health care inequity problems. For example, SEER has begun making available more detailed extent of disease information, including tumor size, extension of tumor, and lymph node involvement. Analyses of post-1987 cohorts will be able to incorporate them. Also, although this study was able to assess gatekeeping treatment factors, it lacked surgical and radiation protocol detail, as well as information on chemo and adjuvant therapies, which would go a long way toward facilitating the connection between clinical practice and health care policy development in the United States.

The income variable used in this study was ecological. Its analytic goal, however, was merely to assign individuals to one of three broad SES classifications. Any information bias that may intrude is far less potent when aggregating cancer cases into tertiles, as this study did, than when such ecological measures are analytically employed as direct proxies for each individual's SES.[43–46] Furthermore, the magnitude of such error compares favorably with that encountered in related epidemiological domains and is likely to be non-differential.[47,48] The ecological fallacy notwithstanding, we believe that it is important simply to know that in the United States where people with cancer live is closely associated with how long they live. In other words, place itself becomes an important determinant of cancer survival.[49] This study's contextual inferences are thus most relevant to understanding systemic, community-level phenomena.[50,51] Insurance status is one such factor that fits with this study's findings.

Possible alternative explanations

A number of other factors possibly could explain cancer survival disadvantages among people who live in relatively poor neighborhoods. For example, cultural hypotheses related to differences between class or ethnic groups on cancer-preventive behaviors and rates of cancer screening participation have been developed but remain largely untested. In fact, it is actually the level of achieved education and knowledge, rather than any culture-specific attitude or belief differences, that accounts for much of the observed differences on cancer screening.[52–55] It is also possible that so-called lead time bias could explain the observed SES-cancer survival gradients. It could be that cancers generally are being detected earlier among those of higher SES, so that while observed survival time has been artifactually extended among them because their diagnoses have been moved forward, their real survival times are actually unaffected. We feel confident in ruling out lead time bias as a potent explanation for the following reasons: (1) adjusting for lead time, cancer stage has consistently been found to be associated with survival;[26,56–58] (2) adjusting for lead time and stage, other delays in diagnostic and treatment processes do not seem to be significantly associated with survival;[58] (3) this study's findings were homogeneous across cancers with diverse natural histories including their preclinical phase lengths; and (4) this study found treatment to be associated with survival after stage differences were accounted for. Finally, lifestyle factors that have been observed to be strongly associated with the occurrence of

some cancers are only weakly associated with cancer survival, if at all.[59–62] It is unlikely that these personal factors could account for the consistently observed SES-survival gradients. On the other hand, 8 of every 10 households in this study's low-income neighborhoods were categorically defined as poor or near poor (up to 200 percent of the poverty threshold),[37] and it is precisely such groups of people who are at the greatest risk of being uninsured or underinsured.[18] It seems that the elucidation of possible alternative explanations tends to further support, rather than refute, the plausibility of the health insurance explanation for this study's findings.

The unifying construct of health insurance status

Consistent with the health systems hypothesis, health insurance status in the United States' multitiered system is associated closely with SES and race/ethnicity,[63–65] which themselves are associated closely with the use of cancer screens and physician and hospital services. Insurance status in the United States is also known to be associated with cancer stage, investigations and treatments, and with survival.[19,66–69] Contrary to findings among U.S. samples, SES has generally not been found to be associated with the use of services in Canada,[70–72] and the SES-cancer screen association among Americans is two-thirds larger than the Canadian one.[73] Some delay to treatment problems have been described among Canadian samples, but they have not accounted for SES in any way.[74–76] Such problems seem to be associated with provincial or regional cancer care service endowments, rather than with personal income or other such individual factors.

Perhaps the best evidence that it is predominantly systemic factors that predict cancer survival is the consistent secular trend of a 10 to 25 percent improvement in cancer survival during the past two decades across diverse North American and European countries. As increasingly effective treatments have been made available, more cancer patients have survived for longer periods of time.[77–79] During the mere five years when adjuvant systemic therapy was made available in British Columbia, breast cancer survival increased 15 percent.[79] In the same connection, many (37 percent, breast) and, in some cases, the majority of cancer patients in the United States (colon, rectum) do not receive the best available treatments.[80,81] This research, and that of many others, very strongly suggests that in the United States, access to such best treatments is associated closely with SES, race, and ultimately with insurance status. Thus, it also strongly suggests that movement to a more universally accessible health care system such as Canada's, though not a panacea, certainly would result in more equitable enjoyment of health care resources and consequently more favorable health outcomes among all Americans.

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TABLE 1

THE ASSOCIATION OF SOCIAL, PROGNOSTIC, AND TREATMENT FACTORS WITH FIVE-YEAR CANCER SURVIVAL: COX PROPORTIONAL HAZARDS MODELS

	SELECTED REGRESSION MODEL STATISTICS[a]			
	WOMEN (*n* = 31,855)[b]		MEN (*n* = 26,168)[b]	
MODEL AND FACTOR (RISK GROUP)	HR	(95 PERCENT CI)[c]	HR	(95 PERCENT CI)
Model 1				
Race	1.65	(1.54, 1.77)	1.69	(1.55, 1.84)
Model 2				
Income areas	1.62	(1.46, 1.79)	1.49	(1.32, 1.67)
Race	1.46	(1.30, 1.63)	1.13	(0.99, 1.29)
Model 3				
Stage	12.23	(9.45, 15.85)	8.63	(6.95, 10.72)
Cancer-directed treatment	3.16	(2.59, 3.86)	1.79	(1.40, 2.29)
Income areas	1.38	(1.22, 1.57)	1.28	(1.10, 1.48)
Race	1.31	(1.16, 1.49)	1.00	(0.86, 1.16)

Note: Predictor variables were added to models in life space chronological order. Demographic and social characteristics that necessarily precede cancer diagnosis were entered first (age, race, and income area). Next, a factor assessed at diagnosis (stage) was added. And finally, cancer treatment factors (surgery and radiation therapy) were entered. Dummy variables for specific cancer sites did not enter any models after social, prognostic, and treatment factors were accounted for. Therefore, aggregate survival estimates among cancers of relatively good prognoses are this study's central focus.

[a] All adjusted for age (25–44,45–54,55–64,65–74,75 years or older) and other factors in the model.

[b] Number of cases with valid data on all factors. Among the six regression models, no analytic strata among women or men, respectively, had fewer than 400 or 300 cases.

[c] HR = hazard ratio and 95 percent CI = 95 percent confidence interval. Variables are coded so that a hazard ratio greater than 1.00 is indicative of hypothesis support.