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Time dependent ethnic convergence in colorectal cancer survival in hawaii

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Abstract

Background: Although colorectal cancer death rates have been declining, this trend is not consistent across all ethnic groups. Biological, environmental, behavioral and socioeconomic explanations exist, but the reason for this discrepancy remains inconclusive. We examined the hypothesis that improved cancer screening across all ethnic groups will reduce ethnic differences in colorectal cancer survival.

Methods: Through the Hawaii Tumor Registry 16,424 patients diagnosed with colorectal cancer were identified during the years 1960–2000. Cox regression analyses were performed for each of three cohorts stratified by ethnicity (Caucasian, Japanese, Hawaiian, Filipino, and Chinese). The models included stage of diagnosis, year of diagnosis, age, and sex as predictors of survival.

Results: Mortality rates improved significantly for all ethnic groups. Moreover, with the exception of Hawaiians, rates for all ethnic groups converged over time. Persistently lower survival for Hawaiians appeared linked with more cancer treatment.

Conclusion: Ethnic disparities in colorectal cancer mortality rates appear primarily the result of differential utilization of health care. If modern screening procedures can be provided equally to all ethnic groups, ethnic outcome differences can be virtually eliminated.

Background

After lung, prostate, and breast cancer, colorectal cancer ranks as a leading source of cancer mortality.[1] Nationally, although death rates have been declining since the mid-1980s, this trend is not consistent across all ethnic groups.[2] Specifically, in the past 10 years the death rate for Caucasians has been decreasing at nearly twice the rate as that for African Americans, and for Native Americans the rate has actually been increasing.[3,4] Among Asian ethnic groups, Chinese and Filipinos suffer a higher death

rate than do the Japanese.[5] These ethnic disparities appear largely driven by differential stage distribution (e.g., more advanced stage cases at presentation). Underutilization of cancer screening appears a key factor.[6] However, studies have found that even after controlling for stage at diagnosis, significant ethnic differences remain.[7]

How can one explain cancer survival differences that persist after adjustment for stage? Biological theories suggest that members of certain ethnic groups are genetically

predisposed to more aggressive forms of the disease, differ in host-tumor interactions, or are more likely to have contributing comorbid conditions. Wudel et al. (2002) recently reported that colorectal cancer survival differences between Caucasians and African Americans could not be explained by measurable differences in treatment.[8] Neuhausen has proposed a multi-factorial biology-utilization model.[9] Environmental theories propose that behavioral or socioeconomic factors leading to differential utilization of medical care are responsible. Varying utilization of, as well as access to health care has been reported as an explanation. [10–12] Schrijvers et al. (1997) have described a relation between socioeconomic status and comorbidity.[13] Evidence of interaction between age and socioeconomic status has also been reported.[14]

Hawaii's diverse ethnic composition combined with its long-standing statewide cancer registry, the Hawaii Tumor Registry (HTR), offer an ideal setting for examining ethnic differences in cancer survival. Previous research has documented significant survival disparities among the major ethnic groups (Caucasian, Japanese, Hawaiian, Filipino, and Chinese) in the state. In 1978, Nomura et al. found that Japanese patients had a nearly one-third higher survival rate than Caucasians.[15] Hirohata et al. (1977) described better survival rates among Japanese and Caucasians than among Filipinos and Hawaiians, even after adjusting for age, gender, and extent of disease at diagnosis.[16] Wegner et al. (1982) analyzed HTR data from 1960–1974 and found the same pattern of differences, which also could not be explained by any of the available covariates.[17]

The goal of the present study is to examine trends in recent survival rates. The HTR data that was incorporated in the Wegner (1982) study is still available as is more recent data up to the year 2000, allowing for an examination of survival patterns over time. Improved survival rates for cancer patients were observed by Hinds et al. (1983) during the years 1960–1974.[18] More recently, Maskarinec et al. (1999) have described improved breast cancer survival among all ethnic groups for 1970–1990.[19] Also, for the years 1995–1998 it was found that all ethnic disparities in breast cancer survival were eliminated once TNM Stage had been controlled.[20] These findings largely fail to support purely biologic explanations of disparate colorectal cancer survival. Differential utilization of health care or access to health care appears more important.

In Hawaii, the passage of time has brought general improvements in medical care and also narrowed disparities in access to medical care. Utilization of screening procedures continues to vary among ethnic groups, however. At the onset of this study, we hypothesized that, over the past

30 years, improved cancer screening and treatment, as well as better access to medical care across all ethnic groups has both improved survival rates and reduced ethnic differences in colorectal cancer survival. We further predicted that stage at diagnosis, age, and gender could explain most remaining survival differences, although we questioned the role of other factors such as treatment utilization and co-morbid disease.

Methods

Population and Sample

The population of Hawaii resides on seven islands with 80% on the island of Oahu and is estimated at 1.2 million with approximately 580,000 women. [21] Close to 13% of residents are 65 years and older and 40% are 40 years and older. The majority of the population is of Asian and Pacific Islander descent: 24.1% of the population in 1990 were Caucasian, 20.4% Japanese, 18.8% Native Hawaiian, 11.4% Filipino, 4.7% Chinese, and the rest other ethnic groups. However, over the period of this study, differences in age distribution within various ethnic groups in Hawaii have driven some differences in the actual proportions of individuals with cancer.

All data were ascertained through the Hawaii Tumor Registry (HTR), which provides population-based coverage of all newly diagnosed cancer cases and subsequent follow-up status for residents of Hawaii. The HTR was established in 1960 and it became part of the Surveillance, Epidemiology, and End Results (SEER) program in 1973. Quality control reviews have shown that case-ascertainment through HTR is virtually complete. Over 99% of cancer cases reported to the registry are histologically confirmed[22] and less than 2% of cases are identified through death certificates only. Whenever possible, the HTR follows cases until death through regular linkages with the Hawaii Department of Health's death records, hospital-based registries, and additional sources of mortality information. In accordance with SEER rules, less than 5% of cases are lost to follow-up. The ethnicity classification in the HTR is based on self-reports by patients. Information on the first course of treatment (surgery, chemotherapy, radiation, and hormone therapy) is also collected.[23]

From the HTR, all patients diagnosed with colorectal cancer (ICD-O-2 codes: C18.0-C18.9, C19.9, C20.9, C21.0-C21.2, C21.8) from 1960–2000 were extracted. Of the 17,416 pathologically confirmed cases of invasive colorectal cancer, we excluded 757 patients who were not from the five major ethnic groups (Caucasian, Japanese, Hawaiian, Filipino, and Chinese) and 235 patients for whom the diagnosis date was unknown, leaving a total sample of 16,424 cases for analysis.

Statistical Analyses

Data were first examined for ethnic differences by cohort across stage at diagnosis, age, sex, and cause of death using the likelihood ratio χ^2 statistic. This statistic is interpreted in the same manner as the Pearson χ^2 , but provides greater precision. Next, the SAS procedure PHREG,[24] which performs regression analyses based on the Cox proportional hazards model, was used to conduct survival analyses. As a test of the validity of the proportional hazards assumption (that the hazard ratio does not change over time), the Cox proportional hazards regression was performed with a variable calculated as the mean deviated natural log of time. Significance of this variable would imply a violation of the proportional hazards assumption. Survival (survivor function) estimates (used for figures) were based on the fitted proportional hazards model, and can be interpreted as the estimates for the survivor functions controlling for the effects of the covariates.[25] The same analyses were conducted in each of three separate cohorts determined by the year of diagnosis: 1960–1974, 1975–1987, and 1988–2000. The years for the first cohort were chosen to be consistent with the study conducted by Wegner et al.[17]

The starting year for the third cohort was chosen as 1988 because that was the first year in which TNM staging data (tumor size, node status, and metastases) became available in the HTR.[26] With TNM stage data, a comparison between the predictive value of this more comprehensive form of staging (0, I, IIA, IIB, IIIA, IIIB, and IV) and the SEER staging (local, regional, distant) could be made.[26] This was accomplished by computing the increment in model fit after the TNM stage variable had been added to model containing the SEER stage variable. The likelihood ratio statistic provides this information and is distributed as chi-square, allowing for determination of statistical significance. The years for the second cohort consisted simply of the years between cohorts one and three.

Within each cohort two sets of survival analyses were performed: In the first, an event was considered to have occurred if a patient died as a result of colorectal cancer; in the second, death by any other cause was considered an event. This allowed for an assessment of whether or not changing colorectal cancer survival trends were consistent with general survival trends. Censored values included patients alive at the last data collection and patients lost to follow-up. In all analyses the effect of ethnicity on survival, while controlling for the variables stage at diagnosis (local, regional, distant), age, sex, and year of diagnosis (to control for any linear time trends existing within cohorts), was assessed using a hierarchical approach in which a model including ethnicity was compared to one that did not. Age and year of diagnosis were treated as con-

tinuous variables, as examinations did not reveal any non-linear associations.

Results

Tables 1 and 2 provide frequency and percentage distribution data for stage at diagnosis, age, sex, and cause of death by ethnicity and cohort. The average ages for each stage at diagnosis were 66.6 years for local, 65.9 years for regional, and 65.5 years for distant. For each variable, significant ethnic differences were observed. When compared to the other ethnic groups, Hawaiians in all three cohorts were diagnosed at a more advanced stage [Likelihood Ratio χ^2 (8) = 36.8, 25.0, and 46.0; $p < .0001$, $p < .01$, and $p < .0001$ respectively] and were more likely to have died from colorectal cancer (as opposed to death by other causes or still alive) [Likelihood Ratio χ^2 (8) = 36.5, 71.2, and 69.6; $p < .0001$ for all]. Hawaiians also were significantly younger within cohorts 2 and 3 [Likelihood Ratio χ^2 (4) = 92.3 and 180.5; $p < .0001$ for both]. When compared to the other ethnic groups, Filipinos had a significantly higher proportion of males in all three cohorts [Likelihood Ratio χ^2 (4) = 140.1, 92.7, and 32.1; $p < .0001$ for all].

Figure 1 presents the survivor function plots (stratified by ethnicity) for each cohort and for each cause of death category (controlled for stage at diagnosis, year of diagnosis, age, and sex). The corresponding five-year survivor estimates with 95% confidence intervals are shown in Table 3, and the parameter estimates for each Cox regression survival model are provided in Table 4. Unadjusted five-year survival rates for each ethnic group were 80.5% for Japanese, 79.4% for Caucasian, 78.8% for Chinese, 76.4% for Filipino, and 72.5% for Hawaiian. The test of the validity of the proportional hazards assumption with the variable [$\log_e(\text{time}) - 0.52$] indicated no violation [χ^2 (1) = 0.13, $p = 0.72$].

When an event was considered death by colorectal cancer, significant ethnic differences were found for all three cohorts [Likelihood Ratio χ^2 (4) = 20.0, 23.1, and 12.0; $p < .001$, $p < .001$, and $p < .05$ respectively]. An examination of the confidence intervals for cohort 1 indicated that Japanese and Caucasian patients had significantly longer five-year survival than Filipino and Hawaiian patients. For the second cohort, the confidence intervals indicated that Caucasians had a significantly longer survival time than Filipinos; and in the third cohort, Hawaiians had significantly shorter survival time than all other ethnic groups. When an event was considered any death not caused by colorectal cancer, significant ethnic differences were again found for all three cohorts [Likelihood Ratio χ^2 (4) = 46.3, 73.3, and 57.9; $p < .0001$ for all]. Confidence intervals indicated that the Japanese always had a significantly higher survival rate than at least one other ethnic group.

Table 1: Frequency of Colorectal Cancer Cases Diagnosed in Hawaii from 1960–2000.

ETHNICITY	Caucasian			Japanese			Hawaiian			Filipino			Chinese			TOTAL		
	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3
STAGE																		
local	318	588	994	403	901	1668	59	178	299	90	246	440	79	171	299	949	2084	3700
regional	338	671	712	500	945	1210	57	143	279	116	236	334	97	167	191	1108	2162	2726
distant	240	324	360	208	390	453	58	102	153	83	139	146	59	86	69	648	1041	1181
missing	78	122	168	62	68	106	11	14	37	12	34	60	11	20	22	174	258	393
AGE																		
< 65	545	649	804	600	1033	1026	107	256	417	153	227	359	121	153	154	1526	2318	2760
≥ 65	429	1056	1430	573	1271	2411	78	181	351	148	428	621	125	291	427	1353	3227	5240
SEX																		
male	488	935	1299	669	1392	1985	99	266	427	259	495	637	153	248	299	1668	3336	4647
female	486	770	935	504	912	1452	86	171	341	42	160	343	93	196	282	1211	2209	3353
DEATH																		
cr cancer	331	567	506	422	859	775	93	182	246	142	251	234	99	161	124	1087	2020	1885
other	537	810	636	607	839	764	82	167	156	129	284	248	122	196	127	1477	2296	1931
censored	106	328	1092	144	606	1898	10	88	366	30	120	498	25	87	330	315	1229	4184
TOTAL	974	1705	2234	1173	2304	3437	185	437	768	301	655	980	246	444	581	2879	5545	8000

Notes. Cohort relates years of diagnosis, where cohort 1 is 1960–1974, cohort 2 is 1975–1987, and cohort 3 is 1988–2000. Death relates cause of death information, where *cr cancer* indicates colorectal cancer, *other* indicates any other cause, and *censored* indicates alive or missing. Stage is SEER staging.

Results were largely consistent with our hypothesis, but with one major exception: the persistently low Hawaiian colorectal cancer survival in cohort 3. This unpredicted finding led to post hoc analyses that were identical to the previous Cox regression models, but included the available treatment variables (surgery, chemotherapy, radiation, and hormone therapy) as additional predictors. Table 5 provides the percentages of each ethnic group receiving a given treatment by stage. With the inclusion of treatment variables, ethnic differences were no longer significant in the third cohort, but remained significant in the first two [Likelihood Ratio χ^2 (4) = 25.3, 29.1, and 8.2; $p < .0001$, $p < .0001$, and $p = .08$ respectively]. See Figure 2.

Additionally, we tested the post hoc hypothesis that Hawaiians have lower survival because they were both younger and diagnosed at a more advanced stage than the other groups. If advanced disease is more aggressive in young people, this could explain why the Hawaiians had lower survival. An interaction term between age and stage at diagnosis was created and added to the models run previously. However this interaction term did not show statistical significance, failing to support the post hoc hypothesis.

At least for cohort 3, our data also allowed us to compare the predictive value of the SEER staging variable (local, re-

gion, and distant) with that of the more comprehensive TNM staging variable. TNM staging provided significantly improved predictive value over SEER staging [Likelihood Ratio χ^2 (1) = 126.4; $p < .0001$]. However, inclusion of TNM staging did not eliminate the Hawaiian ethnic disparity in outcome [Likelihood Ratio χ^2 (4) = 11.7, $p < .05$], again suggesting that stage at diagnosis alone does not account for the persistently low survival among Hawaiians.

Discussion

With few exceptions, results clearly supported the stated hypothesis that ethnic disparities in colorectal cancer survival have been diminishing over time. Figure 1, showing the convergence of survival over time, best exemplifies this. The one discrepancy in this overall trend is the unchanged life expectancy for the Hawaiian group in cohort 3. A comparison with the survival curves for other causes of death within cohort 3 reveals that this effect is specific to colorectal cancer and does not reflect a general tendency for Hawaiians to die sooner.

One possible explanation for this is that Hawaiians were not utilizing medical care to treat colorectal cancer to the same degree as other ethnic groups. Our post hoc analyses did demonstrate that ethnic disparities were no longer statistically significant after controlling for treatment differ-

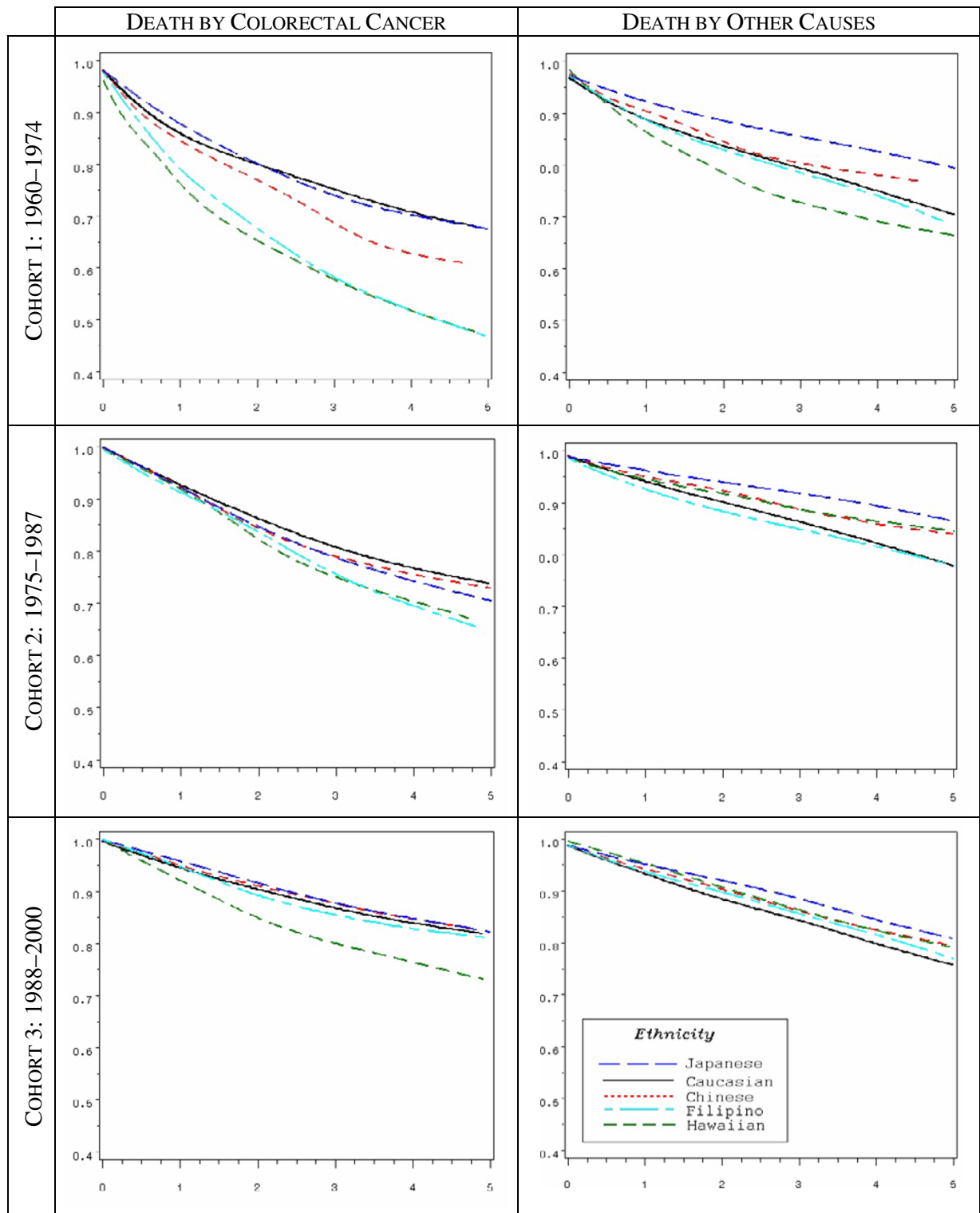


Figure 1
Estimated Survival versus Time (Years) by Ethnicity. Estimated survival (survivor functions) versus time (years) stratified by ethnicity for each cohort (1960–1974, 1975–1987, and 1988–2000) and cause of death category, controlling for the effects of SEER stage at diagnosis, year of diagnosis, age, and sex are provided.

Table 2: Percentages of Colorectal Cancer Cases Diagnosed in Hawaii from 1960–2000.

ETHNICITY	Caucasian			Japanese			Hawaiian			Filipino			Chinese			TOTAL		
	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3
STAGE																		
local	32.6	34.5	44.5	34.4	39.1	48.5	31.9	40.7	38.9	29.9	37.6	44.9	32.1	38.5	51.5	33.0	37.6	46.3
regional	34.7	39.4	31.9	42.6	41.0	35.2	30.8	32.7	36.3	38.5	36.0	34.1	39.4	37.6	32.9	38.5	39.0	34.1
distant	24.6	19.0	16.1	17.7	16.9	13.2	31.4	23.3	19.9	27.6	21.2	14.9	24.0	19.4	11.9	22.5	18.8	14.8
missing	8.0	7.2	7.5	5.3	3.0	3.1	5.9	3.2	4.8	4.0	5.2	6.1	4.5	4.5	3.8	6.0	4.7	4.9
AGE																		
< 65	56.0	38.1	36.0	51.2	44.8	29.9	57.8	58.6	54.3	50.8	34.7	36.6	49.2	34.5	26.5	53.0	41.8	34.5
≥ 65	44.0	61.9	64.0	48.8	55.2	70.1	42.2	41.4	45.7	49.2	65.3	63.4	50.8	65.5	73.5	47.0	58.2	65.5
SEX																		
male	50.1	54.8	58.1	57.0	60.4	57.8	53.5	60.9	55.6	86.0	75.6	65.0	62.2	55.9	51.5	57.9	60.2	58.1
female	49.9	45.2	41.9	43.0	39.6	42.2	46.5	39.1	44.4	14.0	24.4	35.0	37.8	44.1	48.5	42.1	39.8	41.9
DEATH																		
cr cancer	34.0	33.3	22.6	36.0	37.3	22.5	50.3	41.6	32.0	47.2	38.3	23.9	40.2	36.3	21.3	37.8	36.4	23.6
other	55.1	47.5	28.5	51.7	36.4	22.2	44.3	38.2	20.3	42.9	43.4	25.3	49.6	44.1	21.9	51.3	41.4	24.1
censored	10.9	19.2	48.9	12.3	26.3	55.2	5.4	20.1	47.7	10.0	18.3	50.8	10.2	19.6	56.8	10.9	22.2	52.3
TOTAL	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100

Notes. Cohort relates years of diagnosis, where cohort 1 is 1960–1974, cohort 2 is 1975–1987, and cohort 3 is 1988–2000. Death relates cause of death information, where *cr cancer* indicates colorectal cancer, *other* indicates any other cause, and *censored* indicates alive or missing. Stage is SEER staging.

Table 3: Probabilities of Surviving Five Years Among Three Cohorts of Colorectal Cancer Patients

COHORT	ETHNICITY	CAUSE OF DEATH	
		Colorectal Cancer	Other
1 1960–1974	Japanese	.68 (.65 – .71)	.79 (.77 – .82)
	Caucasian	.68 (.64 – .71)	.71 (.67 – .74)
	Chinese	.61 (.54 – .69)	.76 (.71 – .83)
	Filipino	.47 (.41 – .55)	.69 (.62 – .76)
	Hawaiian	.48 (.39 – .59)	.67 (.58 – .76)
2 1975–1987	Japanese	.70 (.68 – .72)	.86 (.84 – .88)
	Caucasian	.74 (.72 – .77)	.77 (.75 – .80)
	Chinese	.73 (.69 – .78)	.84 (.81 – .88)
	Filipino	.66 (.62 – .70)	.77 (.74 – .81)
	Hawaiian	.67 (.62 – .72)	.83 (.80 – .87)
3 1988–2000	Japanese	.82 (.81 – .84)	.81 (.79 – .83)
	Caucasian	.82 (.80 – .84)	.75 (.73 – .78)
	Chinese	.82 (.79 – .86)	.79 (.75 – .83)
	Filipino	.81 (.78 – .84)	.76 (.72 – .80)
	Hawaiian	.73 (.69 – .77)	.79 (.75 – .83)

Notes. Probabilities (with 95% confidence intervals) of surviving five years among three cohorts of colorectal cancer patients by ethnicity and cause of death are provided. Values reflect the estimates controlling for the effects of SEER stage at diagnosis, year of diagnosis, age, and sex.

Table 4: Determinants for Five-year Survival Among Three Cohorts of Colorectal Cancer Patients.

COHORT	VARIABLE	DEATH BY COLORECTAL CANCER				DEATH BY OTHER CAUSES			
		β	s.e.	$\chi^2(1)$	e^β	β	s.e.	$\chi^2(1)$	e^β
1 1960–1974	Stage	1.28	.050	659.0*	3.61	0.35	.044	65.5*	1.42
	Year	-0.43	.071	36.6*	0.65	-0.04	.071	0.3	0.96
	Age	0.18	.025	50.4*	1.20	0.56	.025	521.2*	1.75
	Sex	-0.08	.066	1.5	0.92	-0.28	.056	25.6*	0.75
2 1975–1987	Stage	1.66	.037	2029.3*	5.25	0.29	.036	68.8*	1.34
	Year	-0.14	.064	4.8	0.87	0.05	.061	0.7	1.05
	Age	0.16	.020	64.2*	1.17	0.70	.022	997.9*	2.01
	Sex	-0.13	.047	7.4	0.88	-0.35	.045	61.3*	0.71
3 1988–2000	Stage	1.80	.037	2398.7*	6.07	0.37	.036	102.1*	1.44
	Year	-0.01	.052	0.1	0.99	0.37	.079	22.0*	1.45
	Age	0.16	.021	58.6*	1.17	0.58	.023	616.2*	1.79
	Sex	-0.10	.048	4.7	0.90	-0.29	.048	37.5*	0.75

Notes. Determinants for five-year survival among three cohorts of colorectal cancer patients by cause of death are provided. All values were obtained using the method of partial maximum likelihood estimation in Cox regression. β is the regression coefficient, and is equivalent to the log of the hazard ratio. s.e. is the standard error of the regression coefficient and is used for calculating chi-square, which in turn is used for determining the statistical significance of β . $\chi^2(1)$ is the chi-square value with one degree of freedom (each variable provides a single degree of freedom) and is calculated as $(\beta/s.e.)^2$. e^β is the hazard ratio and is interpreted in the standard fashion. For Year (of diagnosis) and Age, the parameters reflect the estimated change per 10-year increment. Sex is coded with male as the control. An asterisk indicates significance at the .0001 level; none of the others was significant within the experimentwise α -level set to .005.

ences. Interestingly, however, Hawaiians did not appear to be receiving less treatment; and with respect to chemotherapy and radiation, appear to have been receiving more than the other ethnic groups. One possible explanation for this is that treatment is causing adverse effects and death. Another is that doctors see prognostic signs of severe disease that are not measured by our covariates, and therefore prescribe more treatment. That is, Hawaiians may have more advanced disease than staging alone indicates.

The implications of these findings are important. If differential screening constitutes the primary reason for ethnic survival disparities, it should be possible to achieve equally favorable outcomes in all ethnic groups. With the exception of the Hawaiians, the evidence presented here reflects a convergence in terms of screening, medical care, and colorectal cancer survival among all ethnic groups. Further efforts are needed to examine why Hawaiians do not follow the overall trend, and how to make improvements. In this regard, a Native Hawaiian cancer network called the Imi Hale is attempting, along with support from the National Cancer Institute, to increase screening for colorectal cancer in Native Hawaiians.[27]

One limitation of this study is that data are restricted to the state of Hawaii. However, even though there are clearly potential regional differences in ethnic patterns of survival, the results of this study could be important beyond Hawaii. For example, in national studies, it has been shown that African-Americans are less likely than others to receive adjuvant chemotherapy.[28] Differential treatment utilization may drive ethnic outcome disparities. The role of individual patient choice and the role of complicating co-morbid conditions in treatment selection probably play some role, and another limitation of our study is not having access to this information. In future studies, however, we hope to elucidate the impact of such factors.

To this end, an important area for future research is detailed analysis of specific treatments received by cancer patients. For example, beginning in 1988 (the start of the third cohort in the present study) colorectal cancer survival has been improved through the use of 5-fluorouracil-leucovorin as adjuvant chemotherapy.[29] This factor, as well as improving stage distribution through screening, has undoubtedly contributed to the greatly improved colorectal cancer survival rates in the third cohort. Unfortunately, the HTR does not provide adequate detail with

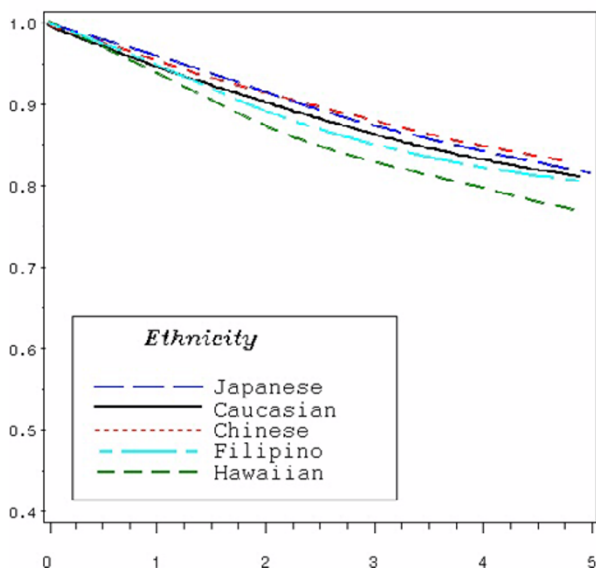


Figure 2
Estimated Survival versus Time (Years) by Ethnicity.
 Estimated survival (survivor functions) versus survival time (years) stratified by ethnicity for the third cohort (1988–2000) controlling for the effects of SEER stage at diagnosis, year of diagnosis, age, sex, and treatment are provided.

respect to specific chemotherapy treatments, so this hypothesis could not be examined here. However, future studies incorporating expanded data sources should examine whether Hawaiians have been receiving adjuvant 5-FU-leucovorin to the same degree as others, and if not, why not (e.g., access, informed choice with refusal of recommended treatment, or co-morbid disease).

Conversely, if Hawaiians receive apparently similar adjuvant therapy (i.e., same agents, dosage, number of courses, etc.), do they benefit to the same degree as others? Also, do they show a similar degree of treatment compliance? These issues may be of particular relevance, because results from this study suggest that Hawaiians are equally likely, if not more likely, to receive treatments.

Hawaiians have been reported to have relatively high rates of diabetes, renal and vascular disease, and tend to be afflicted at a younger age. Perhaps an interaction between cancer treatment and comorbid conditions is having a negative effect on Hawaiians. We speculate that co-morbid illness might play a role in treatment selection for some individuals with colorectal cancer. Collection of ICD-9 diagnosis codes from non-HRT sources with appropriate record linkage would allow us to study this.

Table 5: Frequencies and Percentages of Treatments by SEER Stage and Ethnic Group for Cohort 3 (1988–2000).

STAGE	ETHNICITY	TREATMENT							
		Surgery		Chemo		Radiation		Hormone	
		N	%	N	%	N	%	N	%
Local	Japanese	1613	96.9	98	5.9	49	2.9	0	0.0
	Caucasian	947	95.5	90	9.1	58	5.9	4	0.4
	Chinese	293	98.3	7	2.3	5	1.7	0	0.0
	Filipino	425	96.6	29	6.6	25	5.7	1	0.2
	Hawaiian	290	97.3	32	10.7	23	7.7	1	0.3
Regional	Japanese	1190	98.4	581	49.2	173	14.4	11	0.9
	Caucasian	685	96.3	281	40.7	123	17.4	3	0.4
	Chinese	188	98.4	88	47.1	30	15.8	1	0.5
	Filipino	326	98.2	124	37.6	56	16.9	0	0.0
	Hawaiian	265	95.0	149	54.4	66	23.8	3	1.1
Distant	Japanese	314	69.5	240	54.3	53	11.8	2	0.4
	Caucasian	251	69.9	126	36.2	31	8.7	4	1.1
	Chinese	42	60.9	34	50.8	10	14.5	1	1.5
	Filipino	103	70.6	79	55.2	21	14.5	2	1.4
	Hawaiian	107	70.4	86	57.7	32	21.1	2	1.3

Other results from this study indicate that age at diagnosis is another significant predictor of survival, with older individuals having a shorter life expectancy after diagnosis. However, a comparison of hazard ratios by cause of death showed that the values were much lower for death due to colorectal cancer than for other causes. This suggests that, while age is clearly related to overall survival, it is less relevant to colorectal cancer survival. That is, colon cancer is not more deadly for older individuals than for younger ones. Similarly, sex appears to predict colorectal cancer survival. A small beneficial effect was observed for women when considering death due to colorectal cancer, but a strong effect when considering death due to other causes. The impact of co-morbid disease on survival might explain these age and gender differentials.

Stage at diagnosis represents the most important prognostic variable. In this study the SEER staging system was used so that identical analyses could be performed across all three cohorts. However, for the most recent cohort (cohort 3), TNM staging clearly improved survival predictions over the less comprehensive SEER staging. In future studies, we will use TNM staging whenever possible.

Conclusions

This study provided longitudinal evidence in support of non-biologic explanations for ethnic disparities in colorectal cancer survival. Specifically, the present analysis suggests that observed ethnic differences result from differential screening. In Hawaii, ethnic disparities in colorectal cancer survival have narrowed considerably over the past 30 years. However, Hawaiian patients did not experience the same degree of improvement in survival as the other ethnic groups.

Competing interests

None declared.

Authors' contributions

IP participated in the design of the study, drafted the manuscript, and performed the statistical analyses. SM, SD, SH, and GM participated in the design of the study.

All authors read and approved the final manuscript.

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