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Choice of survival metric and its impacts on cancer survival estimates for American Indian and Alaska Native people

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Abstract

Background: Different survival metrics have different applicability to clinical practice and research. We evaluated how choice of survival metric influences assessment of cancer survival among American Indian and Alaska Native (AIAN) people relative to non-Hispanic whites (NHW). A secondary objective was to present variations in survival among AIAN people by age, sex, stage, and Indian Health Service (IHS) region.

Methods: Five-year survival was calculated using the North American Association of Central Cancer Registries Cancer in North America dataset. We calculated survival among AIAN people, compared to NHW using four approaches: 1) observed (crude) survival, 2) cause-specific survival, 3) relative survival using age- and sex-adjusted lifetables and 4) relative survival using life tables additionally adjusted for race, geography, and socioeconomic status. For AIAN people, we evaluated how survival varied by age, stage at diagnosis, and IHS region.

Results: Observed survival methods produced the lowest estimates, and – excepting prostate cancer – cause-specific methods produced the highest survival estimates. Survival was lower among AIAN people than NHW for all methods. Among AIAN people, survival was higher among those 20-64 years, females, and tumors diagnosed at local stage. Survival varied by IHS region and cancer sites.

Conclusions: These results support the assertion that using the same methodology to compare survival estimates between racial and ethnic groups is of paramount importance, but that the choice of metric requires careful consideration of study objectives.

Impact: These findings have the potential to impact choice of survival metric to explore disparities among AIAN people.

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Keywords

Native American; cancer survival; survival metric; cause-specific survival; relative survival; observed survival; Cancer in North America (CiNA)

INTRODUCTION

Cancer survival measures are an important tool for cancer patients, clinicians, researchers, and policy makers to understand the burden of cancer at both the individual and population levels.(1) Observed (crude) survival measures, which indicate probability of death from cancer or other causes, are informative for cancer patients and their physicians as an indicator of prognosis. Net survival measures, which indicate cancer survival in the absence of other (non-cancer) causes of death, are more commonly used by researchers and others to indicate progress towards cancer control through examination of trends over time, and comparisons between populations.(2) Net survival metrics can also be used to indicate cancer disparities, and evaluate progress towards elimination of such disparities.(3,4)

Net survival can be considered in two settings: relative, and cause-specific. Relative survival compares survival among a population of cancer patients to that which would be expected in a comparable cancer-free population. Because this framework is not dependent on cause of death information, it has been considered the superior approach, and has been widely used in the cancer surveillance community.(5–7) It may be particularly useful for international comparisons where specific cause of death might not be known for different countries or populations, and is also preferable when background mortality is suspected to differ between populations being compared.(8) However, one key limitation of relative survival is that calculation of this measure requires life-tables that well represent the experience of the population.(9,10) Age and sex-adjusted life-tables are not always accurate for certain population subgroups, biasing relative survival estimates.(11)

Conversely, cause-specific analyses consider only death due to the cancer as being an “event”; individuals dying from any other cause are censored at the date of death. A critical assumption of this method is accuracy of cause of death information;(1) misclassification in cause of death can occur because cancer patients may have complicated medical histories which include many comorbidities that could have contributed to their reason for dying. Furthermore, as time since cancer diagnosis increases, it can become difficult to distinguish and classify death due to that specific cancer versus other causes. Cause-specific survival is considered the superior methodologic approach when cause of death information is known to be accurate, and in patients diagnosed with localized disease, or who have been heavily exposed to specific risk factors including infectious agents and smoking.(12) Cause-specific analysis has also been used among populations for whom the general age- and sex-adjusted lifetables were thought not to reflect that population’s life expectancy experience.(13)

Choice of survival metric may affect our ability to understand health disparities affecting minority populations in the U.S. We are interested in cancer disparities that affect American Indian and Alaska Native (AIAN) people.(13–16) Previous work examining survival among AIAN people has used a cause-specific framework to indicate improvements in

survival from lung and colorectal cancers among Alaska Native people,(13) as well as to examine racial and ethnic disparities in survival in New Mexico.(17) In 2018, the National Cancer Institute developed and released lifetables accounting for differences in mortality by geography (county-level), socioeconomic status (SES), and race/ethnicity, including among AIAN people.(11) These more specific lifetables have been shown to more accurately estimate relative survival among minority groups.(11) In the present study, we were interested in exploring how choice of survival metric influences assessment of cancer survival disparities specifically among AIAN people for all cancer sites combined, as well as specific cancer types; thus, we calculated survival estimates using different available approaches (observed, net: relative, cause-specific), and compared estimates between AIAN people and non-Hispanic whites (NHW). As a secondary aim, we compared survival estimates among AIAN people stratified by age, sex, cancer stage, and IHS region (all cancer sites combined, and leading cancers).

MATERIALS AND METHODS

Data sources

We used the North American Association for Central Cancer Registries (NAACCR) Cancer in North America (CiNA) Survival dataset, a subset of the CiNA Deluxe Analytic File, for diagnosis years 2000 to 2017. Data are available upon application to NAACCR at naaccr.org. To be included in CiNA Survival data, registries must meet the following criteria for at least three consecutive years: case completeness (≥ 90%), passing edits (100%), low numbers of death certificate only cases (≤ 5%) and duplicate reports (≤ 2/1,000 cases), and small proportion of cases missing information on race (≤ 5%), or sex, age and county (≤ 3%). Registries must also meet the Surveillance, Epidemiology, and End Results (SEER) follow-up standard or ascertain all deaths through the study cutoff date.

Data from registries that did not give permission for their data to be used for this study or who did not contribute data to CiNA Survival for the entire study period were not provided by NAACCR for analysis. We also excluded three registries which had > 25% missing or unknown cause of death among those known to be dead, and registries without any Purchased/Referred Care Delivery Area (PRCDA) counties.(18) Registries included in this analysis were Alabama, Alaska, Arizona, California, Colorado, Connecticut, Florida, Idaho, Iowa, Kentucky, Louisiana, Maryland, Michigan, Montana, Nebraska, Nevada, New Mexico, North Carolina, North Dakota, Oklahoma, Oregon, Pennsylvania, South Carolina, Texas, Utah, Virginia, Washington, Wisconsin. Analyses were restricted to PRCDA counties, as AIAN racial misclassification is known to be lower in these counties.(18) All NAACCR registries conduct linkage with the Indian Health Service to reduce racial misclassification.(18) We estimate that our analysis included approximately 62% of AIAN people.

Ethics Statement

The 2018 revised common rule considers secondary analysis of public health surveillance data to be “not research”; the University of Iowa Institutional Review Board determined this study to be not human subjects research.

Data Availability

NAACCR data are available to qualified researchers through application available at naaccr.org.

Statistical analysis

We calculated five-year survival for people diagnosed aged 20+ years using four methods: 1) relative survival ratio with general lifetables (hereafter: relative survival – general lifetables); 2) relative survival ratio with race, geography, and SES-specific lifetables (hereafter: relative survival – specific lifetables); 3) cause-specific survival; and 4) observed (crude) survival. Analyses were conducted for all malignant cancer sites combined,(19) as well as the following cancer sites (SEER Site recode; International Classification of Diseases for Oncology, Third Edition (ICD-O-3) anatomic site codes in parentheses): female breast (C500-509), colon and rectum (C180-189, C199, C209, C209), prostate (C619), stomach (C160-169), pancreas (C250-259), liver (C220), lung and bronchus (C340-349), and kidney and renal pelvis (C649-659). These sites were chosen as they were the most common among AIAN people, and therefore were likely to have adequate case counts to support a robust survival analysis.

Age-adjusted five-year survival estimates were calculated among AIAN people, and compared to those among NHW. Choice of NHW as a comparison group was made a) because NHW are the largest (and therefore most statistically stable) racial/ethnic group for comparison, and b) to maintain consistency with the large body of disparities literature that compares AIAN people to NHW.(15,16,20,21) However, we recognize that this choice is not necessarily in line with anti-colonial research approaches;(22,23) for this reason, our secondary aim focuses solely on AIAN people without such comparison. Among AIAN people only, we calculated survival estimates by strata of age (20-64 years, 65+ years), stage (SEER Combined Summary Stage, 2004-2017: local, regional/distant/unknown), and IHS region. All analyses excluded individuals with non-malignant behavior, no survival time, death certificate/autopsy only cases, and included first primary cancers only (i.e., sequence # 00 or 01).(19)Analyses were conducted using the Surveillance Research Program, National Cancer Institute's SEER*Stat software (www.seer.cancer.gov/seerstat) version 8.3.9.

Among registries meeting SEER follow-up standards (SEER-18 registries plus Idaho, Montana, and New York), the survival time for alive patients was calculated through the first of date of last contact, date of death, or December 31, 2017. For registries not meeting SEER follow-up standards, survival time was calculated through date of death, or December 31, 2017; patients who were not known to be deceased were presumed to be alive.(24)

All survival estimates were calculated using the actuarial method. Relative survival – general lifetable estimates were calculated using the age- and sex-adjusted lifetables provided within SEER*Stat for the U.S. population (1970-2017). Relative survival – specific lifetable estimates were calculated using the more recently released race, geography, and SES-specific lifetables (1992-2016) also available in SEER*Stat.(11) We used the Ederer II approach to calculate expected five-year survival proportions.(25) Estimates of cause-specific survival were calculated using the SEER cause-specific death classification as the

outcome of interest; individuals with no known cause of death were excluded from cause-specific analyses. Survival estimates were standardized using International Cancer Survival Standard (ICSS) 1 weights as described elsewhere.(26)

RESULTS

Case counts utilized for observed and relative survival analyses are given in Table 1. There were 75,485 AIAN cancer cases (all sites) included in this study. The most common tumor was female breast, followed by cancers of the lung and bronchus and colorectal cancers. Females comprised a little over half of the AIAN study population (52%). Over half (58%) of the AIAN study population was aged 20–64 years at the time of diagnosis, compared to 45% among NHW. Most AIAN patients (58%) were diagnosed with a cancer at regional, distant or unknown stage, compared to 51% among NHW. Reflective of the overall AIAN population by region, the largest proportion of cases among AIAN people were seen in the Southern Plains region, followed by the Southwest and the Pacific Coast.

Comparison of survival measures

Figure 1 shows five-year survival estimates for select cancer sites, calculated using the four survival methods (observed survival, cause-specific survival, relative survival – general lifetables, relative survival – specific lifetables), comparing AIAN people and NHW. As expected, we observed differences in five-year survival estimates between the four methods for both AIAN and NHW populations. For instance, among both populations, observed survival methods produced the lowest estimates, and with the exception of female breast and prostate cancers, cause-specific methods produced the highest survival estimates. For several cancer sites, absolute differences in survival estimated by the methods yielding the highest and lowest estimates varied by greater than 10% (AIAN: prostate 17.6%, female breast 12.4%, kidney and renal pelvis 11.7%; NHW: prostate 14.9%, female breast 11.5% kidney and renal pelvis 10.0%). Among AIAN people, absolute differences in relative survival estimates calculated using the general versus the race-, geography-, and SES-adjusted life tables ranged from 0.5% to 8.6% (Figure 2). Differences among NHW were < 1.0% for all primary site categories.

Survival estimates tended to be lower among AIAN people than NHW: all sites five-year survival was 11% lower among AIAN people that NHW (AIAN relative survival - specific lifetable estimate: 55.3% [95% CI: 54.7, 55.8]; NHW relative survival - specific lifetable estimate: 65.5% [95% CI 65.4, 65.5] (Figure 1). When looking at site-specific data, the smallest differences in relative survival – specific lifetable estimates between AIAN people and NHW were observed for pancreatic cancer (1.6%) and the largest for stomach cancer (7.4%).

Cancer survival among AIAN people

A secondary objective of these analyses was to compare survival estimates among AIAN people across strata of age, stage at diagnosis, and IHS region (Figure 1, Supplementary Figures 1–4). We base our description here in text on relative survival – specific lifetable estimates; however, estimates generated using all four methods are presented in the figures.

Overall, we observed the highest five-year survival for cancers of the prostate (93.6% [95% CI: 91.9, 95.0]) and female breast (86.0% [95% CI: 84.4, 87.5]). The lowest relative survival estimates were seen for cancers of the pancreas (7.8% [95% CI: 6.4, 9.3]), stomach (20.9% [95% CI: 18.6, 23.3]), lung and bronchus (15.6% [95% CI: 14.6, 16.5), and liver (11.9% [95% CI: 10.1, 13.8). When examining survival by strata of age, stage at diagnosis, sex, and IHS region, we observed higher survival among those aged 20–64 years versus those aged 65+ years; those diagnosed at local stage versus regional, distant, or unknown stage. For many of the sites examined, survival was higher among females than males. Survival also varied by IHS region; for example, CRC-specific survival was highest in Alaska (67.5%) and lowest in the Southern Plains region (57.7%).

DISCUSSION

Understanding and addressing cancer disparities among minority populations is of interest to the National Institutes of Health, professional associations including the American Cancer Society, clinicians, and the communities themselves. Although changes in cancer survival are most accurately evaluated in the presence of incidence and mortality,(27) cancer survival can illuminate differential effects of post-diagnosis factors such as access to treatment, treatment effectiveness, and pre-diagnosis factors such as access to screening. Different survival metrics (observed, net: cause-specific and relative) reflect different underlying methodologies, and as such provide different information suitable for different purposes. The purpose of this study was to evaluate how the use of different survival metrics might influence investigations into cancer survival disparities affecting AIAN people.

Our findings have direct implications for studies of disparities. We found that differences in survival estimates between AIAN people and NHW varied greatly depending method used, including referent lifetables. In our analyses, differences between methods were different between AIAN people and NHW (Figure 2); this was particularly pronounced for relative survival estimates calculated using different lifetables. Specifically, we observed differences between relative survival calculated with race-, SES-, and geography-specific and general population lifetables for AIAN people, but not NHW. This likely occurs because general population lifetables mainly reflect the mortality experience of the largest group (NHW), thus underestimating referent mortality of AIAN populations in the context of relative survival. We found relative survival ratios calculated using general population and race-, SES-, and geography-specific lifetables to be similar for those cancer sites with the lowest survival (liver, stomach, pancreas, lung and bronchus), but sometimes very different for sites with higher survival (female breast, prostate, colorectal, kidney).(11) One potential explanation for this is that female breast, prostate and colorectal cancers are all screenable cancers. Socioeconomic status is positively correlated with cancer screening, impacting stage at diagnosis and subsequent survival.(28) Race-, geography-, and SES-specific lifetables adjust for these confounding factors at the area-level, generating more accurate estimates of death associated with cancer than general lifetables, as reflected in research by Mariotto et al.(11) This is particularly useful when evaluating changes in survival over time. Alternatively, it may be that for higher survival sites where relative survival is closer to 100% (i.e., the relative survival ratio comparing cancer patient to general population survival is closer to 1), that the background mortality of the population (and the lifetable used to

calculate that mortality) has a larger impact on the relative survival estimates. Regardless of mechanism driving these differences, we conclude that choice of lifetable may have drastic effects on estimates, and in turn, interpretation of disparities. Furthermore, we recognize that depending on the study question, the comparisons of survival metrics calculated via different methods and with different life tables may be illuminating.

While race-, geography-, and SES-specific lifetables are useful when evaluating survival disparities between groups, the presentation of survival estimates using general lifetables may also be useful in illuminating disparities between groups with different population-level health behaviors or experiences. Depending on the research question – and in particular in the investigation of health disparities – investigators may find it equally or more revealing to present relative survival estimates based on general and race-, geography-, and SES-specific lifetables, as a means by which to help explain the “crude” but real disparities in survival observed from general lifetables. Further, the relative survival estimates presented herein do not, for example, account for distributions of stage at diagnosis, smoking status, or primary site, all of which impact survival and may be differentially distributed between populations. We used a widely-available and commonly used tool (SEER*Stat) to conduct these analyses; however, we recognize that should one desire to account for these factors in elucidating survival disparities, and/or answer more complex questions that require simultaneous adjustment for multiple factors, a modeling approach may be more appropriate. In particular, flexible parametric models have wide applicability, including in situations where the assumption of proportional hazards may be violated.(29,30)

In our analysis, observed (crude) survival produced the lowest survival estimates, whereas cause-specific methods produced the highest estimates (Figure 1). This latter finding is consistent with those previously reported in the literature.(1,9,10,31,32) and is expected because observed survival uses the broadest definition of an “event” (i.e., death from any cause), whereas cause-specific methods have the narrowest definition (i.e., death from that specific cancer).(1) Furthermore, estimates from the different survival methods were more similar among cancer sites with low survival (lung, pancreas, stomach), relative to those with higher survival (female breast, colorectal, kidney). In situations of low competing risks (i.e., highly fatal cancers), cause-specific and observed survival are expected to be more similar than in situations of high competing risk (i.e., less fatal cancers).

To our knowledge, only one paper by Withrow and colleagues has analyzed how choice of survival method impacts estimates among Indigenous populations;(10) this study showed that, among Canadian First Nations and Inuit populations, cause-specific survival when calculated using a narrow definition of the event produced survival estimates that were much higher than those calculated using cause-specific methods with a broader definition of the event, or relative survival. This finding was particularly pronounced for cancers of continuous organ systems (e.g., digestive and respiratory systems). Our present work adds to this body of literature by examining methods and data pertinent to the U.S. Indigenous context. We anticipate that this information will be of interest to individuals working with U.S. Indigenous communities to reduce their burden of cancer.

Secondary objectives of this study were to describe survival for leading cancer sites among AIAN people by age, sex, IHS region, and stage at diagnosis, and differences in survival estimates between AIAN people and NHW. We observed slight differences in survival between most IHS regions, but Alaska had markedly lower all-site survival and the East region having markedly higher all-site survival. This observation may be explained in part by underlying differences in the primary cancer site distribution by region; for example, incidence of highly fatal lung cancer is lower in the Southwest region than it is in Alaska.(16) Site-specific cancer survival also varied by region: for example, survival from colorectal cancers was 10% lower in the Southern Plains region compared to Alaska, potentially identifying an area where increased screening efforts are warranted. Differences in site-specific survival between regions are attributable to stage at diagnosis, and access to and effectiveness of post-diagnostic treatment services. To our knowledge, there are few recent studies that examine cancer survival by region among AIAN people; however, several recent studies from authors at the Centers for Disease Control and Prevention have shown variations in incidence of and disparity from several leading cancers by IHS region.(15,20,33)

For almost all cancer sites examined, five-year survival was lower among AIAN people than NHW. The magnitude of disparity varied by cancer site, but was highest for colorectal cancer, where net survival measures calculated approximately 10% lower survival among AIAN people. Again, differences were largest for cancer sites that are screenable (e.g., colorectal cancer, female breast cancer), and with high survival (e.g., prostate cancer), and lowest for cancers with high mortality (e.g., lung cancer, pancreatic cancer).

This manuscript has several strengths and limitations. A key strength of this work is the use of the NAACCR CiNA dataset, which includes data from both National Program of Cancer Registries (NPCR) and SEER registries from across the U.S. Therefore, our analyses benefitted from increased sample size and statistical power relative to many survival analyses examining data from AIAN people, which have either used data from a single registry(13) or the SEER system alone.(34,35) A key methodological consideration when interpreting the results of this study are the different methods and resources registries are able to use to ascertain patient follow-up. U.S. registries are supported by, and participate in, the National Cancer Institute's SEER Program, and/or the Center for Disease Control and Prevention's (CDC) NPCR. U.S. registries utilize local and national resources to ascertain patient vital status, e.g., state death tape linkage and National Death Index linkage. Registries adhering to SEER Program standards additionally conduct active follow-up on cases to ascertain a date of last follow-up for ≥ 90% of alive patients for the study time period. Registries funded by the SEER Program are able to leverage additional resources, e.g., the Social Security Administration Service to Epidemiological Researchers, to ascertain date of last follow-up among alive patients with efficiency, greatly improving their ability to get more accurate estimates of follow-up time.(36) Registries that are not funded by the SEER Program and do not have resources to ascertain date of last follow-up on all alive patients rely on complete death clearance to estimate survival; this presumed alive model can bias survival estimates upwards in certain populations relative to the observed survival time used for registries with active follow-up for alive patients.(19,37) Because data included in the CiNA Research File for Survival meet stringent data quality standards

and because follow-up practices are internally consistent within registry for the time period under study, we anticipate that using “blended” survival follow-up for this study yielded appropriate and internally valid results.

Another limitation of these analyses is that the analytic sample was different between observed/net: relative, and net: cause-specific analyses, due to the requirement for known cause of death in cause-specific analyses; this is not expected to greatly impact results. We describe differences in results produced by four different survival methods; however, the magnitude of these differences will be affected by underlying differences in the populations being compared. For example, if access to and utilization of screening services is similar in the two populations, we might expect to see lower differences between the measures. However, if screening prevalence differs between populations, this may result in observing a larger disparity. Finally, an important limitation of a large majority of studies using population-based cancer registry data to understand the AIAN experience: our analyses were limited to those living in PRCDA counties. This choice is often made because of the potentially higher racial misclassification in counties outside of those areas served by IHS facilities(18,38,39). Yet, it neglects the experience of AIAN people in non-PRCDA counties, which are often urban, and in the East of the U.S. Thus, it should be noted that these results may not reflect the experience of 47.7% AIAN people living outside of PRCDA counties.(40) Future work should continue to explore the cancer burden experience of AIAN people living outside of PRCDA counties.

This manuscript provides two key pieces of information that will be of use to scholars who are interested in cancer disparities among AIAN people. First, we provide information to compare different observed and net measures of survival and conclude that consistency in metric is imperative; studies conducted using different methods should be compared with caution. Additionally, these results – as seen in the differences in relative survival by lifetable – underscore the importance of careful consideration of research objectives in the selection of analytic method. Second, we provide data on survival for leading cancers among AIAN people by sex, age, stage at diagnosis, and IHS region. In general, we observed lower survival among AIAN people than NHW. The magnitude of disparity varied by cancer site, but these data suggest that continued efforts should be made to explain these disparities, and to address them using Tribally-driven approaches.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

AI/AN	American Indian/Alaska Native
AN	Alaska Native
CI	Confidence Interval
CiNA	Cancer in North America
CRC	colorectal cancer
HR	Hazard Ratio
IHS	Indian Health Service
ICD-O-3	International Classification of Diseases for Oncology – Third Edition
L	Local stage
NAACCR	North American Association of Central Cancer Registries
NHW	non-Hispanic whites
NPCR	National Program of Cancer Registries
PRCDA	Purchased/Referred Care Delivery Area
R/D/U	Regional/Distant/Unknown stage
SEER	Surveillance, Epidemiology and End Results

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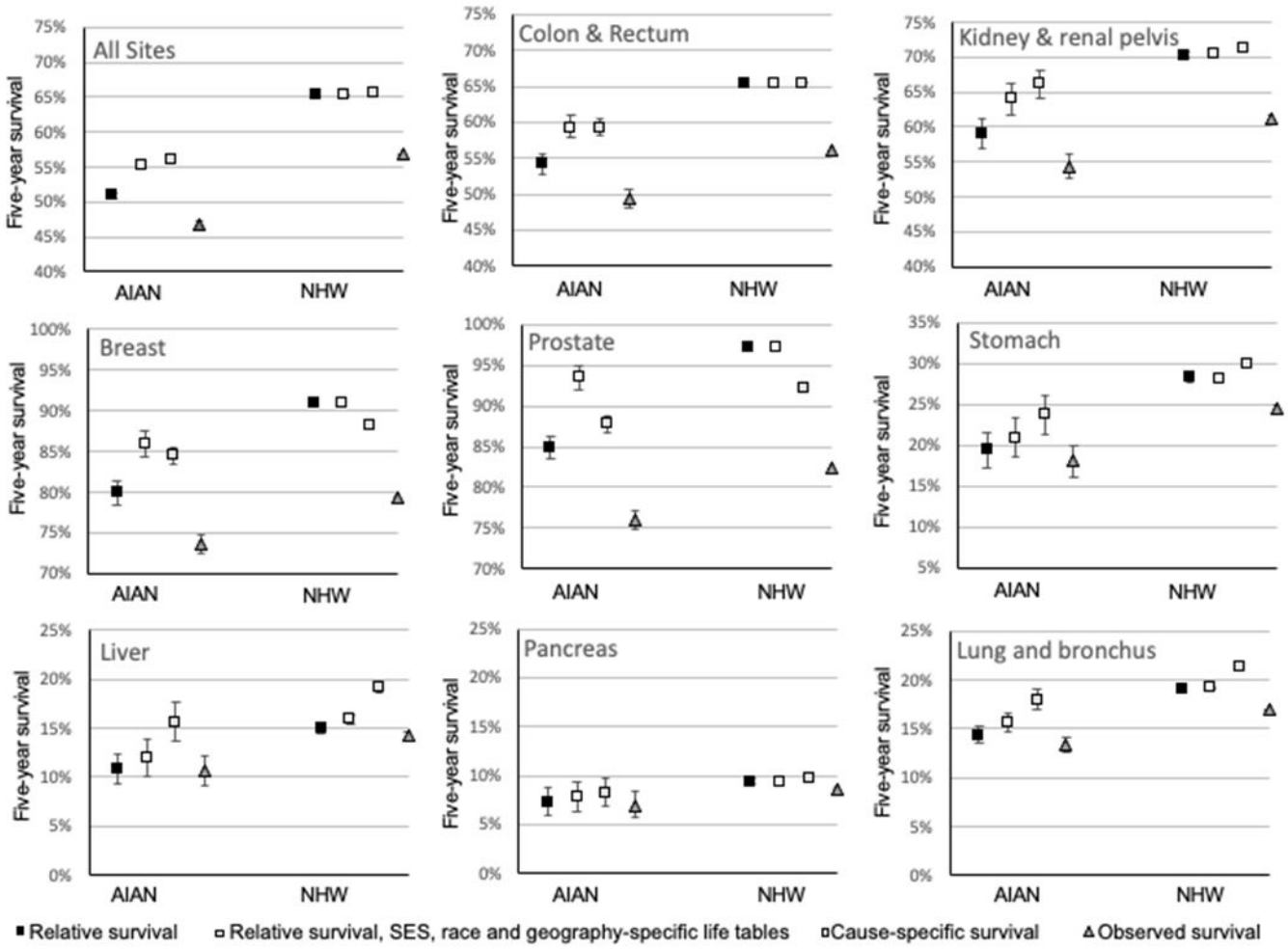

Figure 1.

Survival calculated for AIAN and NHW people calculated using different survival measures, NAACCR's Cancer in North America database, 2000-2017. A) All sites, B) Stomach C) Colon and rectum, D) Female breast, E) Prostate, F) Kidney and renal pelvis, G) Liver, H) Pancreas, I) Lung and bronchus.

[a]Net measures of survival are indicated using a square marker; observed survival is indicated by a triangular marker, to differentiate between the different measure types.

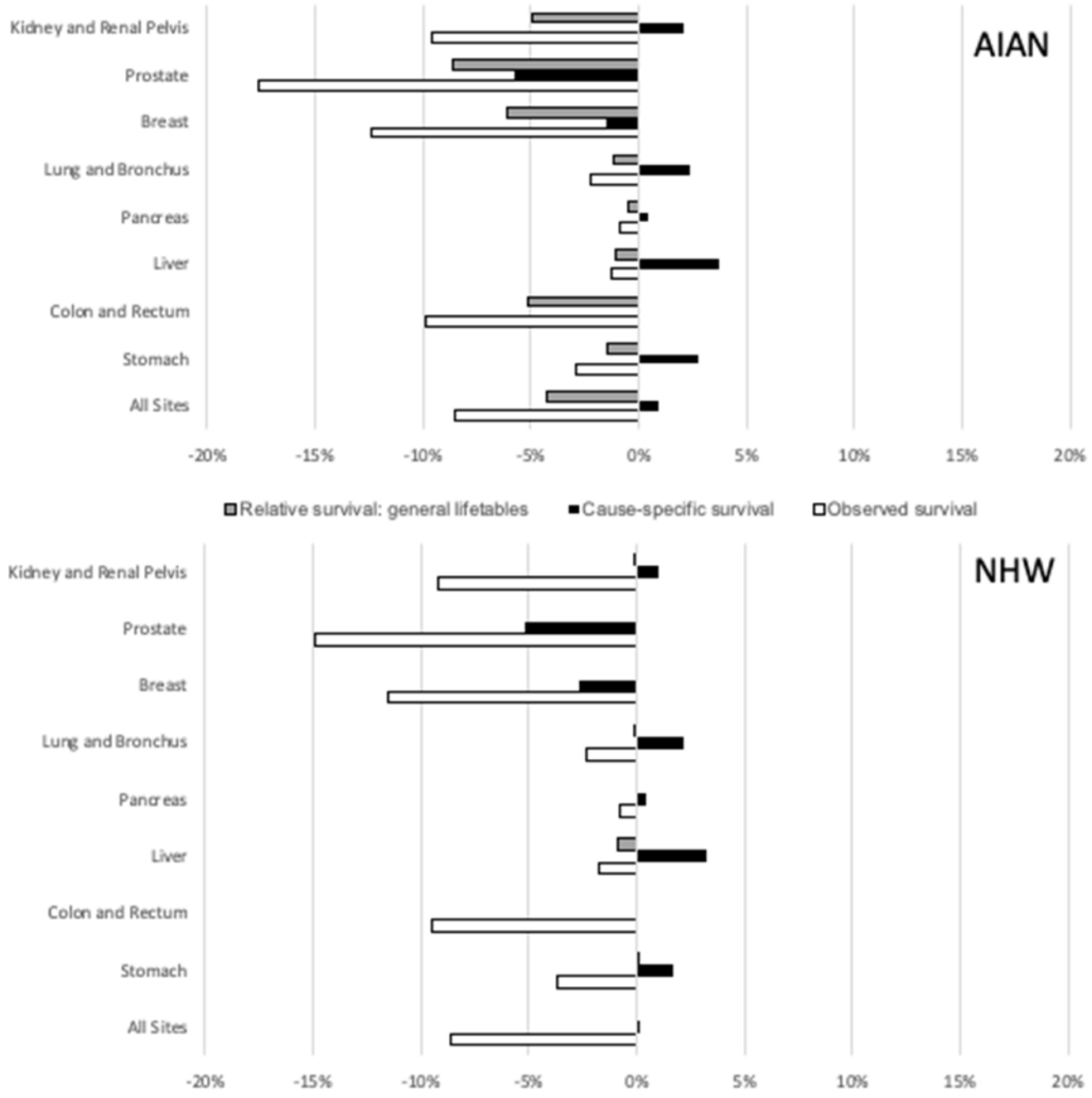

Figure 2.

Absolute differences in survival estimates between survival metrics, compared to overall survival estimates among A) AIAN people, and B) NHW people, NAACCR's Cancer in North America database, 2000-2017.

TABLE 1.

Numbers of cancer cases diagnosed among AIAN people and included in the present analysis, NAACCR's Cancer in North America database, 2000-2017.

	AIAN		NHW	
	n	%	n	%
Cancer site[a]				
All Sites	75,485	100	3,473,975	100
Breast	10,639	14.1	516,734	14.9
Lung and Bronchus	9,486	12.6	463,997	13.4
Colon and Rectum	8,525	11.3	313,397	9.0
Prostate	7,882	10.4	523,983	15.1
Kidney and Renal Pelvis	4,574	6.1	107,033	3.1
Liver	2,378	3.2	40,374	1.2
Pancreas	1,909	2.5	88,722	2.6
Stomach	1,738	2.3	38,803	1.1
Sex[a]				
Male	36,144	47.9	1,810,747	52.1
Female	39,341	52.1	1,663,228	47.9
Age[a]				
20-64 years	42,726	57.8	1,557,513	45.2
65+ years	31,168	42.2	1,886,026	54.8
SEER Combined Summary Stage 2000 [a,b]				
Local	24,844	42.5	1,253,210	49.4
Regional	11,215	19.2	447,725	17.7
Distant	15,951	27.3	614,656	24.2
Unknown	6,434	11.0	219,552	8.7
IHS Region[a]				
Alaska	6,229	8.3	30,010	1.0
East	2,558	3.4	886,899	30.3
Northern Plains	9,713	12.9	494,413	16.9
Southern Plains	23,524	31.2	239,709	8.2
Pacific Coast	16,289	21.6	1,273,858	43.6
Southwest	17,172	22.7	549,086	18.7
Known Cause of Death	74,434	98.6	3,421,610	98.4

[a]Calculated using the numbers for relative and observed survival. Numbers included in cause-specific analyses differ, due to the requirement for known cause of death in these analyses.

[b] Numbers included in SEER Combined Summary Stage 2000 differ from the overall count as SEER Combined Summary Stage 2000 is only available for cases diagnosed during 2004–2017.