

Cancer in Guam and Hawaii: A comparison of two U.S. Island populations



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ABSTRACT

Background: Cancer disparities within and across populations provide insight into the influence of lifestyle, environment, and genetic factors on cancer risk.

Methods: Guam cancer incidence and mortality were compared to that of Hawaii using data from their respective population-based, central cancer registries.

Results: In 2009–2013, overall cancer incidence was substantially lower in Guam than in Hawaii for both sexes while overall cancer mortality was higher for Guam males. Cervical cancer incidence and prostate cancer mortality were higher in Guam. Both incidence and mortality were higher among Guam men for cancers of the lung & bronchus, liver & intrahepatic bile duct, and nasopharynx; Chamorro men were disproportionately affected by these cancers. Filipinos and Whites in Guam had lower overall cancer incidence compared to Filipinos and Whites in Hawaii. Although breast cancer incidence was significantly lower in Guam compared to Hawaii, women in Guam presented at younger ages and with rarer disease histologies such as inflammatory carcinoma were more prevalent. Guam patients were also diagnosed at younger ages for cancers of bladder, pancreas, colon & rectum, liver & intrahepatic bile duct, lung & bronchus, stomach, non-Hodgkin lymphoma, and leukemia. **Conclusion:** Smoking, infectious agents, and betel nut chewing appear to be important contributors to the burden of cancer in Guam. Earlier onset of cancer in Guam suggests earlier age of exposure to key risk factors and/or a more aggressive pathogenesis. Contrasting cancer patterns within Guam and between Guam and Hawaii underscore the potential influence of genes, lifestyle, and environmental factors on cancer development and progression.

1. Introduction

The burden of cancer varies globally by geographic regions, locations and across racial and ethnic populations. Guam and Hawaii are each comprised of unique ethnically diverse populations including indigenous peoples and individuals of Asian, European, and Pacific Island ancestry. Guam, a U.S. territory located in the Western Pacific, is the largest island in Micronesia with a population of approximately 159,000 [1]. Guam's population includes indigenous Chamorros (including part-Chamorros) (42.2%), Filipinos (26.3%), Chuukese and other Micronesians (7.2%), Whites (6.8%), other Asians (6.2%), and other race/ethnic groups (11.3%) [1,2]. Hawaii, the 50th U.S. state located in the Central Pacific, consists of a population of 1,360,000 residing on six main islands [3]. Hawaii's population is comprised of indigenous Native Hawaiians (including part-Hawaiians) (21.3%), Whites (22.8%), Filipinos (17.2%), Japanese (16.3%), Chinese (6.8%), and other race/ethnicities (15.6%) [3].

The contribution of Hawaii's multiethnic population to its cancer

burden has long been recognized based on numerous epidemiologic studies conducted over more than four decades [4–11]. These studies have provided important insight into cancer development and progression across Hawaii's population and the interacting influence of genes with lifestyle, diet, environment, and other factors. In contrast, infrastructure and resources for cancer surveillance and cancer research were not established in Guam until relatively recently. Consequently, there is limited knowledge of the epidemiology of the cancer in this island population. Ethnic variation in cancer incidence and mortality across Guam's population has been observed [12,13]. Prevalent exposures such as cigarette smoking and *Areca* (betel) nut chewing likely influence disease risk [14,15].

The present report utilizes cancer surveillance data to characterize and compare the current burden of cancer in Guam and Hawaii. Ethnic comparisons focus on variation within Guam's major ethnic groups. Elucidation of factors influencing cancer risk and progression is key to informing future research and public health efforts for Guam's population.

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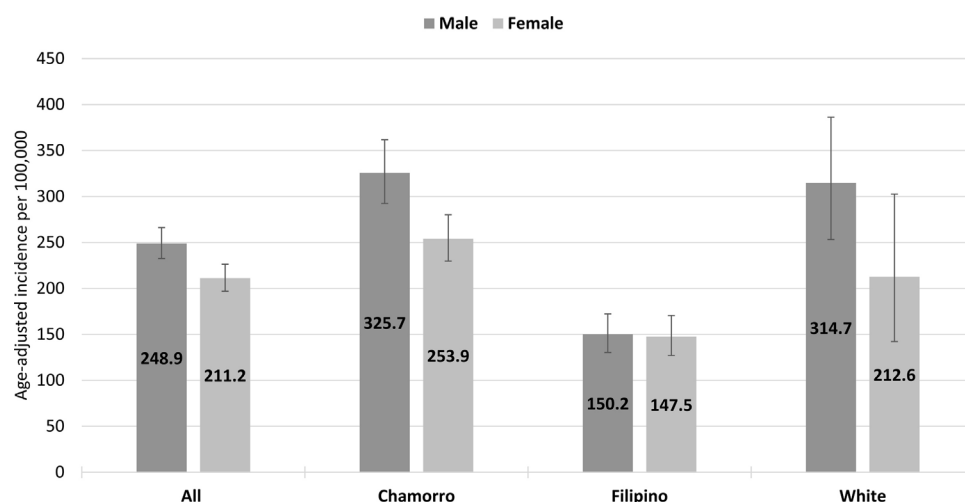


Fig. 1. Overall Cancer Incidence, ¹ Guam, 2009–2013.
¹ Average annual rates age-adjusted to the World (WHO 2000–2025) Standard Million Population

2. Materials and methods

The present analysis utilized cancer registry data from cases diagnosed in 2009–2013 in Guam and Hawaii. The Guam Cancer Registry (GCR) was established as a unit of the University of Guam (UOG) in 2004 through a partnership of the UOG, the Guam Department of Public Health and Social Services, and the University of Hawaii Cancer Center. The GCR is partly supported through the University of Hawaii–University of Guam Partnership (NCI 5 U54 CA143727). The Guam Cancer Registry is also a member and reporting registry of the Pacific Regional Central Cancer Registry (PRCCR) (CDC U58 DP000976 and U58 DP003906). PRCCR consists of cancer registries covering the U.S. Affiliated Pacific Islands including Guam, American Samoa, the Commonwealth of the Northern Mariana Islands, the Federated States of Micronesia, the Republic of the Marshall Islands, and the Republic of Belau (Palau). The GCR offices at the UOG serve as the central host location for PRCCR. The GCR is responsible for the collection of data on newly diagnosed cancer cases and annual follow-up of existing cases throughout the territory of Guam. Data is collected, coded, and maintained based on standards of the CDC National Program of Cancer Registries and the North American Association of Central Cancer Registries (NAACCR).

The Hawaii Tumor Registry (HTR) of the University of Hawaii Cancer Center (UHCC) was established in 1960 and has been a part of the National Cancer Institute's Surveillance Epidemiology and End Results (NCI/SEER) Program since 1973. The HTR is responsible for cancer surveillance for the state of Hawaii and contributes to U.S. cancer incidence, mortality, and survival data [16]. The HTR works closely with the GCR to provide technical assistance and training.

Comparisons of cancer in Guam and Hawaii necessitate consideration of certain limitations in the quality of data from the GCR as a relatively new central cancer registry. For 2009–2013, GCR data met the standards of data completeness [17] for the proportion of cases with unknown age, sex, and residence (0% for all). However, the proportions of unknown race/ethnicity and death certificate-only cases were 7.1% and 11%, respectively, which did not meet data quality standards.

Site, and histology were coded according to the International Classification of Diseases for Oncology (ICD-O), Third Edition [18]. Cancer sites and stage at diagnosis were categorized according to WHO and SEER definitions [19]. The present analysis was limited to invasive cancers with the exception of bladder cancer, which includes both in situ and invasive cancers consistent with SEER standards. Demographic, clinical, and pathologic information was available from both registries. The GCR data also included cancer-screening history for a subset of cases.

Average annual age-adjusted incidence and mortality rates per

100,000 were calculated for the 5-year period, 2009–2013. Rates were age-standardized to the World Health Organization 2000–2025) World Standard Million Population. Ninety-five percent confidence intervals were calculated for all rates. To ensure the stability and reliability of rates, incidence and mortality rates were limited to sex-ethnic categories with at least 10 cases or deaths over the 5-year period. Overall incidence comparisons in Guam included Chamorros, Filipinos, and Whites (Caucasians). Hawaii comparisons included Whites (Caucasians), Japanese, Native Hawaiian, Filipino, and Chinese. Unpaired *t*-tests, Wilcoxon two-sample tests, and Pearson's chi square statistics were used to compare continuous and categorical variables; *p*-values less than 0.05 were considered significant.

3. Results

3.1. Cancer incidence

In 2009–2013, cancer was diagnosed in 1708 individuals (342 per year) in Guam and 33,521 individuals (6704 per year) in Hawaii, respectively. The overall cancer incidence was significantly lower in Guam than in Hawaii for both sexes (Males: 248.9, 95% CI 232.5–266.2 and 329.3, 95% CI 324.2–334.5 per 100,000, respectively; Females: 211.2, 95% CI 196.9–226.3 and 317.3, 95% CI 312.1–322.4 per 100,000, respectively). (Hereafter all incidence and mortality rates shown exclude “per 100,000”).

Overall cancer incidence varied across the major race/ethnic groups of both island populations. In Guam, among both sexes, overall incidence was significantly higher in Whites and Chamorros compared to Filipinos (Fig. 1). In Hawaii, overall incidence among males was highest for Whites, followed by Native Hawaiians, then Filipinos and Japanese—whose rates were comparable—, and Chinese, who had the lowest incidence (Fig. 2). Overall incidence among Hawaii females was highest for Native Hawaiians and Whites, followed by Japanese, and Filipinos, and lowest in Chinese (Fig. 2).

Cancers of the prostate, lung & bronchus, and colon & rectum were the most frequently diagnosed malignancies among males in both Guam and Hawaii (Table 1). Cancers of the lung & bronchus, liver & intrahepatic bile duct, and nasopharynx were of significantly higher incidence among Guam compared to Hawaii males. Rates of liver & intrahepatic bile duct cancer among Guam males was nearly double and nasopharyngeal cancers more than four times higher than that of men in Hawaii.

Melanoma of the skin, the 4th most common malignancy among Hawaii males, was rare in Guam. Other cancers with significantly lower incidence among Guam compared to Hawaii males included bladder, kidney & renal pelvis, pancreas, and non-Hodgkin lymphoma. The

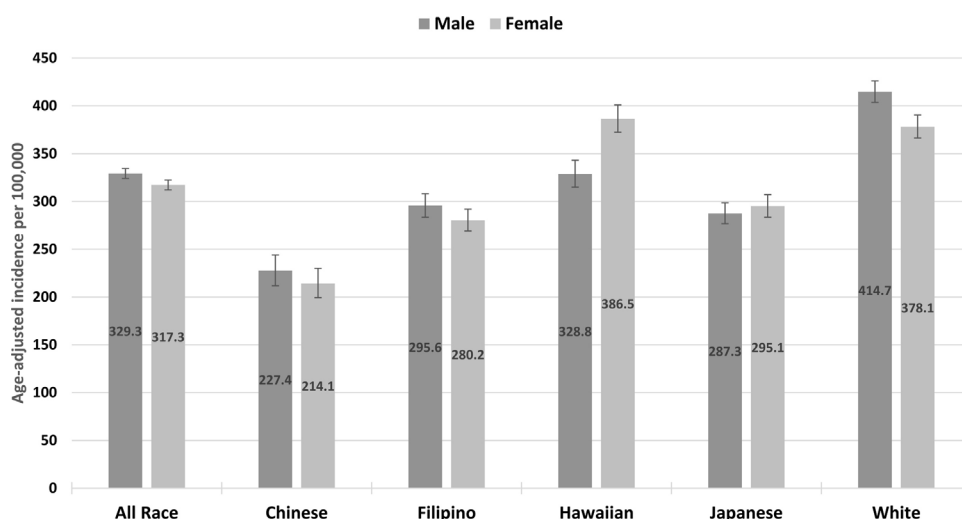


Fig. 2. Overall Cancer Incidence, ¹ Hawaii, 2009–2013.
¹ Average annual rates age-adjusted to the World (WHO 2000–2025) Standard Million Population

incidence of pancreatic cancer and non-Hodgkin lymphoma was more than two-fold lower among Guam compared to Hawaii males.

In 2009–2013, cancers of the breast, lung & bronchus, colon & rectum, uterus/endometrium, and thyroid were the most frequently diagnosed malignancies among females in both Guam and Hawaii (Table 2). Cancers with significantly lower incidence among Guam compared to Hawaii females included breast, colon & rectum, uterus/endometrium, non-Hodgkin lymphoma, skin melanoma, pancreas, leukemia, ovary, and kidney & renal pelvis. Cervical cancer was the only major cancer with higher incidence in Guam females; rates were was nearly double that of Hawaii.

Ethnic differences in incidence were observed for some of the major cancers in Guam. The incidence of liver & intrahepatic bile duct cancer among Chamorro men (41.9, 95% CI 31.3–54.9) was significantly higher than that of Filipinos (10.3, 95% CI 5.6–17.6) and Whites (10.5, 95% CI 2.8–28.2) in Guam as well as Native Hawaiians (17.5, 95% CI 14.5–21.0) who had the highest incidence in Hawaii. Similarly, Chamorro men had an elevated incidence of lung & bronchus cancer (73.6, 95% CI 59.4–90.2) compared to Filipinos (31.9, 95% CI 23.2–43.1) and Whites (42.5, 95% CI 22.6–72.4) in Guam. Their rates also exceeded that of Native Hawaiians (52.7, 95% CI 47.1–58.7) who had the highest statewide rates. Non-significant higher rates of nasopharyngeal cancer were observed in Chamorro males (8.1, 95% CI 4.3–14.3) compared to Filipino (4.2, 95% CI 1.5–9.5) and White (2.5,

95% CI 0.1–15.8). Among Guam females, cervical cancer incidence was highest in Chamorros (14.8, 95% CI 9.5–22.1) compared to Filipinos (4.2, 95% CI 1.3–10.2) and Whites (9.3, 95% CI 1.0–35.6).

3.2. Cancer mortality

In 2009–2013, there were 760 (152 per year) cancer deaths in Guam and 11,144 (2229 per year) in Hawaii. Overall cancer mortality was significantly higher among Guam males (130.6, 95% CI 118.7–143.5) compared to Hawaii males (111.5, 95% CI 108.6–114.4). Among females, mortality was comparable in Guam and Hawaii (80.2, 95% CI 71.3–89.8) and (78.2, 95% CI 75.9–80.6), respectively.

Overall cancer mortality varied by ethnicity in both Guam and Hawaii. In 2009–2013, among males in Guam, mortality was significantly higher in Chamorros (198.3, 95% CI 170.6–229.0). and Whites (160.6, 95% CI 114.6–217.6) compared to Filipinos (74.1, 95% CI 60.2–90.3). Similarly, among females, mortality was significantly higher in Chamorros (105.2, 95% CI 89.7–122.6) and Whites (96.5, 95% CI 51.7–160.9) compared to Filipinos (35.5, 95% CI 26.2–47.3). In Hawaii, the highest cancer mortality was observed among Native Hawaiians. Cancer mortality in Native Hawaiian males (156.6, 95% CI 146.9–166.7) was significantly lower than Chamorro men. In contrast, mortality in Native Hawaiian females (130.3, 95% CI 122.2–138.8) was significantly higher than Chamorro women.

Table 1
Major Cancers in Guam and Hawaii, Males, 2009–2013.

Guam						Hawaii					
	Average Annual Cases ^a		Incidence ^{b,c}				Average Annual Cases ^a		Incidence ^{b,c}		
Site	No.	%	Rate	95% CI		Site	No.	%	Rate	95% CI	
Prostate	40	22.5%	60.0	51.8	69.1	Prostate	743	22.2%	70.6	68.3	72.9
Lung & Bronchus	40	22.5%	57.0	49.1	65.6	Lung & Bronchus	435	13.0%	40.0	38.3	41.8
Colon & Rectum	23	12.9%	31.6	25.9	38.1	Colon & Rectum	406	12.1%	40.1	38.4	42.0
Liver & Intrahepatic Bile Duct	19	10.7%	24.9	20.1	30.5	Melanoma of the Skin	204	6.1%	20.8	19.5	22.1
Bladder	6	3.4%	8.9	5.9	12.8	Bladder	172	5.1%	15.4	14.4	16.5
Kidney & Renal Pelvis	6	3.4%	7.6	5.1	11.0	Non-Hodgkin Lymphoma	162	4.8%	16.2	15.1	17.4
Non-Hodgkin Lymphoma	5	2.8%	6.3	4.0	9.5	Kidney & Renal Pelvis	141	4.2%	14.4	13.3	15.6
Nasopharynx	5	2.8%	6.4	4.2	9.5	Liver & Intrahepatic Bile Duct	130	3.9%	12.8	11.8	13.9
Oral Cavity & Pharynx (excluding nasopharynx)	5	2.8%	6.1	3.9	9.2	Oral Cavity & Pharynx (excluding nasopharynx)	122	3.6%	12.2	11.3	13.3
Stomach	4	2.2%	5.4	3.2	8.5	Pancreas	117	3.5%	10.9	10.0	11.8

^a All cases are invasive except for bladder cancer which are in situ and invasive.

^b Average annual rates age-adjusted to the World (WHO 2000–2025) Standard Million Population.

^c Incidence rates (95% CI) not shown: Nasopharynx 1.5 (1.2–1.9) (Hawaii); Stomach 8.2 (7.5–9.1) (Hawaii); Melanoma of the skin 0.7 (0.1–2.3) (Guam); Pancreas 5.0 (3.0–7.9) (Guam).

Table 2
Major Cancers in Guam and Hawaii, Females, 2009–2013.

Guam						Hawaii					
	Average Annual Cases ^a		Incidence ^{b,c}				Average Annual Cases ^a		Incidence ^{b,c}		
Site	No.	%	Rate	95% CI		Site	No.	%	Rate	95% CI	
Breast	48	29.3%	60.9	53.3	69.1	Breast	1107	33.0%	108.1	105.1	111.1
Lung & Bronchus	21	12.8%	26.9	21.9	32.6	Lung & Bronchus	341	10.2%	27.4	26.1	28.8
Colon & Rectum	16	9.8%	21.2	16.8	26.3	Colon & Rectum	316	9.4%	27.1	25.7	28.6
Uterus/Endometrium	15	9.2%	19.1	15.1	24.0	Uterus/Endometrium	248	7.4%	25.4	23.9	26.9
Thyroid	14	8.5%	17.9	14.0	22.6	Thyroid	171	5.1%	21.8	20.3	23.3
Cervix	9	5.5%	11.9	8.8	15.9	Non-Hodgkin Lymphoma	127	3.8%	11.1	10.2	12.1
Non-Hodgkin Lymphoma	5	3.1%	6.7	4.4	9.8	Melanoma of the Skin	116	3.5%	12.5	11.4	13.6
Ovary	5	3.1%	6.3	4.0	9.3	Pancreas	108	3.2%	8.1	7.4	8.9
Liver & Intrahepatic Bile Duct	4	2.4%	5.1	3.1	8.1	Ovary	76	2.3%	7.9	7.1	8.8
Stomach	4	2.4%	5.1	3.1	8.0	Leukemia	76	2.3%	7.9	7.0	8.8

^a All cases are invasive except for bladder cancer which are in situ and invasive.

^b Average annual rates age-adjusted to the World (WHO 2000–2025) Standard Million Population.

^c Incidence rates (95% CI) not shown: Cervix 6.4 (5.6–7.3) (Hawaii); Stomach 5.0 (4.5–5.7) (Hawaii); Liver & Intrahepatic bile duct 4.2 (3.7–4.8) (Hawaii); Melanoma of the skin 0.2 (0.0–1.4) (Guam); Pancreas 2.1 (0.9–4.1) (Guam); Leukemia 3.6 (2.0–6.1) (Guam).

Table 3
Major Causes of Cancer Death in Guam and Hawaii, Males, 2009–2013.

Guam						Hawaii					
	Average Annual Deaths ^a		Mortality ^{b,c}				Average Annual Deaths ^a		Mortality ^{b,c}		
Site	No.	%	Rate	95% CI		Site	No.	%	Rate	95% CI	
Lung & Bronchus	29	31.8%	42.8	36.0	50.5	Lung & Bronchus	303	24.7%	27.4	26.0	28.8
Liver & Intrahepatic Bile Duct	13	14.2%	16.7	12.8	21.3	Colon & Rectum	128	10.4%	11.8	10.9	12.8
Colon & Rectum	9	9.9%	13.6	9.9	18.1	Prostate	99	8.1%	7.7	7.0	8.4
Prostate	8	8.8%	13.1	9.4	17.7	Pancreas	94	7.7%	8.5	7.7	9.3
Pancreas	3	3.3%	4.3	2.3	7.1	Liver & Intrahepatic Bile Duct	85	6.9%	8.3	7.5	9.1
Nasopharynx	4	4.4%	4.8	2.8	7.7	Non-Hodgkin Lymphoma	50	4.1%	4.5	4.0	5.1
Non-Hodgkin Lymphoma	3	3.3%	4.0	2.1	6.7	Leukemia	47	3.8%	4.5	3.9	5.1
Kidney & Renal Pelvis	2	2.2%	3.5	1.8	6.1	Stomach	47	3.8%	4.2	3.7	4.9
Esophagus	2	2.2%	2.3	1.0	4.6	Esophagus	41	3.3%	3.9	3.4	4.5
Stomach	2	2.2%	3.1	1.5	5.6	Bladder	36	3.0%	3.0	2.5	3.5

^a All cases are invasive except for bladder cancer which are in situ and invasive.

^b Average annual rates age-adjusted to the World (WHO 2000–2025) Standard Million Population.

^c Mortality rates (95% CI) not shown: Nasopharynx 0.6 (0.4–0.9) (Hawaii); Kidney & Renal Pelvis 2.8 (2.4–3.3) (Hawaii); Leukemia 3.8 (2.0–6.5) (Guam); Bladder 2.6 (1.2–4.9) (Guam).

Lung & bronchus cancer was the top cause of cancer death among males in both populations although rates were significantly higher in Guam compared to Hawaii (Table 3). For other major causes of cancer death in men, rates were also significantly higher in Guam compared to Hawaii for cancers of the prostate and liver & intrahepatic bile duct. Nasopharyngeal (NPC) cancer deaths also significantly higher among men in Guam compared to Hawaii. Pancreatic cancer mortality was significantly lower among Guam compared to Hawaii males.

Lung & bronchus cancer was also the leading cause of cancer death among females in Guam and Hawaii although rates were highest in Guam (Table 4). Mortality was comparable in Guam and Hawaii females for most other major cancers. Similar to males, pancreatic cancer mortality was higher among females in Guam than in Hawaii.

Mortality rates varied across Guam's ethnic populations. Lung & bronchus cancer mortality among Chamorro men (62.1, 95% CI 47.7–79.1) was more than double that of Filipinos (24.2, 95% CI 16.6–34.2) and Whites (29.2, 95% CI 12.5–56.9). Lung & bronchus cancer mortality among Chamorro males also exceeded that of Native Hawaiians (40.8, 95% CI 35.9–46.1) who had the highest rates in Hawaii. Liver & intrahepatic bile duct cancer mortality was more than two times higher in Chamorro males (27.0, 95% CI 19.2–37.1) compared to Filipinos (5.9, 95% CI 2.5–11.9) and Whites (10.8, 95% CI 2.7–29.1).

3.3. Filipinos and Whites in Guam and Hawaii

Comparison of cancer incidence and mortality in Filipinos and Whites residing in Guam with their ethnic counterparts in Hawaii demonstrated striking differences. Overall cancer incidence was significantly lower among Filipinos residing in Guam than Filipinos in Hawaii (males: 150.2, 95% CI 130.3–172.3 and 295.6, 95% CI 283.5–308.1, respectively; females: 147.5, 95% CI 127.0–170.5 and 280.2, 95% CI 269.0–291.9, respectively). Significantly lower incidence was observed among Filipinos in Guam compared to those in Hawaii for a number of major cancers: prostate (39.1, 95% CI 29.3–51.4 and 76.8, 95% CI 70.9–83.2, respectively); breast (62.0, 95% CI 49.2–77.4 and 86.9, 95% CI 80.7–93.5, respectively); colon & rectum (males: 27.0, 95% CI 19.1–37.4 and 43.8, 95% CI 39.2–48.8, respectively; females: 10.1, 95% CI 5.3–17.7 and 30.1, 95% CI 26.6–34.0, respectively); lung & bronchus (males: 31.9, 95% CI 23.2–43.1 and 47.4, 95% CI 42.7–52.4, respectively; females: 12.9, 95% CI 7.6–20.9 and 24.7, 95% CI 21.7–28.1, respectively); uterus/endometrium (13.2, 95% CI 7.7–21.4 and 20.2, 95% CI 17.2–23.6, respectively); and thyroid (females: 20.2, 95% CI 12.8–30.4 and 35.1, 95% CI 30.8–39.9, respectively). Rates of thyroid cancer among Filipinas in both Guam and Hawaii were the highest in their respective populations. Overall cancer mortality was also substantially lower among Filipinos in Guam compared to Filipinos in Hawaii (males: 74.1, 95% CI 60.2–90.3 and 99.2,

Table 4
Major Causes of Cancer Death in Guam and Hawaii, Females, 2009–2013.

Guam						Hawaii					
	Average Annual Deaths ^a		Mortality ^{b,c}				Average Annual Deaths ^a		Mortality ^{b,c}		
Site	No.	%	Rate	95% CI		Site	No.	%	Rate	95% CI	
Lung & Bronchus	15	24.7%	20.1	15.8	25.3	Lung & Bronchus	223	22.2%	16.7	15.7	17.8
Breast	11	18.1%	13.5	10.1	17.7	Breast	125	12.5%	11.1	10.2	12.0
Colon & Rectum	5	8.2%	7.0	4.5	10.3	Colon & Rectum	96	9.6%	7.3	6.6	8.1
Liver & Intrahepatic Bile Duct	4	6.6%	4.7	2.8	7.5	Pancreas	88	8.8%	6.2	5.6	6.9
Pancreas	2	3.3%	2.9	1.5	5.3	Ovary	47	4.7%	3.9	3.4	4.4
Ovary	4	6.6%	5.5	3.4	8.4	Liver & Intrahepatic Bile Duct	41	4.1%	2.9	2.5	3.4
Uterus/endometrium	4	6.6%	4.6	2.7	7.4	Uterus/endometrium	38	3.8%	3.3	2.8	3.9
Stomach	2	3.3%	2.4	1.1	4.6	Non-Hodgkin Lymphoma	37	3.7%	2.5	2.2	3.0
Cervix	2	3.3%	2.6	1.2	4.8	Leukemia	33	3.3%	2.8	2.3	3.3
Non-Hodgkin Lymphoma	1	1.6%	1.7	0.7	3.6	Stomach	35	3.5%	2.3	1.9	2.8

^a All cases are invasive except for bladder cancer which are in situ and invasive.

^b Average annual rates age-adjusted to the World (WHO 2000–2025) Standard Million Population.

^c Mortality rates (95% CI) not shown: Cervix 1.7 (1.3–2.1) (Hawaii).

95% CI 92.4–106.4, respectively; females: 35.5, 95% CI 26.2–47.3 and 69.8, 95% CI 64.6–75.4, respectively).

Whites in Guam had significantly lower overall cancer incidence than Whites in Hawaii (males: 314.7, 95% CI 253.1–386.2 and 414.7, 95% CI 403.6–426.1, respectively; females: 212.6, 95% CI 142.1–302.6 and 378.1, 95% CI 366.2–390.3, respectively). There were no cases of melanoma among Whites in Guam. In contrast, melanoma was one of the most common cancers among Whites in Hawaii who comprised 84% (1341/1601) of cases. Overall mortality was higher among Whites in Guam than in Hawaii (males: 160.6, 95% CI 114.6–217.6 and 117.1, 95% CI 111.6–122.9, respectively). Mortality rates were similar for White females in Guam and Hawaii (females: 96.5, 95% CI 51.7–160.9 and 86.1, 95% CI 81.0–91.5, respectively).

3.4. Age at cancer diagnosis

Guam cancer patients were diagnosed at significantly younger ages than Hawaii patients (Fig. 3). Overall, the mean age at diagnosis in Guam and Hawaii was 62.8 years and 65.8 years, respectively, for

males ($p < 0.0001$) and 57.8 years and 63.1 years, respectively, for females ($p < 0.0001$). Younger mean age at diagnosis was also observed in Guam compared to Hawaii for cancers of the bladder in men (66.4 vs. 71.8; $p = 0.008$), pancreas in men (57.2 vs. 69.1, $p < 0.0001$), breast in women (57.9 vs. 61.5; $p < 0.0001$), colon & rectum in women (60.6 vs. 66.7; $p = 0.0001$), non-Hodgkin lymphoma in females (58.0 vs. 66.4; $p = 0.009$), leukemia in both sexes (48.6 vs. 61.3; $p = 0.04$ in males; 39.0 vs. 58.5; $p = 0.003$ in females), liver & intrahepatic bile duct in both sexes (57.9 vs. 63.8; $p < 0.0001$ in males; 60.4 vs. 70.7; $p = 0.0009$ in females), lung & bronchus in both sexes (66.0 vs. 70.3; $p < 0.0001$ in males; 64.3 vs. 70.4; $p < 0.0001$ in females), and stomach in both sexes (62.9 vs. 69.6, $p = 0.03$ in males; 62.1 vs. 70.9, $p = 0.0098$ in females). These age differences were also significant based on non-parametric tests (data not shown).

3.5. Breast cancer in Guam and Hawaii

In addition to the significantly lower incidence and younger age of diagnosis of female breast cancer cases in Guam compared to Hawaii,

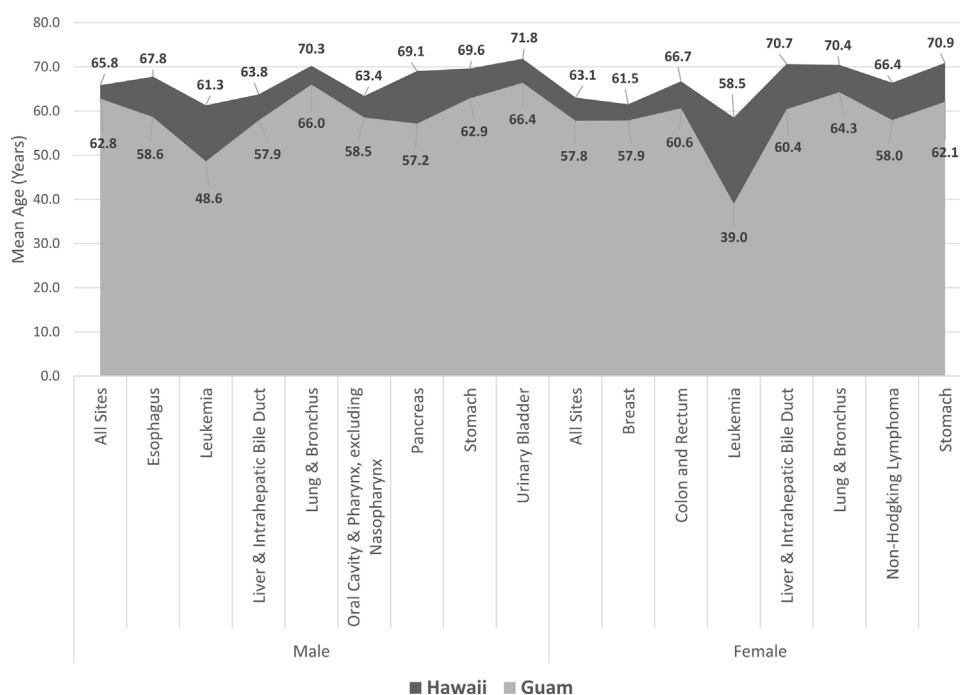


Fig. 3. Younger Age of Cancer Diagnosis ($p < 0.05$) in Guam vs. Hawaii.

histologic differences were observed. Infiltrating duct carcinoma comprised 71% (169/239) of Guam breast cancer cases compared to 81% (4488/5536) of Hawaii cases ($p < 0.0001$). Less common histologies were more prevalent in Guam breast cancers. Inflammatory carcinoma comprised 2% (4/239) of Guam breast cancer cases and only 0.1% (6/5536) of Hawaii cases ($p < 0.0001$). Infiltrating ductular carcinoma made up 2% (4/239) and 0.2% (10/5536) of Guam and Hawaii cases, respectively ($p < 0.0001$). Infiltrating duct mixed with other types comprised 5% (11/239) of Guam cases and 2% (104/5536) of Hawaii cases ($p = 0.0032$).

Molecular subtypes could not be compared due to the lack of complete information on ER, PR, and HER2 for Guam cases. There was no difference in the stage at diagnosis with the localized breast tumors representing 62% (15/185) and 69% (3654/5335) ($p = 0.19$) of cases in Guam and Hawaii, respectively. Information on screening history within the two years prior to diagnosis was available for Guam. Among breast cancer cases, 78% (184/237) had a mammogram within two years prior to diagnosis. There was no difference in stage between screened and unscreened cases (data not shown). Screening history was not available for Hawaii cases.

4. Discussion

Contrasting cancer patterns within Guam and between Guam and Hawaii underscore the potential influence of genes, lifestyle, and environment on cancer development and progression. Guam males and, in particular, Chamorros, are disproportionately affected by poor outcomes for a number of major cancers. Malignancies of the lung & bronchus account for the largest cancer burden in both Guam and Hawaii and is one of the most commonly diagnosed cancers and the leading cause of cancer deaths. The incidence of lung & bronchus cancer in Guam males was far higher than that of Hawaii males and slightly exceeded overall U.S. rates [20]. This is consistent with the historically high prevalence of cigarette smoking in Guam which was estimated at 31% in 2001, the highest of all U.S. states and territories [14]. In Guam, lung & bronchus cancer incidence was highest among Chamorro males. In Guam lung & bronchus patients were diagnosed an average of 4–5 years younger than Hawaii patients. This may reflect an earlier age of smoking initiation in Guam, which is consistent with the observed higher mortality rates as duration of smoking is a strong predictor of lung & bronchus cancer death [21]. Early age of smoking initiation may also account for the younger age of cancer onset in Guam compared to Hawaii for malignancies of the bladder, pancreas, liver & intrahepatic bile duct, and stomach, which are all linked to cigarette smoking [22].

The high incidence of liver & intrahepatic bile duct cancer among men in Guam, which was nearly twice that of Hawaii males, is particularly striking given that Hawaii has one of the highest rates in the U.S. [20]. Liver cancer is one of the fastest rising cancers and causes of cancer death in the U.S. [20]. The extremely high rates in Chamorro men underscores the potential contribution of multiple independent and, possibly, synergistic risk factors. It is likely that liver cancers caused by hepatitis B (HBV) have declined in Guam since 1988 when HBV infant vaccination became universally available [23]. Conversely, liver cancers related to hepatitis C (HCV) may be increasing in Guam as it is in Hawaii and the U.S. resulting from rising rates of chronic HCV in individuals acutely infected decades earlier likely through parenteral exposure, including intravenous drug use, or transfusion-related exposure to contaminated blood products, as well as sexual transmission [20]. Haddock et al. reported that 63% of liver cancer cases were attributed to HCV and Chamorros had the highest incidence of HCV infection [23]. In addition to HCV, smoking, alcohol consumption, and other factors may also be driving the high rates of liver cancer in Guam. Chewing of betel nut, which comes from the *Areca catechu* palm tree, is widely practiced throughout Micronesia including among Chamorros in Guam [15,22]. There is some evidence that betel nut chewing may act synergistically with HBV and HCV to increase the risk of liver cancer

[22,24–26]. Chamorros have a high prevalence of obesity [27], which has been increasingly recognized as a risk factor for liver cancer contributing to the rising rates in the U.S. [28] Notably, betel nut chewing is linked to obesity [29,30].

Nasopharyngeal cancer (hereafter NPC) was a top cancer in Guam particularly among Chamorro men, and a major cause of cancer death in Guam. In contrast, NPC was rare in Hawaii. The incidence of NPC varies widely across the globe with the highest incidence in eastern and southeastern Asia [31]. The high mortality of NPC in Guam is consistent with its typical presentation as an advanced, metastatic tumor [32]. NPC is etiologically linked to Epstein-Barr virus (EBV) [33], a common, orally-transmitted infection with most individuals infected by early adulthood [33]. Primary EBV infection in early childhood typically occurs in developing areas where crowded living conditions as well as practices such as pre-chewing of foods for young children contribute to transmission [33]. In more developed areas, EBV infection is often delayed until adolescence when transmission typically occurs through kissing and other salivary contact [33]. Following primary infection, EBV is maintained as a latent infection and carcinogenesis may be induced with its reactivation. In addition to EBV, other factors may be influencing the elevated risk of NPC in Guam including the high prevalence of smoking, a risk factor for NPC [22]. The chewing of betel nut with added tobacco is also a risk factor for NPC [22]. In Guam, betel nut is typically chewed alone or combined with betel leaf, tobacco, and/or slaked lime [15].

Cancers of the oral cavity & pharynx (excluding nasopharynx) were among the top malignancies among men in both Guam and Hawaii. Smoking and betel nut chewing are presumably important factors contributing to Guam's high incidence of oral cavity & pharyngeal cancers other than NPC. Betel nut chewing with or without added tobacco is an established risk factor for cancers of the oral cavity and, with the addition of tobacco, it is also causally linked to cancers from other subsites of the pharynx [22]. In Hawaii, where betel nut use is not widespread, human papillomavirus (HPV), primarily genotypes 16 and 18, may play a more important role. HPV has been increasingly recognized as a causal agent in oropharyngeal and, to a lesser extent, oral cavity tumors, in the U.S. [34,35]. In a study of oropharyngeal cancer cases over a twenty-year period in Hawaii, Iowa, and Los Angeles County, HPV-positive cases were shown to increase over time while HPV-negative cases, presumed to be smoking-related, decreased [36].

HPV is also the primary cause of cervical cancer [37], one of the top cancers among women in Guam with rates double that of Hawaii women. The burden of cervical cancer is particularly high among Chamorro women. Steady declines in cervical cancer incidence and mortality in the U.S. over the past several decades have been attributed to widespread Pap screening [38]. Today, the majority of cervical cancers in the U.S. occur in women who have not been appropriately screened and present at advanced stages [38].

The incidence of breast cancer in Guam, which was substantially lower than Hawaii, is lower than all 50 U.S. states [39]. The lower incidence combined with the higher mortality in Guam compared to Hawaii suggests lower rates of breast cancer screening and/or issues related to access to care in Guam resulting in more advanced stage breast cancers. Nonetheless, there was no difference in the stage distribution of breast cancers. Moreover, registry records indicate that most Guam breast cancer patients had received breast screening in the two years prior to diagnosis. The younger age of diagnosis in Guam breast cancer patients compared to Hawaii may account for the higher mortality rates. Premenopausal breast cancers tend to be more aggressive, including a larger proportion of triple-negative tumors [40]. Guam breast cancers included a greater proportion of rare histologic subtypes including inflammatory breast cancer, an aggressive tumor more common in younger women and characterized by rapid onset, progression, and poor survival [41,42].

Cancer incidence among the same ethnic groups residing in Guam and Hawaii illustrate the potential influence of genes and environment

on cancer risk. Hawaii Filipinos experienced higher incidence of a number of major cancers compared to Filipinos in Guam. Hawaii Filipinos may have adopted Western diets and lifestyles to a greater extent than Filipinos in Guam contributing to a higher prevalence of obesity-related cancers including colon & rectum, postmenopausal breast, ovary, endometrium, and thyroid [43]. Although thyroid cancer incidence was higher among Filipinas in Hawaii than in Guam, the rates among Filipinas in Guam was the highest in the population. The excess risk of thyroid cancer among Filipinas has long been recognized in Hawaii [44] and has also been observed among Filipinas residing on the U.S. mainland [45,46] suggesting genetic susceptibility as well as lifestyle and environmental factors.

Melanoma of the skin was top cancer in Hawaii, with over 80% of cases diagnosed in Whites. In contrast, melanoma was a rare malignancy in Guam's population, including Whites. The elevated risk of melanoma among Whites in Hawaii has long been recognized and multiple risk factors include fair complexion and freckling, excess sun exposure and sunburn, and length of residence in Hawaii [11]. Whether the rarity of melanoma in Guam can be attributed to reduced sun exposure or other differences in lifestyle factors is unknown.

Different lifestyle practices and living conditions in Guam compared to Hawaii may enhance exposure to infectious agents that increase the risk of a number of cancers. The prevalence of cigarette smoking, which has fallen in the U.S. general population, may be slower to decrease in Guam leading to the continued prominence of smoking-related cancers. Betel nut chewing also appears to be an important factor influencing cancer risk in Guam.

The present evaluation provides a comparison of cancer incidence and mortality in two U.S. multiethnic populations. The comparison was strengthened by the availability of data from population-based central cancer registries. Some limitations in Guam data completeness were noted. Comparisons of stage were limited by the large proportion of unstaged cases in Guam. The reason for the lack of staging is unclear. There is some evidence that unstaged diagnoses in the U.S. are more prevalent with lethal cancers and in certain patient groups including the elderly [47]. However, we were unable to evaluate this within the context of the present report.

The influence of access to treatment on cancer outcome could not be evaluated as information on medical insurance coverage was not available from registry data in Guam and Hawaii. Ethnic comparisons were limited by the relatively small case and population numbers in Guam. Chuukese and other less populous groups could not be separately evaluated. As this analysis was limited to a 5-year time period, inferences could not be made regarding trends in cancer rates.

Guam and Hawaii uniquely represent among the most ethnically diverse U.S. populations. Cancer disparities in Guam and their contrasts with that of Hawaii provide insight into the potential interaction of genetic, lifestyle, and environmental factors influencing the development of cancer. These disparities also underscore the importance of strategies for cancer prevention and early detection targeted to these multiethnic communities.

Conflicts of interest

None.

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