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The profound oral cavity cancer burden in the United States Commonwealth of the Northern Mariana Islands: A global health opportunity

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ABSTRACT

Purpose: Betel nut consumption contributes to higher rates of oral cavity cancer throughout Micronesia. The purpose of this study is to review local surveys and cancer data to further characterize these issues in the Northern Mariana Islands (CNMI).

Methods: Two commonwealth-wide health inquiries were reviewed: The Non-Communicable Diseases Survey (NCDS), 2016 and The Youth Risk Behavior Survey (YRBS), 2013. Data pertaining to betel nut, tobacco and alcohol use was extracted. Relevant cancer data from the Commonwealth Healthcare Corporation (CHC) of Saipan and the Surveillance, Epidemiology, and End Results (SEER) databases was assessed.

Results: Betel nut chewing was reported by 43% of Asian Pacific Islander (API) adults, with 88% adding tobacco to the chew. Adults aged 20–30 had significantly higher rates of chewing relative to older groups ($p < .0001$). Tobacco smoking and alcohol use were reported by 25% and 23% of adults, respectively. Betel nut chewing was reported by 33% of high school students. From 2007 to 2016, oral cavity cancers contributed to 9% of all cancer diagnoses and 13% of cancer-related mortalities. SEER data supported oral cavity cancer diagnoses at younger ages in APIs.

Conclusion: These results demonstrate concerning trends regarding alcohol, tobacco and betel nut use in the CNMI. Betel nut use is prevalent among APIs of nearly all ages, with the majority adding tobacco to their chew. The available data suggests a drastic oral cavity cancer burden in the CNMI. Efforts should be made to evaluate for effective means of primary and secondary prevention in API regions.

1. Introduction

The Commonwealth of the Northern Mariana Islands (CNMI) is a United States (US) territory that consists of 14 different islands in the western Pacific Ocean. Saipan, the capital of the CNMI, represents the largest of these islands and has a population of roughly 50,000 people [1]. Most are Asian Pacific Islander (API) or other Asian heritage (85%), and betel nut chewing is customary in this population [2]. Consumption of betel nut, a well-established carcinogen, is thought to contribute to considerably higher rates of oral cavity cancer throughout Oceania [3,4]. Prior studies from Guam and other Micronesian islands have commented on the widespread use of betel nut and oral cavity cancer [2,5].

Despite similarities among the Micronesian islands, each territory, including the CNMI, is culturally and socially distinct. In an effort to better understand their own health issues, the CNMI has implemented a variety of population-wide inquiries and databases in recent years. In 2016, the CNMI performed a commonwealth-wide health inquiry titled the Non-Communicable Diseases Survey (NCDS) that addressed a wide variety of health topics. Dietary practices, obesity rates, exercise habits and substance use were broadly evaluated among 1091 adult residents of the CNMI who completed the survey. A subset of data was collected specifically pertaining to alcohol, tobacco and betel nut practices. In 2013, a similar inquiry called the Youth Risk Behavior Survey (YRBS) focused specifically on health issues and substance abuse among middle and high school students. This survey was completed by 3392 students in grades 7–12. Results of similar surveys from 2007, 2009 and 2011 were also compiled in the 2013 edition. In 2007, a cancer database was

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initiated at the Commonwealth Healthcare Corporation (CHC) of Saipan, the only regional hospital complex of the CNMI. This database contains patient demographic, staging and treatment data for patients treated within the CHC system. Lastly, the Surveillance, Epidemiology, and End Results (SEER) database compiles cancer data from population-based registries from all over the US, including territories in the Western Pacific such as the CNMI [6]. SEER 9 (1973–2011) was the latest database that encoded state of birth information.

In this study, an inquiry of the NCDS, YRBS, CHC, and SEER databases was performed in an effort to better characterize alcohol, tobacco, betel nut use, and the oral cavity cancer burden in the CNMI.

2. Methods

A targeted query of the NCDS and YRBS was performed. Data pertaining to alcohol, tobacco and betel nut use was extracted and compiled. The CNMI cancer database was queried with respect to oral cavity disease. Demographic, staging, and survival data were assessed and collated. Extracted data was compiled, manipulated, and analyzed using Microsoft Excel (Microsoft, Seattle, WA). Statistical analysis was performed using Chi-squared tests, and data was considered significant at $p < .05$. From the SEER database, subjects of Asian/Pacific Islander ethnicity that were born in the CNMI, Guam, Samoa, Palau, and Federated States of Micronesia and had tumors of the oral cavity (ICD-10 codes: tongue: C02.0, C02.1, C02.2, C02.3, C02.8, C09; gingiva: C03.0, C03.1, C03.9, floor of mouth: C04.0, C04.1, C04.8, C04.9) were extracted with age and survival data. These data were compared to whole population level data for the selected ICD-10 codes using Kaplan-Meier curves.

Given the use of exclusively pre-existing, de-identified variables from all data sources, the CHC approved this study for an exemption from an Institutional Review Board assessment.

3. Results

In the 2016 NCDS, 23.0% of adults in the CNMI reported binge drinking alcohol, with 3.1% drinking every day within the past 30 days (Table 1). Drinking was most prevalent in younger adults ($p = .04$), males ($p < .0001$), and native ethnicities (Chamorro, Carolinian, other API) ($p < .0001$). Cigarette smoking was reported by 25.3% of adults, with 20.4% smoking every day within the past 30 days. Smoking was not significantly different between age groups ($p = .7$) and was most prevalent in males ($p < .0001$) and native ethnicities ($p < .0001$). Betel nut use was reported by 19.1% of adults, with 16.2% chewing every day within the past 30 days. Chewing was far more prevalent among native ethnicities ($p < .0001$); 43.0% of people of API heritage reported regular betel nut use. Chewing was not significantly different between males and females ($p = .8$). A majority of chewers mixed tobacco into their betel nut chew (87.5%). Betel nut use was over twice as common in younger adults relative to older adults ($p < .0001$).

Table 1
Alcohol, tobacco, and betel nut use among adults 18 years or older in the CNMI, N = 1091.
Data was extracted from the Non-Communicable Diseases Survey, 2016.

	Alcohol (binge drink)[1]	Cigarettes	Betel nut
% Adults that use	23.0	25.3	19.1
% Adults that use every day	3.1[2]	20.4	16.2
% Males that use	34.9	33.3	19.3
% Females that use	11.1	17.2	18.8
p-Value[3]	$p < .001$	$p < .001$	$p = .8$
% Usage among API ethnicities[4]	31.0	34.7	43.0
% Usage among non-API ethnicities[5]	17.3	18.7	2.3
p-Value[6]	$p < .001$	$p < .001$	$p < .001$
% Usage among 18–34 year olds	29.5	25.1	37.3
% Usage among 35–64 year olds	22.7	26.4	14.9
p-Value[7]	$p = .04$	$p = .7$	$p < .001$
% Mixing tobacco into betel nut chew	N/A	N/A	87.5

[1] Binge drink: ≥5 drinks at a time for men, ≥4 for women.
[2] Frequency of alcohol consumption, not necessarily binge alcohol consumption.
[3] χ^2-Likelihood that % usage among males is equal to that of females for a particular substance.
[4] API ethnicities: Chamorro, Carolinian, other Asian Pacific Islander.
[5] Non-API ethnicities: Filipino, other Asian, other.
[6] χ^2-Likelihood that % usage among API ethnicities is equal to that of non-API ethnicities for a particular substance.
[7] χ^2-Likelihood that % usage among 18–34 year-olds is equal to that of 35–64 year-olds for a particular substance.

In the 2013 YRBS, alcohol, tobacco and betel nut use were assessed by asking participants about use within the past 30 days. Among high school students, roughly one-third used alcohol (33.6%), and over half of these respondents reported binge drinking (57.7%). Roughly one-third of the respondents reported having used some form of tobacco (33.5%). One-third of the respondents used betel nut (33.0%) with a vast majority adding tobacco to their chew (94.5%). Relative to prior years, rates of alcohol, tobacco and betel nut use generally decreased however the rate of mixing tobacco with betel nut slightly increased (Table 2). Among middle school students, roughly one-quarter of the respondents reported having used some form of tobacco (27.4%). Roughly one-third of the respondents used betel nut (31.9%) with a majority adding tobacco to the chew (78.7%). Relative to prior years, rates of betel nut use generally decreased, while rates of mixing betel nut with tobacco have varied.

A query of the CNMI cancer database revealed that head and neck cancers comprised 16.2% of all cancers diagnosed, making them the fourth most commonly diagnosed cancer (87/536, 16.2%) (Fig. 1). Roughly half of the head and neck cancers were of oral cavity origin (46/87, 52.9%) whereas the remainder was distributed as follows: 8.0% nasopharynx, 8.0% thyroid, 5.7% oropharynx, 5.7% larynx, 4.6% nasal cavity and paranasal sinuses, 1.1% salivary gland, and 13.8% unknown origin. Roughly three-quarters of the patients diagnosed with oral cavity cancer were male (34/46, 73.9%), and the majority were of API ethnicity (42/46, 91.3%). The average age of diagnosis was 47, and roughly one-quarter were diagnosed between the ages of 20–39 (13/46, 28.2%). Of the 28 patients for which staging data was available, the distribution was as follows: stage 1 (3/28, 10.7%), stage 2 (3/28, 10.7%), stage 3 (7/28, 25.0%), stage 4 (15/28, 53.6%) (Table 3). Head and neck cancers contributed to nearly 20% of the overall cancer mortality, making them the second most common cause of cancer death (34/173, 19.7%). This was largely driven by oral cavity disease which accounted for 67.6% of deaths (23/34, 67.6%) (Fig. 2).

The SEER database captured 18 subjects with oral cavity carcinomas born in API regions (Table 4). Compared to the 35,515 oral cavity carcinomas in the entire SEER dataset over the same time period, the

Table 2
Alcohol, tobacco, and betel nut use among high school students (grades 9–12, N = 2004) and middle school students (grades 7–8, N = 1388) in the CNMI.
Data was extracted from the Youth Risk Behavior Survey, 2013.

		Percentage of high school/middle school students who have used the following substances on one or more of the past 30 days			
		2007	2009	2011	2013
High school	Alcohol	41.1	38.8	41.4	33.6
	Tobacco	45.3	38.6	37.3	33.5
	Betel nut	48.7	43.6	41	33
	Betel nut + tobacco[1]	89.5	89.7	92	94.5
Middle school	Tobacco	32.8	32	34.1	27.4
	Betel nut	44.5	39.6	37.6	31.9
	Betel nut + tobacco[1]	75.1	79	80.6	78.7

[1] Percentage of betel nut chewers who add tobacco to the chew.

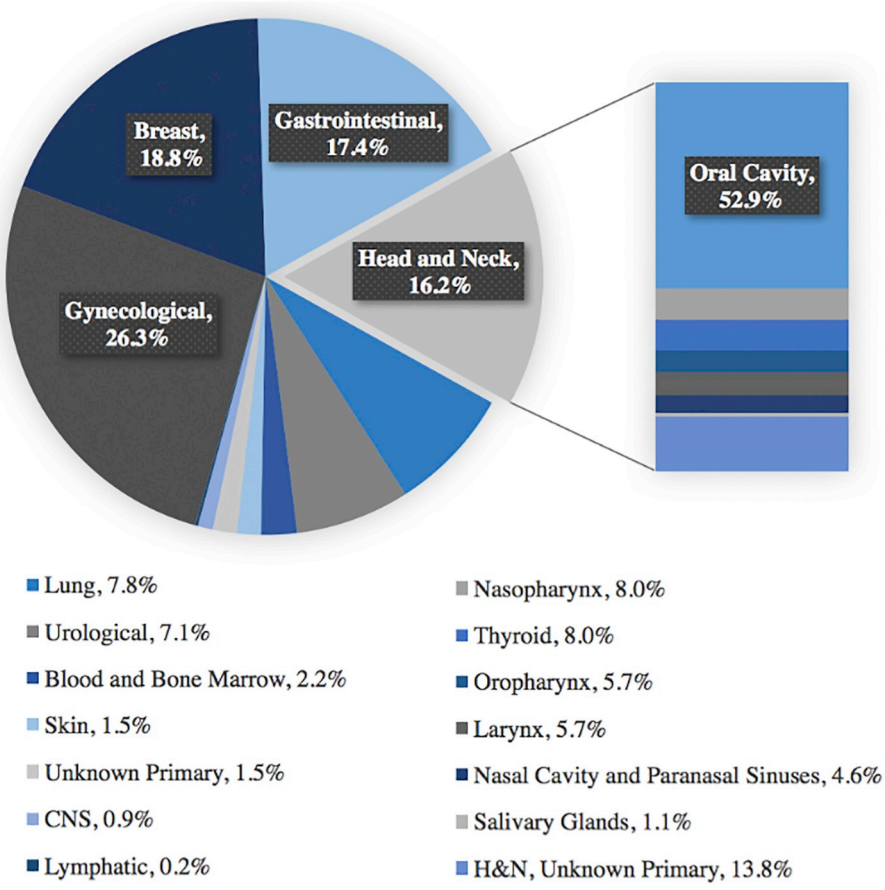

Fig. 1. 2007–2016 CNMI cancer diagnoses by cancer region, N = 536.
Data was extracted from a cancer database maintained by Commonwealth Healthcare Corporation, Saipan, CNMI.

mean age at diagnosis was significantly younger (53.3 ± 3.5 vs. 63.7 ± 0.7, mean ± SEM, $p < .01$). Tumor subsite was not significantly different between groups (10 tumors of the tongue, 3 of the floor of mouth, and 5 in the gingiva in Western Pacific US territories compared to 13,223 of the tongue, 9354 of the floor of mouth, and 12,938 of the gingiva in the entire population, chi-squared 2.62, $p = .27$). Median overall survival was 30 months in subjects born in API territories compared to 54 months for the entire population. There was no significant difference in Overall and Cause-Specific Survival (Fig. 3).

4. Discussion

The results of the NCDS, YRBS, CHC, and SEER databases are suggestive of a profound oral cavity cancer burden in the CNMI that is likely heavily influenced by betel nut consumption. Between 2007 and 2016, oral cavity cancers comprised 8.6% of all cancer diagnoses in the CNMI, as compared to 1.8% in the US in 2015 [7]. Oral cancers contributed to 13.3% of cancer deaths in the CNMI versus 1.0% in the US. Also of note is the proportion of patients presenting with advanced disease; 78.6% of patients presented with stage III or IV disease. This elevated rate of late presentations is likely contributing heavily to disease-specific mortality. Furthermore, the average age at diagnosis in the CNMI was 47, as compared to 62 in the US [8]. A query of the SEER database corroborates these results and suggests that individuals from US territories with high rates of betel nut use such as the CNMI also may have a reduced overall survival.

Rates of alcohol and tobacco use were comparable to estimates from the US mainland [9–11]. However, betel nut use, a practice that is rare in the US mainland, was prevalent. Betel nut use was most common among API ethnicities, with roughly half of adults reporting regular use. Additionally, chewing rates were similar among men and women; this practice is different from other countries like Taiwan, China, and Nepal where men have significantly higher rates of chewing [12]. Prior studies have shown that many people of API descent view the practice as integral to their cultural identity [13]. The majority of both adult and youth users reported mixing tobacco into their chew. Historically, the

Table 3
Primary site, gender, ethnicity, age at diagnosis, and stage at diagnosis of the 46 oral cancer patients diagnosed from 2007 to 2016 in Commonwealth Healthcare Corporation's cancer database, N = 46.

Primary site (N, %)	Buccal mucosa (14, 30.4%)	Tongue (13, 28.2%)	Lip (8, 17.4%)	Gingiva (5, 10.9%)	Hard palate (1, 2.2%)	Mouth, NOS[1] (5, 10.9%)
Gender (N, %)	Male (34, 73.9%)	Female (12, 26.1%)				
Ethnicity (N, %)	Chamorro (28, 60.9%)	Carolinian (4, 8.7%)	OPI[2] (10, 21.7%)	White (2, 4.3%)	Japanese (1, 2.2%)	Unknown (1, 2.2%)
Age at diagnosis (N, %)	20–29 (1, 2.2%)	30–39 (12, 26.1%)	40–49 (16, 34.8%)	50–59 (10, 21.7%)	60–69 (6, 13.0%)	70–79 (1, 2.2%)
Stage at diagnosis[3] (N, %)	4 (15, 53.6%)	3 (7, 25.0%)	2 (3, 10.7%)	1 (3, 10.7%)		

[1] NOS: not otherwise specified.
[2] OPI: Other Asian Pacific Islander.
[3] 18 out of 46 patients did not have staging information available, therefore N = 28.

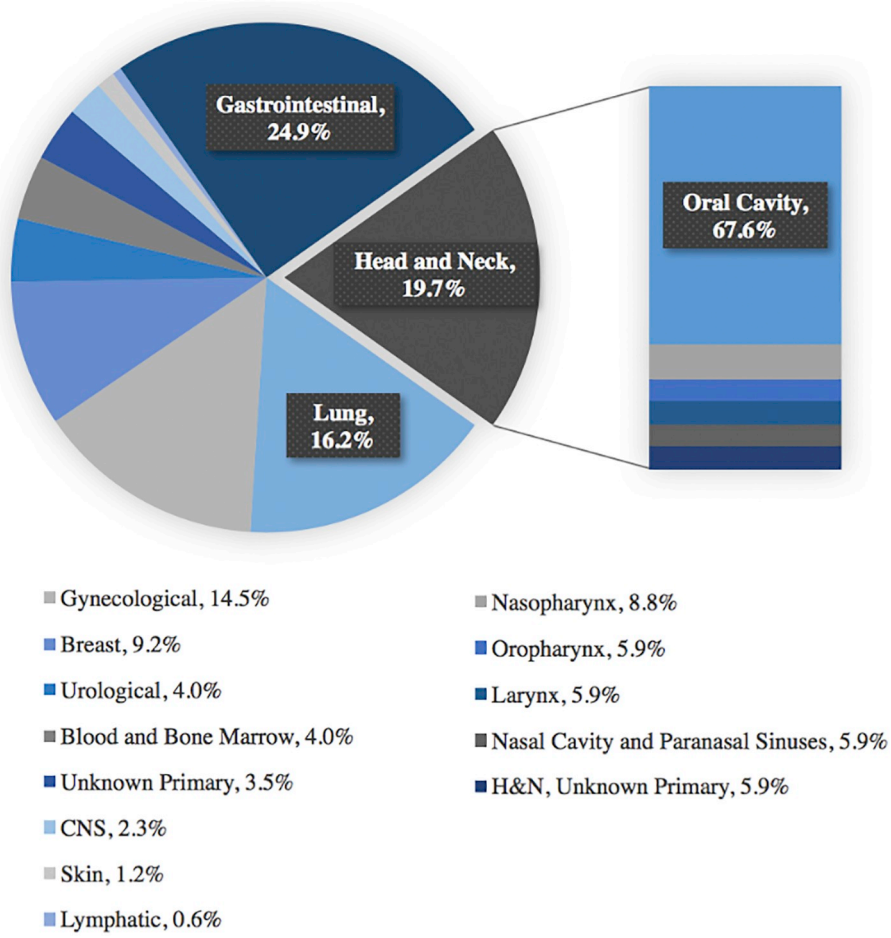

Fig. 2. 2007–2016 CNMI cancer deaths by cancer region, N = 173.
Data was extracted from a cancer database maintained by Commonwealth Healthcare Corporation, Saipan, CNMI.

Table 4
Gender, age at diagnosis, survival, and primary site of the 18 oral cancer patients treated from 1973 to 2011 in the Surveillance, Epidemiology, and End Results (SEER) database, N = 18.

Patient	Sex	Age at diagnosis (years)	Survival (months)	Site
1	Male	31	9	Tongue
2	Male	33	53	Gum and other mouth
3	Male	38	91	Tongue
4	Female	39	17	Tongue
5	Male	40	217	Tongue
6	Female	40	27	Tongue
7	Male	48	12	Gum and other mouth
8	Female	51	14	Floor of mouth
9	Female	52	38	Floor of mouth
10	Male	54	217	Tongue
11	Male	55	23	Gum and other mouth
12	Male	60	6	Gum and other mouth
13	Male	60	51	Tongue
14	Female	64	160	Floor of mouth
15	Male	64	6	Tongue
16	Male	72	17	Tongue
17	Female	79	30	Gum and other mouth
18	Male	80	34	Tongue

practice of mixing tobacco has varied based on geography. Many other regions in Asia where betel nut is used, such as northern Vietnam, Taiwan, and the Hunan and Hainan provinces of China, typically do not add tobacco [12,14–16]. Although there is limited data regarding the carcinogenic effects of directly adding tobacco to the chew, it has been shown that comorbid tobacco smoking and betel nut use can synergistically increase the risk of oral cancer. Lin et al. reported an odds ratio of 11.95 to develop oral cancer in chewers that increased to 26.56 with concurrent smoking [17]. This odds ratio jumped to 46.87 for those who used betel nut, smoked tobacco and drank alcohol. Although our data does not delineate the proportion of comorbid users in the CNMI, the large proportion of substance abuse among API ethnicities implies a significant number of comorbid users, which is likely contributing to the increased oral cavity incidence. A survey conducted in the neighboring region of the Freely Associated States of Micronesia demonstrated significantly elevated rates of concurrent tobacco smoking and alcohol use in betel nut users [5].

The rates of betel nut use among younger adults, high school and middle school students are hugely concerning. These elevated rates of use among the youth are not always typical of betel nut regions. Prior research has shown that chewing in Asian countries such as Taiwan, Malaysia, and Indonesia is much more prevalent among the older adults [12]. Although longitudinal studies examining long-term effects of chewing betel nut are scarce, there is evidence of a dose-dependent relationship with oral cancer, indicating that chewing early in life is a highly dangerous behavior [18]. These trends suggest that the oral cavity cancer problem in the CNMI is likely to persist, and very well may become even more of a problem.

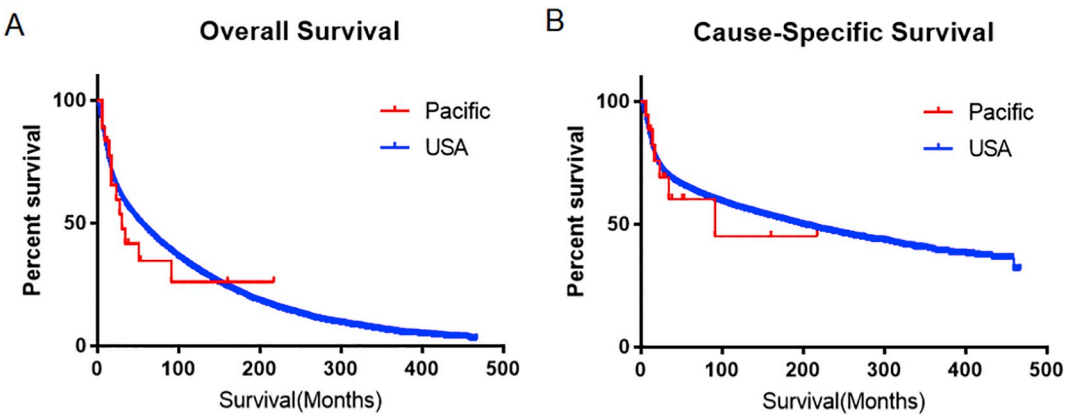

Fig. 3. Overall and cause-specific survival comparisons between oral cancer patients treated in 1973–2011 from US territories in Western Pacific (N = 18) vs those from the entire US population (N = 35,515).
Data was extracted from the Surveillance, Epidemiology, and End Results (SEER) database.

This study is limited by its use of exclusively observational, retrospective data and the associated risk of bias and data inaccuracies. The results of the NCDS and YRBS are at risk of reporting biases. Cancer data from the CHC database were not always complete for individual patients. Inaccurate or incomplete coding would result in cancer patients not being captured within the CHC database. As such, the represented cancer data is most-likely an underestimate of the overall cancer burden at CHC. Furthermore, the CHC cancer database data is not a complete representation of the oncologic burdens in the CNMI as patients treated outside of the CHC system are not included. It is estimated that a minimal number of patients pursue treatment completely outside of the CHC system, such that this limitation is expected to have minimal impact in the oncologic data presented. The SEER database is also limited in a number of ways as it only indicates location of birth rather than ethnicity. Additionally, the extracted 18 patients born in API regions is a very modest figure.

As has been commented on previously, cancer-oriented global health efforts are relatively lacking [19,20]. Surgeons, particularly otolaryngologists, have yet to play as significant a role in global health efforts as their medical colleagues. As a largely preventable, easily detectable, and surgically-treated disease, oral cavity outreach programs provide promising opportunities. Although geographically remote and underserved, there are several attributes about the CNMI that would facilitate global health efforts. Firstly, as US citizens, the vast majority of API residents in the CNMI are eligible for, or already have Medicare. Patient evaluations and data collection would be simplified by the existence of one central hospital (CHC), which has an electronic medical record. CHC is centrally located on the most populous island of the CNMI (Saipan), such that a majority of the population is no > 9 miles away from the hospital. Public transportation is available for those do not have their own means of transportation. Future investigations aimed at evaluating betel nut cessation programs are indicated. Educational outreach should be performed to ensure that CNMI communities are aware of the myriad dangers of betel nut use. Warning labels on betel nut packages, similar to those found with cigarettes, may be effective in decreasing chewing rates. Oral cavity screening programs in high risk populations have shown significant promise in Asia and elsewhere in Micronesia [2,21]. Given the disproportionate rates of oral cavity disease in the CNMI, commonwealth-wide screening efforts should be seriously considered.

5. Conclusion

This review of local surveys and cancer data demonstrated alarming trends regarding alcohol, tobacco, betel nut and oral cancer in the CNMI. Betel nut use is most common among younger adults of API ethnicities. There are significant rates of alcohol, tobacco and betel nut use among high school and middle school students. A large majority mix tobacco into the chew which may be contributing to the disproportionate rates of disease. Proportionally to the population, the CNMI may have the highest oral cavity cancer burden within US jurisdiction. Future studies are indicated to optimize methods of outreach, education, and to investigate the potential for screening programs.

Declaration of Competing Interest

None.

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Disclosures

None.

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