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D. Varez

Exploring the Relationship between Health Insurance, Social Connectedness, and Subjective Social Status among Residents of O'ahu

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Abstract

Relative position in a social hierarchy, or subjective social status, has been associated with indicators of socioeconomic status and may be influenced by social connectedness. The primary purpose of this study is to explore the relationship between health insurance status and subjective social status, using the MacArthur Scale of Subjective Social Status (SSS, community version), in the state of Hawai'i with its highly insured population. The secondary purpose is to examine other social determinants that influence social status, including social connectedness. Data were drawn from a convenience sample of 728 O'ahu residents in 2011-12. Social connectedness was measured if participants stated that family, friends, or community were strengths that could address their social and health concerns. In the final adjusted linear regression model, those with Medicaid/Quest insurance (β -0.40; P<*.05), those who had not completed high-school (β -0.51;* P<*.01), adults of working age (27-64 years) (β -0.59;* P<*.01), and Native Hawaiians (β -0.57;* P<*.05) ranked themselves lower on the SSS ladder. Social connectedness was highly valued, with over 30% of participants stating strong community and family ties as one of Hawai'i's greatest strengths. However, these strengths were not found to be statistically associated with subjective social status in our sample. Future studies should assess whether reinforcing social connectedness through public health and educational interventions improves subjective social status among low-income and ethnically diverse communities in Hawai'i.*

Introduction

Two significant pieces of the United States' Affordable Care Act, Medicaid expansion and the national Healthcare Marketplace, were implemented in January 2014.[1] If all states were to participate in the Medicaid expansion, an estimated 21.6 million uninsured Americans would be newly covered by Medicaid, or 52% of the uninsured population.[2] This legislation has expanded health insurance throughout the United States, although the effect of increased access to insurance on improved health outcomes remains unknown.

Hawai'i residents are highly insured; only 8% of residents between the ages of 18 and 64 are uninsured.[3] In fact, Hawai'i has the second highest percentage of insured residents of any state, falling behind Massachusetts.[3] This is largely attributed to Hawai'i's sweeping 1974 legislation mandating that employers offer health insurance to all non-seasonal employees working twenty hours per week or more.[4] In addition to employer-provided health insurance, Hawai'i has a network of publicly-provided plans, as well as a state-run health insurance exchange for residents whose needs are not met by employer-provided plans.[5] In 2013, more than 290,000 individuals, or 20% of the 1.4 million individuals living in Hawai'i, were enrolled in the federal Medicaid program (referred to as Quest).[6,7] The health insurance landscape is likely to change in the coming years as the Affordable Care Act rolls out and as new health plans become available and the penalty for being uninsured is implemented.

Honolulu County is the most densely populated county in the state, with more than 998,000 residents in 2015.[8] Asian residents make up a high proportion of the population (43%).[8] Nineteen percent of Honolulu County residents were born outside of the United States, and approximately 28% over 5 years of age speak a language other than English at home.[12] Poverty is a significant problem, with 10% of individuals living below the poverty level.[8] In 2013, approximately 4,500 individuals were homeless.[9] Poverty and homelessness both create significant barriers to accessing healthcare and other social services. Strengthening connectedness to community organizations may have important ramifications for improving the wellbeing of immigrant, poor, and homeless groups in Hawai'i.

Social connectedness, demonstrated by positive relationships with family, friends, or community, may decrease social isolation, assist communities in socializing to normative values, and reduce the conflicts that may arise in societies that are culturally and linguistically heterogeneous.[10] Social connectedness, which can be measured by the number, strength, and intensity of social group interactions with family, friends, and community groups strongly impacts health,[11] leading to reduced mortality[12,13] and improved physical and emotional well-being.[14,15] Social connectedness was found to improve self-esteem among homeless youth,[16] increase volunteerism among retirees,[17] and moderate the effect of perceived racial discrimination among Chinese students,[18] but was not associated with maternal smoking patterns[19] or depression.[20] Social connectedness may increase the sense of social status within a given community, and this relationship may be independent of other sources of status measures, such as income and education.[21]

The MacArthur Scale of Subjective Social Status (SSS) is an instrument designed to measure where individuals see themselves within a given hierarchy. When asked what influenced perception of their SSS, respondents often mentioned volunteering or other giving activities, leadership roles, and parenting activities.[22] The MacArthur Scale of Subjective Social Status has been used widely since its development,[23] including among elders in Taiwan,[24] low-income Mexican immigrants living in Texas,[25] biracial adolescents in Ohio,[26] and civil servants in London.[27] In these studies, SSS was found to be a significant predictor of the health status of individuals, independent of income, ethnicity, and gender.

The purpose of this study was to explore the relationship between health insurance status and SSS among Hawai'i residents. The second aim was to examine other social determinants that influence SSS, such as identified community strengths that build social connectedness.

Methods

This cross-sectional study was conducted in 2011 and 2012 on the island of O'ahu, Hawai'i. A convenience sample (N=728) was recruited from nine community sites: Association of Hawaiian Civic Clubs conference, the Children and Youth Day Fair, Hispanic Heritage Festival, Women's Expo conference, Food Bank and Ohana Learning Center in Palolo public housing, Next Step Homeless Shelter, Senior Fair, and St. Philomena Health and Safety Fair. Community members were eligible to participate if they spoke English and were aged 16 years or older. They were approached by trained undergraduate nursing students from Chaminade University (Honolulu, HI) and asked to participate in a short 30-item survey. Nursing students received four hours of didactic training on ethical conduct of research, consent and questionnaire administration, and piloting of questionnaire, before conducting the community surveys. Surveys were verbally administered using a semi-structured questionnaire. The research team chose to verbally administer the questionnaire so that literacy level of the respondents would not be a factor in participant selection. Among the 1,106 who were approached, 728 individuals completed the survey (65.8 % response rate). Participants were given a $5 gift card to a local grocery store for participating in the study.

MacArthur Scale of Subjective Social Status

The outcome variable of interest was the MacArthur scale of SSS, which has been used to assess an individual's relative socioeconomic status as well as their place within their community. For this study, we used the community ladder to explore SSS and asked participants to state their position on a 10-rung ladder (1 through 10, with one being the lowest rung of society and 10 being the highest). A picture of a ladder was shown to participants and they were asked to point to the rung that best described their current position relative to other community members.[22,28]

Demographic Measures

We adapted a demographic survey based upon research previously done in Hawai'i[29-31] and tested in a cohort of undergraduate nursing students.[32] Questions included age, gender, current occupation, education and household income levels, primary language spoken at home, place of birth, and length of residence in Hawai'i. We used laminated cards and asked them to point to the income category that corresponded to their household income. We asked participants to state their race and ethnicity, allowing them to state more than one category. Due to small sample size of some of the groups, Japanese, Chinese, Korean, Vietnamese, Thai, and Lao were coded as "Asian," and Native Hawaiian were examined separately and together with other Pacific Islanders.

Health insurance was the primary predictor variable of interest. We asked two questions: "Do you have health insurance?" (yes/no) and "What type of insurance do you have?" (private health insurance, either provided by employer or self; Medicaid/Quest; Medicare, or Military Health System). We grouped responses into three categories: no insurance, insurance provided by federal or state government to low-income residents based on federal poverty level (Medicaid/Quest), and private/other insurance. Because Medicare and Military Health System insurance are provided to those 65 years of age and to those who serve in the military, regardless of income status, we grouped them into the private/other insurance category. Sixteen respondents had more than one type of insurance, but all included private/other insurance, thus they were classified as private/other insurance.

Participants were asked open-ended questions about the three greatest health and social concerns in Hawai'i, and asked to identify the greatest strengths in Hawai'i to address these concerns. Two researchers independently categorized these open-ended responses. Responses were grouped into themes; for instance, "verbal language barriers" and "getting used to Hawaiian dialect" responses were collapsed into the category "communication barriers." Responses that indicated that positive aspects of community, family, religious groups, or societal support were strengths, were categorized as "yes, socially connected," while responses such as "good weather" and "financial resources" were not categorized as such. A data coding manual was created prior to data entry to categorize text response answers for subsequent analysis.

Statistical Analyses

Demographic variables were explored using descriptive statistics. Bivariate analysis was employed to assess covariates using Chi-square test, Kruskal-Wallis, and simple linear regression. Variables were included in a multiple linear model if they were statistically related to the primary independent (insurance status) or dependent (SSS) variables at $P < .10$ or found to be associated with SSS in the literature. The dependent variable was normally distributed. Covariates that were initially assessed for inclusion in the model included: gender (male or female), age (16-26 years old, 27-44, 45-64, or 65+), income (<$25,000/year, $25,000-$49,999, $50,000-$74,999, $75,000-$99,999, $100,000+), occupation (employed or unemployed), ethnicity (Native Hawaiian, Asian, Pacific Islander, White, Hispanic, African American, and Native American), language (English as primary or secondary language), whether they were born in Hawai'i, and place of interview (Hawaiian Civic Clubs, youth and senior fairs, food bank, public housing community center, or a homeless shelter). We assessed whether they mentioned social connectedness as one of Hawaii's greatest strengths (yes/no). Income and insurance were collinear ($r_s = -.37$, $P = .033$), and income had a 19% non-response rate. Those with Medicaid and the uninsured were less likely to report income than those with private insurance (26.8%, 24.7%, and 15.3%, respectively), thus income was not included as one of the variables in the multiple regression model. The best model was fit after detecting influential data using residual plots, testing for normality

of residuals, and assessing collinearity between variables using variance inflation factor and tolerance statistics. The final model, which included insurance status, education, age, race/ethnicity, and social connectedness to family and community, was chosen based on these regression diagnostics and the model that had the smallest root mean square error. Stata 13 was used for data analysis.

Human Subjects Review and Informed Consent

The study received ethical approval from the Committee for Human Research at University of California, San Francisco and from Papa Ola Lokahi, a federally registered Institutional Review Board that reviews and approves research studies conducted with Native Hawaiians. Participants signed an informed consent before the interview and were informed they could decline to answer any questions and stop the survey at any time.

Results

Description of Sample

Of the 728 individuals surveyed, 67% were women and 53% were born in Hawai'i (Table 1). Two hundred and thirty (31%) participants reported being Native Hawaiian (n=149) or Other Pacific Islander (n=81). More than 30% reported speaking a first language other than English. Twenty-nine languages were spoken, represented primarily by Hawaiian/Pacific Islander and Asian languages. Eighty-eight percent of all participants reported having current health insurance, ranging from 78% to 100% depending on interview site. The median age of respondents was 42 years old, ranging from 16 to 91 years old. Nine percent reported less than a high school education. More than 25% of the participants (n=193) were interviewed at centers serving low-income communities, including homeless shelters and food banks.

Respondents were divided into three groups based on health insurance status: uninsured (n=85), Medicaid/Quest (n=160), and private or other insurance (n=483). There was a statistically significant difference in median rank scores of SSS among the three groups with different health insurance coverage ($P<.001$). Those with private insurance were more likely to have been born in Hawai'i ($P<.01$), had longer length of residence in Hawai'i ($P<.05$), and spoken English as their first language ($P<.001$) compared to the uninsured or those with Medicaid/Quest (Table 1**).** There were proportionally more Asians and Whites in the private/other insurance group and more Native Hawaiian and other Pacific Islanders in the uninsured and Medicaid/Quest groups *(*$P<.05$). The education gradient was markedly different with higher levels of education achieved in the private/other insurance group ($P<.001$). Men were more likely to be uninsured compared to women (16.0% versus 9.6%, $P<.05$). Although limited by a 20% rate of nonresponse, for respondents who reported income (n=589), those receiving Medicaid/Quest were most likely to report less than $25,000 a year (75.9%), as compared to those who were uninsured (68.7%) and those otherwise insured (24.7%) ($P<.001$).

Participants were asked to state Hawai'i's greatest strengths; social connectedness was the predominant theme (n=230, 31.6%). Elements of social connectedness ranged from community support (n=89, 38.7%); the people and culture of Hawai'i (n=80, 34.8%), which included specific reference to aloha spirit, referring to a spirit of peace and compassion (n=38, 16.5%); family support (n=58, 25.2%), which included mention of *ohana*, the binding and internal support in families (n=10, 4.3%); and participation in religious organizations (n=3, 1%) (data not shown).

Participants were asked to report what they perceived as the top social and health problems in Hawai'i (Figure 1). Diabetes, obesity, and cardiovascular disease were the top three health concerns among all three insurance groups. The top three social problems affecting residents of Hawai'i were identified as drug and alcohol abuse, homelessness, and domestic violence/violent crime.

Regression Analysis for Subjective Social Status

Linear regression was used to evaluate the relationship between demographic variables and SSS. Insurance, site of enrollment, education, unemployment, age, and being Native Hawaiian were significantly related to SSS in the initial analysis (Table 2**)**. Site of enrollment and employment were removed from the final model because they did not improve model fit. Those with Medicaid/Quest viewed themselves lower on the ladder compared to those with private/other insurance (adjusted β -0.40; $P<.05$). Those with less than a high school degree also placed themselves lower on the SSS ladder than those with a high school degree or higher (adjusted β -0.51; $P<.001$). Respondents 26-64 years of age were lower on the ladder than those over 65 years of age (adjusted β -0.59; $P<.01$) but there was no statistically significant difference between those between the ages of 16-26 and those over 65 years of age (adjusted β -0.12; $P=.65$). Native Hawaiians (adjusted β -0.56; $P<.05$) reported being on a lower rung compared to White participants.

In the multivariate linear regression model, participant report of social connectedness to family and community increased SSS (adjusted β 0.18; $P=.25$) although this finding was not statistically significant (Table 3). The final model was statistically significant (F 3.9, $P<.001$); variables included in the model explained 7% of the variance in SSS.

Table 1. Characteristics of O'ahu Community Participants Based on Insurance Status				
	Total	**Private/Other[a]**	**Medicaid/ Quest**	**Uninsured**
	(N=728)	(n=483)	(n=160)	(n=85)
SSS Ladder rank,* median (IQR)**	7 (5-8)	7 (6-8)	6 (5-7)	6 (4-8)
Born in Hawai'i, n (%)**	389 (53.4)	283 (58.5)	74 (46.2)	32 (37.6)
Lived in Hawai'i,* mean age in years (SD)	29.8 (21.6)	31.6 (22.5)	26.9 (19.1)	25.6 (20.3)
Male	237 (32.6)	153 (31.7)	46 (28.9)	38 (44.7)
Age group, n (%),**				
16-26	143 (19.6)	99 (20.5)	27 (16.9)	17 (20)
27-64	471 (64.7)	292 (60.5)	119 (74.4)	60 (70.6)
65 and older	107 (14.7)	88 (18.2)	13 (8.2)	6 (7.1)
No response	7 (1)	4 (0.8)	1 (0.6)	2 (2.3)
All race/ethnicities (n=984)*[b]				
Native Hawaiian/Pacific Islander	340 (46.7)	212 (43.9)	87 (54.4)	41 (48.2)
Native Hawaiian	149 (20.5)	95 (19.7)	35 (21.9)	19 (22.4)
Asian	290 (39.8)	210 (43.5)	50 (31.3)	30 (35.3)
White, Non-Hispanic	200 (27.5)	148 (30.6)	31 (19.4)	21 (24.7)
Hispanic	109 (14.9)	82 (17.0)	15 (9.4)	12 (14.1)
Native American	23 (3.2)	16 (3.3)	4 (2.5)	3 (3.5)
African American	22 (3.1)	13 (2.7)	8 (5.0)	1 (1.2)
Languages spoken***				
First language English	489 (67.2)	354 (73.3)	92 (57.5)	43 (50.6)
Highest education level achieved (n=725)***				
Less than high school	65 (8.9)	24 (5.0)	27 (17.0)	14 (16.6)
High school/GED	343 (47.3)	203 (42.0)	94 (76.5)	46 (54.7)
Associate's degree	102 (14)	78 (16.4)	18 (11.4)	6 (7.1)
Bachelor's degree	127 (17.4)	103 (21.3)	11 (6.9)	13 (15.5)
Master's degree	59 (8.1)	53 (11.0)	3 (1.8)	3 (3.5)
Doctorate/MD	15 (2.0)	13 (2.6)	0	2 (2.4)
Other	14 (1.9)	9 (1.7)	5 (3.1)	0
Missing[c]	3	–	2	1
Currently unemployed**	150 (20.6)	27 (7.5)	95 (34.1)	28 (33.3)
Annual Income (n=589)***				
< 25,000	233 (39.5)	101 (24.7)	88 (75.9)	44 (68.7)
$25,000 - $49,999	144 (24.6)	117 (28.6)	13 (11.2)	14 (21.9)
$50,000 - $74,999	96 (16.3)	89 (21.8)	4 (3.4)	3 (4.7)
$75,000 - $99,999	58 (9.8)	48 (11.7)	9 (7.7)	1 (1.5)
$100,000 or more	58 (9.8)	54 (13.2)	2 (1.8)	2 (3.1)
Missing[c]	139	74	44	21
Social connectedness to family and community*	230 (31.6)	166 (34.4)	36 (22.5)	28 (32.9)

*$P<.05$; **$P<.01$; ***$P<.001$ (two-tailed tested)

[a]Private insurance is provided by employer, self-purchased, or Medicare and Military Health Systems.

[b]The total number of responses is greater than 728 because participants could state more than one race/ethinicity.

[c]Percentages exclude missing data.

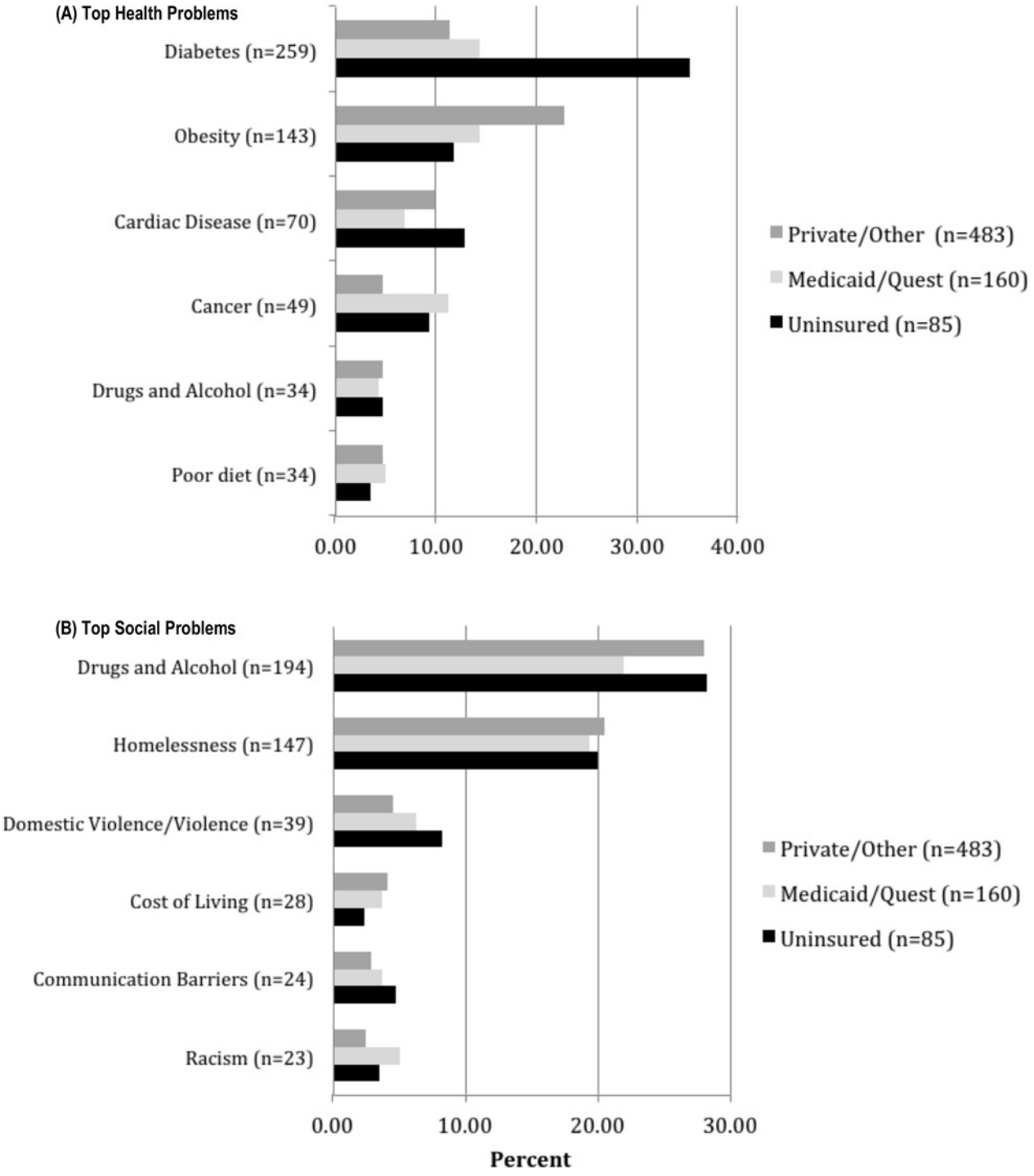

Figure 1. Major Health and Social Problems in Hawai'i as Identified by O'ahu Community Participants, Based on Health Insurance Status (A) Top Health Problems; (B) Top Social Problems

Table 2. Association between Independent Variables and Subjective Social Status as a Continuous Dependent Variable among O'ahu Community Participants

Variable	β (SE)	*P*-value
Insurance Status		
Uninsured	-.75 (0.22)	<.001
Medicaid/Quest	-.36 (0.22)	.10
Private/other insurance[a]	Reference	.
Site of Enrollment		
Food bank, homeless shelter	-.67 (0.16)	<.001
Community events, including fairs and workshops	Reference	.
Education		
High school or less	-.64 (0.14)	<.001
More than high school	Reference	.
Employment		
Unemployed	-.40 (0.18)	<.05
Currently employed	Reference	.
Age (continuous)	.004 (0.04)	.34
Age (years)		
16-26	-.29 (0.25)	.22
27-64	-.64 (0.21)	<.01
65+	Reference	.
Gender		
Women	-.07 (0.15)	.66
Men	Reference	.
Born in Hawai'i		
No	-.05 (0.14)	.74
Yes	Reference	.
First Language English		
No	-.13 (0.15)	.40
Yes	Reference	.
Race/Ethnicity		
Other[b]	Reference	.
Native Hawaiian	-.44 (0.17)	<.05
Social Connectedness to family and community		
No	-.22 (0.15)	.16
Yes	Reference	

[a]Private/other insurance is provided by employer, self-purchased, or Medicare and Military Health Systems
[b]Other are not Native Hawaiian, including White, Asian, Other Pacific Islander, Hispanic or African American race/ethnicities

Table 3. Multivariate Linear Regression Model of Insurance, Education, Age, Ethnicity, and Social Connectedness on Subjective Social Status among O'ahu Community Survey Participants [n=655]

Parameter	β	Standard Error	[95% Confidence Interval]	
Insurance Status				
Private/other insurance[a]	Reference			
Medicaid/Quest*	-.40	0.19	-0.77,	-0.02
Uninsured	-.28	0.24	-0.75,	0.18
Education				
More than high school	Reference			
High school or less**	-.51	0.15	-0.82,	-0.21
Age (years)				
65+	Reference			
27-64**	-.59	0.22	-1.01,	-0.16
16-26	-.12	0.25	-0.62,	0.38
Race/Ethnicity				
White	Reference			
Asian	-.25	0.25	-0.74	0.25
Pacific Islander	-.25	0.25	-0.74,	0.24
Native Hawaiian*	-.57	0.26	-1.07,	-0.06
Other[b]	-.40	0.29	-0.95,	0.14
Social Connectedness to Family and Community				
Yes	Reference			
No	.18	0.16	-0.13,	0.48

**P*-value <.05; ***P*-value <.01
[a]Private/other insurance is provided by employer, self-purchased, or Medicare and Military Health Systems
[b]Other are African American, Native American, or Hispanic race/ethnicities

Discussion

This is one of the first studies to examine the association between health insurance, an essential element for the protection of health, and subjective social status, the perception of one's social position in a community. We found that among residents of O'ahu those who were uninsured or had Medicaid/Quest had lower subjective social status than those with private/other insurance. This relationship persisted for those with Medicaid/Quest even after adjusting for age, education, race/ethnicity, and social connectedness in a multivariate model. People between 27 and 64 years of age, potentially prime members of the workforce, had lower SSS than older adults. In our study, 19.3% in this age group reported being unemployed, compared to the 5%-6% official unemployment reported in Honolulu County during the survey period.[33] Education was an important indicator of SSS; those with high school education or less (57% of the sample) reported lower SSS. Our sample was comparable to census data from Hawai'i, where 9.3% completed high school and 32.5% completed bachelor's degree or higher.[8] In our study, Native Hawaiians reported lower SSS compared to other racial/ethnic groups. Our findings of an association between race, insurance status, and community SSS are similar to a recent study conducted in Texas among 394 homeless adults.[34]

This study highlights some of the health problems identified by community members residing in Hawai'i. The top health concerns were diabetes and obesity. However, while the uninsured were three times more concerned about diabetes compared to the private/other insured group (35% versus 11%), the converse was true for obesity, a risk factor for diabetes, with 11% concerned about obesity in the uninsured compared to 23% in the private/other insured group. Given that health care costs for people with diabetes are 2.3 times higher than for people without diabetes,[35] the high cost of diabetes management is a tangible concern. Cancer and cardiac disease were two other health concerns mentioned by the uninsured in this sample. Both conditions lead to significant health care expenditures. Substance use was mentioned equally across the three insurance groups and is a significant problem in Hawai'i. Self-reported heavy alcohol use in the past month among those 21 years and older was 8.6% in Hawaii compared to the national rate of 6.9%, and enrollment in substance use treatment centers for drug and alcohol use has increased dramatically in the past decade.[36]

Although we drew our participants from a non-probability convenience sample, which leads to selection bias and limits generalizability of findings, nursing students canvased a wide variety of community meeting sites and captured a cross section

of Honolulu residents at public events and gathering spaces, including community fairs, senior centers, and low-income housing and homeless shelters. Our sample was more racially and ethnically diverse than the composition of the state of Hawai'i, primarily due to outreach in communities where a greater proportion of Hawaiian/Pacific Islanders (74% Native Hawaiian at Hawaiian Civic Club event and 44% Pacific Islander at the Palolo Housing center) and Hispanics (33% Latino/Hispanic at Hispanics Hispanic Heritage Festival) gather. Additionally, the surveys were verbally administered, relatively short in duration, and participants were interviewed at public events, which may influence the validity of study findings. However, the research team found similar results when this survey was self-administered, with no time limitations, to a group of student nurses.[32]

Except for Native Hawaiian study participants, other racial/ethnic groups in our study did not have lower SSS compared to whites. This may point to less discrimination and marginalization among these groups than might exist in racially and ethnically homogeneous areas of the United States.[37-39] A limitation of the current study was our inability to explore objective health disparities, such as increased rates of morbidity and perception of "everyday discrimination" among Native Hawaiians,[40,41] important factors that impact subjective social status and could explain the differences that we found. When comparing findings to prior research conducted with residents of Hawai'i and Hawaiians who have migrated to other states, there are multiple factors that affect an individual's SSS that were beyond the scope of this study.[42-44] Although we hypothesized that uninsured respondents would place themselves lower on the SSS ladder than those with either Medicaid/Quest or other insurance, the heterogeneity of response among the uninsured did not give a clear picture of this relationship. Other studies found that SSS has a significant relationship with objective health outcomes, something that we did not measure in the current study. A more complete understanding of how SSS affects physical and emotional wellbeing in a racially and ethnically diverse population, such as exists in Hawaii, may lead to targeted actions that improve the health of these groups.[22,28]

We assessed the influence that social connectedness may exert on the association between health insurance and SSS. Social connectedness has been found to improve health resilience[45] and may improve subjective social status. There are three purported dimensions to social connectedness: numbers of close ties, frequency of interactions, and quality of interactions between the closely tied members.[10] In this study, we measured the presence but not the intensity or frequency, of social connectedness. However, asking a simple open-ended question about "greatest strengths in Hawaii" led 30% of participants to freely mention that family, friends, or community strengths were among Hawaii's significant strengths. Future studies should work with community members to illuminate some of the critical elements of social connectedness that are unique to populations living in Hawai'i, such as aloha spirit[46] and *ohana*. This may, in turn, allow for more targeted, collective public health actions, such as strategies that enhance high school completion or that increase health care access among new immigrants. Ultimately, the goal is to "move people up the ladder" and to improve the health and wellbeing of low-income and ethnically diverse communities in Hawai'i.

Conflict of Interest

None of the authors identify any conflict of interest.

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A Pilot Dental Survey on Maui

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Abstract

Routine dental screening surveys of third graders have proven to be a useful tool to monitor the dental health of a community, especially those of highest risk. In 2010 the PEW Charitable Trust (PEW) conducted state-by-state oral hygiene assessments, giving Hawai'i a poor grade, with routine dental surveys of children one of several criteria not met. The Maui Oral Health Task Force piloted its own survey for the island of Maui to assess the challenges in implementing a dental screening and to gain an understanding as to how obstacles might be addressed. Three issues were identified: technical (sampling methodology, data interpretation, and analysis), administrative (approvals of protocols, consent forms, and confidentiality), and operational (participation rates, dental referrals, and missing data of socio-economic status). These issues were relatively easy to resolve over the course of a few months due to the public's and providers' outcry over the negative findings of the PEW report. Two hundred and eighty-one students were surveyed, which represents 46% of the children whose forms were sent home for parental consent and approval. Of those returning the forms, 77% had parent's consent to participate. Based on our island survey, the estimated sample size and participation rate for the State of Hawai'i would be comparable to those of other states, which had met the PEW survey criteria. Comparative exploratory analysis between Maui and survey data from other states underscores the value of prevention in averting dental treatment.

Keywords

Oral Health, Dental Survey, PEW

Introduction

The United States Surgeon General's report on oral health states that dental caries in children ages 5 to 17 years of age is the most frequent chronic childhood disease — at 58.6%.[1] Caries are a result of bacteria covering the tooth, forming dental plaque, then dissolving the inside minerals within the tooth enamel.[2] There are a variety of subsequent effects of caries including nutrition, growth, and development issues. Untreated caries can lead to extended mouth pain, disturbances of facial structure, abscesses, deterioration of bone and increased risk of infection.[3] Research has shifted away from the causes of dental caries to their effect on general health.[4] Periodontal disease (PD) is a result of bacterial infection on the gums, which stimulates chronic inflammation. Its prevalence (2009 and 2010) is 47% in adults under the age of 65 and 64% for those over this age.[5] Although PD is not as common in children, poor oral hygiene knowledge, attitudes, and practices during childhood may result in variety of problems in adulthood.[6] Research has shown that PD may be associated with cardiovascular diseases, cancer, chronic respiratory diseases, and diabetes.[7] Evidence also shows that coronary heart disease associated with PD is extremely costly, with health related expenses and the loss of productive work adding up to approximately $258 billion in 2006 for the United States.[8]

In response to the Surgeon General's report, an informal group of dental and medical health practitioners on the island of Maui met for a number of years as the Maui Oral Health Task Force (MOHTF). This task force focused on improving access to treatment services for the underserved. MOHTF efforts included legislative initiatives supporting new types of State community dental licenses for dentists who served underprivileged populations. New clinics were established to serve those without access to treatment.

The PEW is an independent non-profit, non-governmental organization (NGO) founded in 1948. Its stated mission is to serve the public interest by "improving public policy, informing the public, and stimulating civic life."[8] PEW's public policy areas address the environment, state policy, economic policy, and health and human services.[8] The PEW conducted two national surveys in 2010 and 2011 assessing the practices and the policies that affect American children's oral health.[9] Each state was graded on eight criteria: (1) Enrollment and access of Medicaid eligible children to dental care, (2) Coverage of children with dental sealants, (3) Use of a hygienist to place dental sealants, (4) Use of fluoridated water, (5) Authorizing new types of primary care dental providers, (6) Tracking children's dental status with periodic surveys, (7) Adequate Medicaid reimbursement for dentists, and (8) Reimbursement to providers for preventive care. Each criterion was graded as a pass or fail, with a state's overall grade depending on the number of criterion passed. In 2010 the PEW gave an "F" grade to several states, including Hawai'i, which met only two out of the eight criteria. The following year PEW repeated its survey with Hawai'i only fulfilling one criterion.[9,10] In 2012, the MOHTF decided to conduct a pilot study to assess the feasibility of meeting one of the PEW criteria—a dental screening survey of 3rd graders. The proposed survey would be patterned after states that had earned an "A (6-8 criteria)" or "B (5 of 8 criteria)" and had completed a successful survey. PEW evaluations are based on standard guidelines for children's dental surveys promulgated by the Association of State and Territorial Dental Directors (ATSDD) and available on their website.[11] While the guidelines are somewhat flexible to accommodate each state's specific situation, four guiding principles emerge: (1) At a minimum 3rd graders enrolled in public schools should be targeted (eg, private schools inclusion are optional), (2) There must be some marker of socio-economic status, with the portion of each school enrolled in the Free Reduced School Lunch (FRL) as the recommended marker, (3) Schools refusing to participate must be replaced at random from the same strata (eg, approximately same proportion FRL and/or region), and (4) Response rates and FRL proportions of the

sample need to be tracked and adjusted by weighted-analysis to best represent the target population. For logistical reasons, the ATSDD discourages random sampling among individual students and instead suggests cluster sampling by schools.

The ATSDD guidelines also cover sample size calculations based on statistical power to detect relevant differences in measured outcomes. This determination is somewhat variable depending on what comparisons are to be made (eg, among counties, states, FRL status, gender, etc).

A secondary goal of this project was to use the results of the pilot survey for comparison to surveys from other states — but only if Maui's Pilot Dental Survey was successful (representative of the target group with an adequate response rate). This would be important since the PEW criteria focus on policies and guidelines that may translate to specific outcomes assessed by the surveys.

Methods

Since Maui planned to contribute county data for a comparison of survey outcomes among states, we envisioned a successful Hawai'i survey would have a sample size and response rate similar to others states that had met the survey criteria. Thus, Maui Island with approximately 10% of Hawai'i's population would target 10% of the sample size envisioned for Hawai'i. The three general areas in this section will describe: (1) How administrative issues were addressed, (2) Over what time period administrative issues were addressed, and (3) Technical issues of survey design.

The investigators of the study prepared a brief background information document describing the need for improving Hawai'i's oral health policies based on the Surgeons General's report and PEW grades. Then a brief technical plan was written based on dental survey reports of several states that had fulfilled the survey criteria. Key points to be addressed were the sampling methods, informed consent, and need for follow-up dental care when urgent conditions were discovered in subjects. Meetings were arranged for oral presentations to the Principals of all Maui elementary schools, as well as the Maui Superintendents of the Department of Education (DOE). In turn, the two Superintendents presented and obtained approval from the State Director (DOE is a State Agency). Ethical approval was obtained from the Institutional Review Board of New York University's Lutheran Medical Center, which placed dental residents on Maui Island and allowed this survey to fulfill the residency requirement for a community project.

The following is an administrative timeline of this project:

February 2012:
MOHTF considers different unmet criteria of the Pew survey (sealants, extended care by Hygienists, 3rd grade survey, etc.).

May 2012:
Third grade screening chosen and project plan written, discussions with county school Superintendents and private school Principals.

August 2012:
Protocol, consent forms written and approved by Maui's representatives for DOH, University of Hawai'i Maui Campus and DOE. Begin screening of schools.

April 2013:
Last School screened

June 2013:
Data entry and analysis begins.

June 2014:
First drafts of reports written and presented to MOHTF.

The DOE required that participation be by active consent (written affirmation). Children were sent home with written informed consent forms to be filled out by parents. Those who did not return forms could not participate in the study. Survey results were kept as confidential as possible, but notes were sent home to the parents of examined children regarding the need to see a dentist (routine/soon/urgent). To keep outcomes as standardized as possible, a single team consisting of dentists, hygienists, dental assistants, and public health outreach workers conducted all the examinations.

The technical development of the study was modeled from three sources. The Basic Screening Surveys: An Approach to Monitoring Community Oral Health,[12] was a referenced source by the PEW that gave an overview of standard procedures, demographic data to be collected, outcome indicators, and specific examples of forms for parent questionnaires (by mail), informed consent, data collection, and data analysis. Analysis of the data was descriptive and then compared to other states that measured similar outcomes. Demographic data included age, gender, and enrollment in the subsidized school lunch program (alternatively using the proportion of each school's third grade class receiving FRL). Outcomes surveyed included presence of: sealants, filled cavities, un-filled cavities, and need for dental visit "routine, soon or urgent." Another PEW reference[11] addressed methodology of sampling and analysis to insure that samples represent target populations and have sufficient statistical power. The third source of recommendations for study design came from descriptions of surveys of several states,[13-15] which met the PEW criterion, and received an overall A or B grade. A high scoring state of the PEW survey, Maryland, targeted about 5000 students with a 50% participation rate.[13-15] Therefore, we envisioned that Hawai'i would target 6000 children with a similar participation rate resulting in 3000 in the sample. Maui Island is 10% of the state's population. Assuming a 50% participation rate, we sent consent forms to approximately 600 children with the goal of reaching a final sample size of about 300 students.

Following the above guidelines 3rd graders were targeted as the study population. Schools were stratified by private or public status. Within each strata, schools were randomly selected (cluster design), with entire third grade classes for each school sampled (not sampling with a probability proportional to school size,)[11] with the intent of having the proportion of public to

private students of the sample reflect Maui's public to private student ratio. For public school students, parents were asked for their child's FRL status. However, after a parent complained, this question was eliminated during the early stages of student recruitment.

Instead, the FRL proportion of each school's third grade class was obtained for weighting of FRL status in the analysis stage.[11] In the analysis stage, for each participating student, a weighting score was introduced (in accordance with the FRL proportion for his/her school) so that the FRL proportion of the sample represented that of all (sampled and non-sampled) public school third graders. Thus the analysis weights for FRL status and adjusts for non-participation.

Data Analysis

Statistical analyses were conducted using Excel and Epi Info 7. Proportions and their confidence interval were calculated. For outcomes, point estimates of proportions and their 95% confidence interval (95% CI) are given. When these outcomes are compared to those of other States, only point estimates of Maui's public school children are used, similar to how the outcomes are reported by other selected states. States chosen for comparison all weighted their data for FRL status and most adjusted for participation.

Results

Administrative Issues

Some important issues arose and needed to be resolved prior to survey implementation. Parents were concerned about outside reporting of their FRL status. This issue of FRL confidentiality occurred when parents reviewed letters sent home for informed consent. Investigators decided to omit this item from data collection and substitute it with aggregate FRL data by school (third grade students). School officials worried that parents would question the study if only some of the children or only some of the classes within each selected school were selected at random. Thus study participation was offered to entire third grade classes of the randomly selected schools. School officials insisted on active enrollment (enrolling students only for affirmative responses from parents) to obtain parental agreement that participating children would not have procedures beyond those described in the study.

Target and Sample Populations

In 2012-13, the school year of the survey, Maui Island had a total of 11,610 third graders with 10,100 (87%) enrolled in 15 public schools and 1509 (13%) in 14 private ones. Of the public school third graders 63% use the FRL program. Seven public and two private schools were randomly chosen to meet the targeted sample size with 90% of students of this sample from public schools. Consent forms and questionnaires were sent home to 607 students in the sample of which 367 (47%) were returned. Of those returned, 281 (77%) consented to participate. Of those consenting, 90% were from public schools. All children with parental consent were enrolled and examined. Of this, 281 (combining the private school children and the FRL weighted values of the public school children), 58% and 39% were ages 8 and 9 respectively, 52% were males, 89% had parents report that the child had a dentist, and 51% reported fluoride use. Of the sample's 281 children 51% were using FRL (using each participating subject's third grade FRL proportion).

Survey Results and Comparison to Other States

The outcomes of the examinations were as follows:

- 29% had sealants
- 68% had treated decay
- 29% had untreated decay
- 78% had experienced one or more caries in their lifetime (treated, untreated, or both)
- 72% had no active dental problems (needed routine follow-up)
- 23% needed early care
- 4.7% needed urgent care

Table 1 is a comparison of Maui's outcomes from this study to other selected states with "A" and "B" grades from the PEW survey.[9] All met the survey criteria,[13-15] some based on surveys done a few years prior to the PEW survey of 2011. The urgency of a follow-up dental visit was not a standard question of the third grade dental surveys required by PEW, so this data is not uniformly reported by states. Maui's sample size (proportional to Hawai'i's population) and participation rates are similar to those for other states. Maui's untreated caries rate (29%) is comparable to rates of other states. However, the proportion of students who had ever experienced caries was substantially higher; therefore, it appears that in order to attain this level, a substantially greater amount of dental treatment was provided on Maui, about twice that of other states.

Table 1. 2011 PEW survey results Maui pilot survey and selected states (all fulfilling 3rd grade survey Criteria)

State (date survey)	Overall Grade*	N Examined	% Providing Consent	% Ever Experienced Caries	% With Untreated Caries	% With Sealants
Maui (2012-13)	F	281	46-77	78	29	29
Maryland (2001-2)	A	2482	50	42	26	24
Connecticut (2006-7)	A	8755	81	40	18	38
Rhode Island (2007-8)	A	2010	66	47	28	36
Arizona (2009-10)	B	3150	37	75	42	47
Colorado (2006-7)	B	3012	79	57	24	37
New Hampshire (2008-9)	B	3015	64	44	12	60

Discussion

A pilot study for Maui Island was done to assess the feasibility of conducting dental surveys in children statewide. The administrative and technical issues that arose were not surprising and the community partners were ready to respond, partly because media coverage of the PEW reports for Hawai'i pointed to a crisis in this area, the lack of surveillance being one of several unmet criteria. A standard survey design and format was chosen, executed, and analyzed. It is unlikely that expanding the survey statewide would encounter any insurmountable problems. A strength of this study is that it follows a standardized, recommended protocol for dental surveys that was developed and widely used by other States. There is nothing novel or experimental for investigators or parents to worry about, which should result in a high participation rate. A limitation of the study is that other districts of Hawai'i have much larger proportions of students in private schools, who may potentially be resistant to participating in these kinds of surveys (although Maui's private school participation did not differ significantly from that of the public schools). Important PEW criteria of sample size, representative sampling (private/public, counties, FRL enrollment), and participation rate were met. However, despite meeting the PEW criteria for an adequate participation rate, the 50% participation rate is still low and could introduce sampling bias in the results. In this study no attempt was made to assess this bias by pursuing the non-participants for evaluation. Future studies should attempt this while still respecting the privacy of those choosing to not participate. The DOE required affirmation by written informed consent to participate. Many consent forms were not returned and the reasons for this needs to be further investigated, although this problem occurred with other states judged by PEW to have met the survey criteria.

We also explored how outcomes for Maui compared to other states with very good grades. States with very bad grades had poor or no surveys done, so no comparison could be made. Four of the six states that met the survey criteria and received A or B PEW grades had roughly the same proportion of students with unfilled dental caries (Table 1). What is striking is that five of these six states had much lower proportions of children who had filled caries. One could interpret this observation to mean that to achieve the same level of unfilled caries as other well performing states Maui has to perform many more treatments (fillings). One initiative that may have positively contributed to this outcome may be Maui's initiative since the 2001 Surgeon General's report describing the dental care crisis, which focused on increasing access to dentists among Medicaid eligible children.

The authors recommend that the comparisons across communities presented in Table 1 be interpreted cautiously, as it is possible that the PEW preventive measures enacted at one point in time may have a measurable impact years later due to a lag effect. Moreover, such comparisons suffer from ecological biases: if a community were in a steady state then any survey would reflect a constant set of PEW interventions. However, if a state is undergoing changes, perhaps stimulated by Dr. Satcher's declaration in 2001, then a point in time survey of outcomes may represent the impact of prevention programs that existed years earlier — or analogously, a point in time PEW survey of interventions may manifest outcomes in a survey years later. Along these lines, New Hampshire conducted surveys in 2004 and 2008, and observed a rise in sealants and a reduction in untreated decay as well as urgent dental care needs.[16,17] This data potentially demonstrates the positive impact of efforts by New Hampshire to implement PEW's recommended preventive measures in 2004 (which earned them a good overall grade in 2009). If Maui, or the State of Hawai'i as a whole, does not enact similar preventive measures (beyond the recommended survey) our outcomes may never improve.

In conclusion, a standardized protocol for a dental survey among children has been conducted quite easily in Maui County. Beyond the mechanics of the study, community participation was comparable to that of other states. Hopefully the lessons learned in this pilot study will be applicable to expand the survey statewide. This survey is but one of eight interventions recommended by the PEW to improve the oral health of children. Hawai'i has to address the other interventions to show some improvement in our newly acquired survey. Hawai'i should repeat on a wider scale this type of standardized survey carried out on Maui. Based on other states' survey programs and the changes that they see in survey results, conducting surveys every 4-5 years should suffice.

Conflict of Interest

None of the authors identify any conflict of interest.

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Comparing Obesity-Related Health Disparities among Native Hawaiians/Pacific Islanders, Asians, and Whites in California: Reinforcing the Need for Data Disaggregation and Operationalization

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Abstract

Since the 2000 Census, Asians and Pacific Islanders have been categorized as separate races. Government initiatives have called for greater study of Asian, Native Hawaiian, and other Pacific Islander (NHPI) health outcomes. NHPI often have worse health outcomes than Asians and Whites. Despite this, the lack of operationalization of racial definitions may affect the magnitude of health disparities. This analysis examined how utilizing different sociological race definitions could influence NHPI health outcomes when compared to Asians and Whites. Utilizing data from the 2009 California Health Interview Survey, NHPI had significantly higher age adjusted obesity prevalence than Whites under the UCLA Center for Health Policy Research (CHPR) (OR = 1.72, P = *.03) and Self-Report (OR = 1.57,* P = *.01) definitions, but not the Census definition (OR = 1.42,* P = *.11). NHPI had significantly higher age adjusted obesity prevalence than Asians under all definitions (Census OR = 4.05,* P < *.01; CHPR OR = 4.81,* P < *.01; Self-Report OR = 4.46,* P < *.01). NHPI had significantly higher age adjusted diabetes/pre-diabetes prevalence than Whites across all definitions (Census OR = 3.27,* P < *.01, CHPR OR = 3.03,* P < *.01, Self-Report OR = 1.99,* P = *.01) but only the Census (OR = 2.12,* P = *.01) and CHPR (OR = 1.86,* P = *.04) when NHPI were compared to Asians. Overall, race definition changed the identification of health disparities. Future studies should operationalize racial definitions, as health disparities are masked post-hoc when utilizing different race definitions.*

Keywords

data disaggregation, Native Hawaiians and Pacific Islanders, Asians and Asian Americans, health disparities, chronic disease, race, ethnicity

Introduction

The crisis surrounding the increasing incidence of obesity in the United States has called for greater efforts to understand the factors attributable to this morbidity and exploration of its disproportionate presence among different ethnic and racial populations.[1] The 2010 National Health Interview Survey (NHIS) found that 34% of Americans were overweight, while another 28% of Americans were obese. The NHIS also found that obesity prevalence among non-Hispanic black adults and Hispanic adults were 37% and 32%, respectively. Obesity prevalence among White adults was 26%, while only 11% of surveyed Asians were classified as obese. Native Hawaiians and Pacific Islanders (NHPI), the smallest reported group, reported 42% of participants as obese.[2] They were classified by sex, age, race and Hispanic origin, education, current employment status, family income, poverty status, health insurance coverage, marital status, and place and region of residence. Obesity has been attributed to poor nutrition and lifestyle and is associated with development of heart disease, diabetes, and cancer. Numerous studies have emphasized disparities of obesity and obesity-related comorbidities such as type II diabetes,[3–7] hypertension,[8,9] and heart disease[6,8] among different ethnic and racial groups.

There is a growing need to understand NHPI health disparities. Over 1.2 million NHPI currently reside in the United States, and this population has increased by 40% since 2000, second to the growth of Asians (45.6%).[10,11] With the exception of research conducted in Hawai'i, NHPI have traditionally been grouped with Asians as "Asian and Pacific Islander" according to US Census definitions. This grouping has masked the health disparities and morbidities experienced by NHPI.[12] Disaggregation of NHPI from Asians since the 2000 Census has revealed the ethnic and health heterogeneity.[13]

The 2012 Pacific Islander Health Study, a health survey of a stratified random sample of Samoan and Tongan households in faith-based organizations in Los Angeles and San Mateo counties, found that more than 95% of NHPI were above normal BMI ranges and 90% of participants were classified as overweight or obese.[14] Nationally, about 57% of NHPI were physically inactive compared to 44.1% of Non-Hispanic Whites. NHPI were 30% more likely to be diagnosed with cancer than Non-Hispanic Whites. NHPI experience greater obesity and obesity-related health disparities compared to other races.[2] The change in Census race definition moved the agenda forward for Asian and NHPI health disparities research.[13,15] Studies since the definition change have revealed that NHPI experience disparities in obesity,[16,17] cardiovascular disease,[6] type II diabetes,[3,7] physical activity,[18] and dietary behaviors.[19]

Despite the inclusion of "Native Hawaiian and Pacific Islander" as a race category by the Census, federal initiatives have called for continued disaggregation of data among Asian Americans and NHPI to better understand the hidden health, economic, and educational disparities within this community.[20] Newly defined racial and ethnic categories address the multifaceted nature of race. Specifically, the University of California Los Angeles Center for Health Policy Research (UCLA CHPR) utilized multiple race definitions (US Census, UCLA CHPR, and Self-Identification) through their biannual health survey.[21] Though each definition is based off self-identification, the Census classifies multiracial individuals as "More than one race,"[22] severely undercounting smaller racial populations by grouping them into a heterogeneous category; this in turn poses methodological difficulties in health disparities research.[23,24] The UCLA CHPR definition asks multiracial persons to choose the race they most identify with, broadening race as a self-determined

attribute.[22] This definition is especially useful for the NHPI population; 56% of NHPI reported more than one race in the 2010 Census.[25] Few analyses examine the multiracial nature of the NHPI population.

Hardy notes that sociological race definitions are often "complex and poorly defined…[which] obscures attempts to identify and address health disparities"(p. 46).[24] It is important to operationalize race, especially for multiracial individuals. Geneticists emphasize a biological/phenotypic definition of race and advocate including genetics in health disparities research.[26,27] While genetic race definitions may elucidate the molecular and physiological factors behind disease, opponents claim that such definitions promote further stigmatization of people of color, eugenics, and may be irrelevant in describing health disparities.[28–31]

Despite the disagreements between the usefulness of socially constructed and genetic definitions of race, it is clear that the definition of race needs to be operationalized. Data disaggregation attempts to understand the multifaceted nature of racial identities, but more research is needed in understanding the relationship between race identification and health outcomes. This study (1) examines differences in obesity-related health outcomes and behavioral correlates among Whites, Asians, and Pacific Islanders utilizing the US Census, UCLA CHPR, and Self-Report definitions of race, (2) examines pairwise health disparities of NHPI compared to Whites and Asians, and (3) seeks to identify concordance in significant pairwise differences between different race definitions.

Methods

Study Design

Data were taken from the UCLA CHPR's 2009 California Health Interview Survey (CHIS). The CHIS is a biannual random digit dialing survey conducted by UCLA CHPR. The CHIS collects data on health status, health conditions, health-related behaviors, health insurance coverage, healthcare access, and health related issues. Surveys were conducted in English, Spanish, Chinese, Korean, Tagalog, and Vietnamese through a computer-assisted telephone interview system. Though the CHIS interviewed both children and adults, adult interviews were examined in this analysis. CHIS data are publicly available and provide statewide and countywide estimates for health in California. The 2009 CHIS received 47,614 total adult responses with response rates of 49.0% and 56.2% for landline and cellphone interviews respectively.[32,33]

Race Definitions

The 2009 CHIS provided two race definitions: the US Census 2000 and UCLA Center for Health Policy Research (CHPR). The Census 2000 race definition was comprised of a combination of six self-reported race questions (Pacific Islander, American Indian/Alaska Native, Asian, African American, White, or Other). Participants selected any race or races they self-identify with. Selection of multiple races will classify multi-racial individuals as "More than one race" under the US Census 2000 race definition.[34] The UCLA CHPR definition utilized the same six self-reported race questions. However, race was determined by asking additional questions as to the race the participants most identified with thereby accounting for the heterogeneity of multi-racial individuals. Participants who do not specifically identify as one race were classified as "More than one race" under the UCLA CHPR definition.[34] The Self-Report race definition was investigator-derived by combining and recoding the CHIS 2009 self-reported race variables. Participants who self-identified as NHPI, regardless of other reported races, were recoded from the sample first. After identifying any self-reported NHPI, self-reported Whites (who were not also NHPI) were recoded, followed by self-reported Asians (who were not also NHPI or White). Recoding was done to maximize the number of self-reported NHPI for analysis.

Responses for each race definition were subcategorized into NHPI, White, or Asian. Sample sizes for groups varied by each definition of race for NHPI, Whites, and Asians. Those who did not identify as NHPI, White, or Asian (eg, identified as Native American/Alaska Native, Hispanic, African American, or Other) by each race definition were excluded from analysis.

Outcome Variables

Participants were examined for the following disease-related variables: classification as overweight or obese based on body mass index (BMI), self-reported diabetes diagnosis (including borderline and pre-diabetes), self-reported high blood pressure or hypertension diagnosis, and self-reported heart disease diagnosis. Participants' physical activity levels and consumption of fruits, vegetables, fast food, and soda were also examined. Adherence to physical activity guidelines was measured dichotomously by identifying if participants did at least 30 minutes of moderate physical activity (MPA) per day for at least five days a week. Adherence to vigorous activity (VPA) guidelines were measured dichotomously by identifying if participants did at least 20 minutes of VPA for at least three days a week.[34] Fruits, vegetables, and soda consumption were asked on a monthly recall basis (eg, "During the past month, how often did you drink regular soda or pop that contains sugar? Do not include diet soda). Fast food consumption was asked on a weekly recall.[35] Dietary behaviors (fruits, vegetables, fast food, and soda) were continuous variables.

Statistical Analysis

Data were analyzed through Statistical Analysis Software (SAS) Version 9.4 (SAS Institute Inc, Cary, NC) to identify significant disparities between each race group. Three conditions were examined: (1) comparison of differences among all three racial groups, (2) comparison of NHPI to Whites only, and (3) comparison of NHPI to Asians only. Participants classified as overweight or obese were clustered within each ethnic group to account for a more comprehensive prevalence calculation. These measures intended to account for potential onset of disease. Participants having pre-diabetes or diabetes and hypertension or high blood pressure were also grouped in order to provide

a more comprehensive prevalence between each ethnic group. Chi-square tests examined significant differences in overweight/obese classification, pre-diabetes/diabetes, hypertension/high blood pressure, heart disease prevalence, and physical activity adherence by racial definition. Significant associations were analyzed post-hoc using logistic regressions, controlling for age. The results of separate analyses are included to examine age adjusted odds ratios between different sexes. Each post-hoc analysis sought to identify if there were differences between NHPI to Whites and NHPI to Asians. Differences in dietary behaviors between races per definition were initially analyzed using one-way ANOVA. Significant associations in dietary behaviors were analyzed post-hoc using the Bonferroni t-test while controlling for age. Additional analyses are included to examine dietary behaviors by sex between NHPI to Whites and NHPI to Asians.

Results

Sample sizes of NHPI, Whites, and Asians differed with each race definition. The Census 2000 sample included 39,204 participants, with 0.23% identified as NHPI (n = 90), 87.25% identified as White (n = 34,205), and 12.52% identified as Asian (n = 4,909). The UCLA CHPR sample included 36,718 participants, with 0.20% identified as NHPI (n = 75), 86.52% identified as White (n = 31,769), and 13.27% identified as Asian (n = 4,874). The Self-Report sample included 40,251 participants, 0.38% identifying as NHPI (including multi-racial NHPI) (n = 153), 87.34% identifying as White-only (n = 35,157), and 12.28% identifying as Asian-only (n = 4,941) (Table 1).

Overweight and Obesity Prevalence

NHPI had significantly higher overweight/obesity (BMI ≥ 25.0)[36] age adjusted prevalence than Whites under the UCLA CHPR (OR = 1.72, $P = .03$) (Table 2) and Self-Report (OR = 1.57, $P = .01$) (Table 3). Only NHPI women were significantly more overweight/obese when compared to White women under each race definition: UCLA CHPR (OR = 2.16, $P = .01$), Self-Report (OR = 2.13, $P < .01$), Census (OR = 2.01, $P = .01$).

Overweight/obesity prevalence was significantly higher among NHPI than Asians under all race definitions after age adjustment: UCLA CHPR (OR = 4.81, $P < .01$), Self-Report (OR = 4.46, P < .01), Census (OR = 4.05, $P < .01$). After stratifying by sex, both NHPI men and women had significantly higher overweight/obesity prevalence compared to Asian men and women (Tables 2-4).

Pre-Diabetes and Diabetes Prevalence

Age adjusted analyses revealed that NHPI had significantly higher odds of diabetes/pre-diabetes than Whites for each race definition: UCLA CHPR (OR = 3.03, $P < .01$), Self-Report (OR = 1.99, $P < .01$), Census (OR = 3.27, $P < .01$) (Tables 2-4). After stratifying by sex, only NHPI women had significantly higher odds of diabetes/pre-diabetes than Whites for each definition: UCLA CHPR (OR = 4.17, $P < .01$), Self-Report (OR = 2.87, $P < .01$), Census (OR = 4.17, $P < .01$).

NHPI had significantly higher age adjusted diabetes/pre-diabetes prevalence than Asians under the UCLA CHPR Definition (OR = 1.86, $P = .04$) (Table 2) and Census Definition (OR = 2.12, $P = .01$) (Table 4). After stratification by sex, NHPI women continued to have signifanctly higher diabetes/pre-diabetes prevalence than Asian women under the UCLA CHPR Definition (OR = 2.58 $P = .01$) and Census Definition (OR = 2.75, $P < .01$). Self-Reported NHPI women also had significantly higher diabetes/pre-diabetes prevalence than Asian women (OR = 1.92, $P = .03$) (Table 3).

Hypertension, High Blood Pressure, and Heart Disease Prevalence

Age and sex adjustment attenuated initial differences in hypertension/high blood pressure prevalence between NHPI, Whites, and Asians. Heart disease prevalence experienced similar results; NHPI had significantly lower heart disease prevalence (5.9%) than Whites (11.5%) ($P = .03$) (Table 1). However, age and sex adjustment attenuated these effects.

Physical Activity

NHPI had significantly higher age adjusted MPA than Whites across Self-Report definition (OR = 1.78, $P < .01$) (Table 3). After stratifying by sex, Male NHPI had significantly higher MPA than White males across Self-Report (OR = 2.36, $P < .01$) and Census (OR = 2.64, $P = .01$) definitions (Table 3 and 4).

NHPI had significantly greater MPA than Asians under Self-Report (OR = 2.02, $P < .01$) and Census definitions (OR = 1.81, $P = .04$) and after controlling for age (Table 3 and 4). NHPI males had significantly greater MPA than Asian males under Self-report (OR = 2.48, $P < .01$) and Census definitions (OR = 2.75, $P = .01$). NHPI also had significantly higher age adjusted VPA than Asians across all definitions. When stratified by sex, NHPI men had significantly higher VPA than Asian men across all race definitions (Tables 2-4). VPA was significantly higher among NHPI women than Asian women under the Census definition VPA (OR = 2.31, $P = .02$) Census definition (Table 4).

Dietary Intake

NHPI fruit consumption was not significantly different from Whites or Asians across each race definition (Table 5). However, NHPI consumed significantly less vegetables than Whites when using the Census ($P = .01$) and Self-Report definitions ($P < .01$). NHPI and Asians did not differ in vegetable consumption. NHPI also consumed more fast food than Whites and Asians across each race definition ($P < .05$). Soda consumption was significantly higher among NHPI than Asians under all race definitions ($P < .05$); no differences were seen between NHPI and Whites.

Table 1. General Demographics, Chronic Disease Prevalence, and Consumption Behavior by Race Definition

	Census 2000				UCLA CHPR				Self-Report			
	NHPI (n=90)	White (n=34,205)	Asian (n=4,909)	*P* -Value[b]	NHPI (n=75)	White (n=31,769)	Asian (n=4,874)	*P* -Value[b]	NHPI (n=153)	White (n=35,157)	Asian (n=4,941)	*P* -Value[b]
Sex (%)												
Female	55 (66.1)	20,391 (59.6)	2,766 (56.3)	< .01 .77 .36	50 (66.7)	18,811 (59.2)	2,739 (56.2)	< .01 .19 .07	90 (58.8)	20,960 (59.6)	2,789 (56.4)	< .01 .84 .56
Male	35 (38.9)	13,814 (40.3)	2,143 (43.7)		25 (33.3)	12,958 (40.8)	2,135 (43.8)		63 (41.2)	14,197 (40.4)	2,152 (43.5)	
Age[a]	45.8 (17.2)	58.3 (16.7)	50.5 (16.7)	< .01 < .01 .02	49.8 (16.0)	59.2 (16.3)	50.6 (16.7)	< .01 < .01 1.0	44.6 (17.0)	58.2 (16.7)	50.4 (16.7)	< .01 < .01 < .01
Chronic Disease (%)												
Overweight or Obese	58 (64.4)	19,368 (56.6)	1,526 (31.3)	< .0 .14 < .01	51 (68.0)	17,721 (55.8)	1,497 (30.7)	< .01 .04 < .01	102 (66.7)	19,951 (56.8)	1,542 (31.2)	< .01 .01 < .01
Diabetic or Pre-diabetic	17 (18.9)	3,649 (10.7)	585 (11.9)	< .01 .01 .05	14 (18.7)	3,308 (10.4)	574 (11.8)	< .01 .02 .07	19 (12.4)	3,777 (10.7)	588 (11.9)	.04 .50 .85
High Blood Pressure or Borderline Hypertension	30 (33.3)	13,594 (39.7)	1,546 (31.5)	< .01 .22 .71	26 (34.7)	12,860 (40.5)	1,534 (31.5)	< .01 .31 .55	47 (30.7)	13,952 (39.7)	1,553 (31.4)	< .01 .02 .85
Heart Disease	6 (6.7)	3,917 (11.5)	302 (6.2)	< .01 .16 .84	6 (8.0)	3,794 (11.9)	300 (6.2)	< .01 .29 .51	9 (5.9)	4,035 (11.5)	304 (6.2)	< .01 .03 .89
Physical Activity (%)												
MPA	14 (15.6)	3,577 (10.5)	457 (9.3)	.01 .11 .05	11 (14.7)	3,382 (10.7)	458 (9.4)	.02 .01 .12	26 (17.0)	3,691 (10.5)	459 (9.3)	< .01 .01 < .01
VPA	23 (25.6)	4,778 (14.0)	565 (11.5)	< .01 < .01 < .01	16 (21.3)	4,452 (14.0)	550 (11.3)	< .01 .07 .01	32 (20.9)	4,914 (14.0)	572 (11.6)	< .01 .01 < .01
Food Consumption[a]												
Fruits	7.5 (6.8)	8.3 (7.0)	7.9 (6.4)	< .01 .31 .56	7.1 (6.8)	8.3 (6.9)	8.0 (6.4)	< .01 .16 .28	7.9 (6.9)	8.3 (7.0)	7.9 (6.4)	< .01 .56 .98
Vegetables	6.4 (5.4)	8.1 (6.0)	7.5 (5.3)	.01 .06	7.1 (5.6)	8.3 (6.0)	7.5 (5.3)	< .01 .09 .56	6.6 (5.6)	8.1 (6.0)	7.5 (5.3)	< .01 < .01 .06
Fast Food	1.7 (1.9)	1.0 (1.7)	.98 (1.5)	< .01 < .01	1.5 (2.0)	1.0 (1.6)	.96 (1.5)	< .01 .02 .01	1.6 (1.8)	1.0 (1.7)	.97 (1.5)	< .01 < .01 < .01
Soda	1.8 (4.1)	1.1 (3.4)	.9 (2.6)	.10 .03	1.6 (4.2)	1.1 (3.4)	.83 (2.6)	< .01 .19 .08	2.1 (5.0)	1.1 (3.5)	.87 (2.7)	< .01 .02 < .01

Note: NHPI = Native Hawaiian and Pacific Islander; UCLA CHPR = University of California, Los Angeles Center for Health Policy Research. MPA = Moderate Physical Activity, indicates percentage of participants who did at least 30 minutes of moderate physical activity for at least 5 days per week. VPA = Vigorous Physical Activity, indicates percentage of participants who did at least 20 minutes of vigorous physical activity, at least 3 times per week. All values are based on self-report data from the 2009 California Health Interview Survey (CHIS). Census 2000, UCLA CHPR, and Self-Report Race Definitions were determined using participants' responses to questions involving race.
[a]Indicates mean and standard deviation; [b]*P*-values indicate overall *P*-value, *P*-value between NHPI and Whites, *P*-value between NHPI and Asian

Table 2. Age Adjusted Odds Ratio for NHPI compared to Whites and Asians for UCLA CHPR Definition of Race

	Adjusted Odds Ratio (95% Confidence Interval)								
	Total (N = 36,718)			Male (n = 15,118)			Female (n = 21,600)		
	NHPI to White	NHPI to Asian	*P* -Value[a]	NHPI to White	NHPI to Asian	*P* -Value[a]	NHPI to White	NHPI to Asian	*P* -Value[a]
Chronic Disease (%)									
Overweight or Obese	1.72 (1.06, 2.80)	4.81 (2.94, 7.81)	.03 < .01	1.32 (.55, 3.16)	3.88 (1.61, 9.34)	.54 < .01	2.16 (1.20, 3.89)	6.33 (3.50, 11.36)	.01 < .01
Diabetic or Pre-diabetic	3.03 (1.66, 5.52)	1.86 (1.01, 3.41)	< .01 .04	1.70 (.50, 5.81)	1.06 (.31, 3.54)	.40 .93	4.17 (2.08, 8.33)	2.58 (1.28, 5.21)	< .01 .01
High Blood Pressure or Borderline Hypertension	1.28 (.77, 2.15)	1.25 (.75, 2.14)	.34 .39	1.59 (.69, 3.68)	1.57 (.68, 3.65)	.28 .29	1.17 (.60, 2.25)	1.13 (.58, 2.19)	.65 .72
Heart Disease	1.15 (.48, 2.76)	1.49 (.61, 3.60)	.76 .38	1.26 (.28, 5.59)	1.85 (.41, 8.26)	.76 .42	1.24 (.42, 3.64)	1.48 (.50, 4.39)	.69 .48
Physical Activity (%)									
MPA	1.46 (.77, 2.77)	1.66 (.87, 3.17)	.25 .12	2.39 (.95, 5.99)	2.49 (.99, 6.32)	.06 .05	1.04 (.41, 2.61)	1.28 (.50, 3.27)	.94 .60
VPA	1.34 (.76, 2.34)	2.14 (1.21, 3.76)	.31 .01	1.72 (.74, 4.05)	2.52 (1.07, 5.95)	.20 .03	1.19 (.55, 2.56)	2.18 (1.00, 4.74)	.66 .05

Note: NHPI = Native Hawaiian and Pacific Islander; UCLA CHPR = University of California, Los Angeles Center for Health Policy Research. MPA = Moderate Physical Activity, indicates percentage of participants who did at least 30 minutes of moderate physical activity for at least 5 days per week. VPA = Vigorous Physical Activity, indicates percentage of participants who did at least 20 minutes of vigorous physical activity, at least 3 times per week. All values are based on self-report data from the 2009 California Health Interview Survey (CHIS). UCLA CHPR Race Definitions were determined using participants' responses to questions involving race.
[a]Indicates *P*-value comparing NHPI to White and NHPI to Asian

Table 3. Age Adjusted Odds Ratio for NHPI compared to Whites and Asians for Self-Report Definition of Race

	Adjusted Odds Ratio (95% Confidence Interval)								
	Total (N = 40,251)			Male (n = 16,412)			Female (n = 23,839)		
	NHPI to White	NHPI to Asian	*P* -Value[a]	NHPI to White	NHPI to Asian	*P* -Value[a]	NHPI to White	NHPI to Asian	*P* -Value[a]
Chronic Disease (%)									
Overweight or Obese	1.57 (1.12, 2.20)	4.46 (3.17, 6.29)	.01 < .01	1.01 (.60, 1.71)	2.99 (1.76, 5.08)	.97 < .01	2.13 (1.37, 3.31)	6.41 (4.46, 10.00)	< .01 < .01
Diabetic or Pre-diabetic	1.99 (1.21, 3.27)	1.31 (.79, 2.16)	.01 .29	1.07 (.42, 2.74)	.71 (.28, 1.83)	.88 .48	2.87 (1.59, 5.18)	1.92 (1.05, 3.48)	< .01 .03
High Blood Pressure or Borderline Hypertension	1.33 (.92, 1.94)	1.32 (.90, 1.93)	.13 .15	1.16 (.65, 2.05)	1.17 (.65, 2.09)	.62 .59	1.49 (.91, 2.44)	1.46 (.88, 2.40)	.11 .14
Heart Disease	1.04 (.51, 2.10)	1.34 (.65, 2.74)	.92 .42	1.03 (.35, 3.01)	1.51 (.51, 4.44)	.95 .46	1.08 (.42, 2.76)	1.30 (.50, 3.37)	.88 .60
Physical Activity (%)									
MPA	1.78 (1.17, 2.72)	2.02 (1.31, 2.13)	< .01 < .01	2.36 (1.32, 4.24)	2.48 (1.37, 4.48)	< .01 < .01	1.36 (.72, 2.55)	1.67 (.87, 3.19)	.35 .12
VPA	1.19 (.80, 1.77)	1.78 (1.19, 2.67)	.39 .01	1.44 (.83, 2.49)	2.02 (1.16, 3.55)	.19 .01	.98 (.54, 1.78)	1.63 (.89, 3.00)	.95 .11

Note: NHPI = Native Hawaiian and Pacific Islander. MPA = Moderate Physical Activity, indicates percentage of participants who did at least 30 minutes of moderate physical activity for at least 5 days per week. VPA = Vigorous Physical Activity, indicates percentage of participants who did at least 20 minutes of vigorous physical activity, at least 3 times per week. All values are based on self-report data from the 2009 California Health Interview Survey (CHIS). Self-Report Race Definitions were determined using participants' responses to questions involving race.
[a]Indicates P-value comparing NHPI to White and NHPI to Asian

Table 4. Age Adjusted Odds Ratio for NHPI compared to Whites and Asians for Census Definition of Race									
	Adjusted Odds Ratio (95% Confidence Interval)								
	Total (N = 39,204)			Male (n = 15,992)			Female (n = 23,212)		
	NHPI to White	NHPI to Asian	*P* -Value[a]	NHPI to White	NHPI to Asian	*P* -Value[a]	NHPI to White	NHPI to Asian	*P* -Value[a]
Chronic Disease (%)									
Overweight or Obese	1.42 (.92, 2.19)	4.05 (2.62, 6.25)	.11 < .01	.85 (.43, 1.69)	2.54 (1.27, 5.05)	.64 .01	2.01 (1.15, 3.51)	6.02 (3.44, 10.64)	.01 < .01
Diabetic or Pre-diabetic	3.27 (1.89, 5.65)	2.12 (1.22, 3.69)	< .01 .01	2.31 (.87, 6.17)	1.51 (.56, 4.05)	.09 .41	4.17 (2.15, 8.06)	2.75 (1.40, 5.38)	< .01 < .01
High Blood Pressure or Borderline Hypertension	1.45 (.90, 2.34)	1.42 (.88, 2.30)	.13 .15	1.31 (.61, 2.80)	1.31 (.61, 2.82)	.48 .49	1.56 (.84, 2.89)	1.52 (.81, 2.82)	.16 .19
Heart Disease	1.15 (.48, 2.73)	1.46 (.61, 3.51)	.76 .39	1.05 (.23, 4.61)	1.52 (.34, 6.71)	.95 .58	1.32 (.45, 3.83)	1.56 (.53, 4.59)	.42 .61
Physical Activity (%)									
MPA	1.62 (.91, 2.87)	1.81 (1.01, 3.24)	.10 .04	2.64 (1.23, 5.65)	2.75 (1.28, 5.95)	.01 .01	.97 (.39, 2.43)	1.18 (.47, 3.00)	.95 .72
VPA	1.59 (.98, 2.58)	2.40 (1.47, 3.92)	.06 < .01	1.95 (.97, 3.92)	2.75 (1.36, 5.59)	.06 .01	1.37 (.68, 2.75)	2.31 (1.14, 4.67)	.38 .02

Note. Note: NHPI = Native Hawaiian and Pacific Islander. All values are based on self-report data from the 2009 California Health Interview Survey (CHIS). MPA = Moderate Physical Activity, indicates percentage of participants who did at least 30 minutes of moderate physical activity for at least 5 days per week. VPA = Vigorous Physical Activity, indicates percentage of participants who did at least 20 minutes of vigorous physical activity, at least 3 times per week. Census 2000 Race Definitions were determined using participants' responses to questions involving race.

[a]Indicates *P*-value comparing NHPI to White and NHPI to Asian

Table 5. Age Adjusted Consumption Behaviors by Racial Definition									
	Adjusted Mean Proportion (95% Confidence Interval)								
	Census 2000			UCLA CHPR			Self-Report		
	NHPI (n=90)	White (n=34,205)	Asian (n=4,909)	NHPI (n=75)	White (n=31,769)	Asian (n=4,874)	NHPI (n=153)	White (n=35,157)	Asian (n=4,941)
Fruits per month	7.90 (6.47, 9.33)	8.26 (8.18, 8.33)	8.16 (7.96, 8.35)	7.43 (5.87, 8.99)	8.25 (8.17, 8.32)	8.21 (8.01, 8.41)	8.34 (7.24, 9.44)	8.24 (8.17, 8.31)	8.14 (7.95, 8.34)
Vegetables per month	6.53 (5.31, 7.75)	8.09 (8.03, 8.15)	7.53 (7.36, 7.70)	7.13 (5.80, 8.45)	8.28 (8.21, 8.35)	7.50 (7.33, 7.66)	6.75 (5.81, 7.69)	8.09 (8.02, 8.15)	7.53 (7.36, 7.69)
Fast food per week	1.45 (1.11, 1.78)	1.04 (1.02, 1.06)	0.83 (0.79, 0.88)	1.39 (1.02, 1.75)	1.02 (1.00, 1.04)	0.82 (0.77, 0.86)	1.38 (1.13, 1.63)	1.05 (1.03, 1.07)	0.83 (0.79, 0.88)
Soda per month	1.45 (0.77, 2.13)	1.16 (1.12, 1.19)	0.62 (0.53, 0.71)	1.43 (0.69, 2.17)	1.09 (1.06, 1.13)	0.59 (0.50, 0.69)	1.65 (1.12, 2.18)	1.17 (1.14, 1.21)	0.63 (0.54, 0.73)

Note. UCLA CHPR = University of California, Los Angeles Center of Health Policy Research. NHPI = Native Hawaiian and Pacific Islander. All values are based on self-report data from the 2009 California Health Interview Survey (CHIS). Census 2000, UCLA CHPR, and Self-Report Race Definitions were determined using participants' responses to questions involving race.

Figure 1. Summary of Chronic Disease and Health Behavior Concordance of Pacific Islanders by Racial Definition			
Indicator	**Census 2000**	**UCLA CHPR**	**Self-Report**
Overweight/Obesity	NHPI = White NHPI > Asian	NHPI > White NHPI > Asian	NHPI > White NHPI > Asian
Diabetic/Pre-diabetic	NHPI > White NHPI > Asian	NHPI > White NHPI > Asian	NHPI > White NHPI = Asian
Hypertension	NHPI = White NHPI = Asian	NHPI = White NHPI = Asian	NHPI = White NHPI = Asian
Heart Disease	NHPI = White NHPI = Asian	NHPI = White NHPI = Asian	NHPI = White NHPI = Asian
MPA	NHPI = White NHPI > Asian	NHPI = White NHPI = Asian	NHPI > White NHPI > Asian
VPA	NHPI = White NHPI > Asian	NHPI = White NHPI > Asian	NHPI = White NHPI > Asian
Fruits per month	NHPI = White NHPI = Asian	NHPI = White NHPI = Asian	NHPI = White NHPI = Asian
Vegetables per month	NHPI < White NHPI = Asian	NHPI = White NHPI = Asian	NHPI < White NHPI = Asian
Fast food per week	NHPI > White NHPI > Asian	NHPI > White NHPI > Asian	NHPI > White NHPI > Asian
Soda per month	NHPI = White NHPI > Asian	NHPI = White NHPI > Asian	NHPI = White NHPI > Asian

Note. UCLA CHPR – UCLA Center for Health Policy Research. NHPI – Native Hawaiian and Pacific Islander. MPA = Moderate Physical Activity, indicates percentage of participants who did at least 30 minutes of moderate physical activity for at least 5 days per week. VPA = Vigorous Physical Activity, indicates percentage of participants who did at least 20 minutes of vigorous physical activity, at least 3 times per week. Concordance is based on identification of obtaining the same statistically significant/insignificant result with a cutoff significance value of $P = .05$ for Native Hawaiians and Pacific Islanders compared to Whites and Asians after adjusting for age.

Discussion

This analysis examined how different definitions of race could influence health disparity outcomes for NHPI when compared to Asians and Whites. Results indicate that race definition did change the types of health disparities that were presented in each analysis (Figure 1). The high overweight/obesity prevalence among NHPI were consistent with nationally representative data and previous studies.[2,3,4,17] NHPI were more likely to be overweight or obese than Whites and Asians. Diabetes prevalence was also comparable to previous studies.[3,7] NHPI had a higher prevalence of diabetes than Whites and Asians. Heart disease and hypertension prevalence was also similar to previous studies.[6] NHPI appeared to engage in greater MPA and VPA than Whites and Asians. This was unexpected, given the high rates of obesity among NHPI. However, measuring obesity through BMI has limitations. BMI may be the standard proxy measure of adiposity, but it does not distinguish between muscle mass and adipose tissue.[37] Future studies of adiposity among NHPI should consider using different adiposity measures to best determine the severity of obesity in this population. NHPI appeared to consume significantly fewer vegetables and significantly more fast food and soda when compared to Whites and Asians.

Strengths of this study include the operationalization of race definitions to account for the multiracial composition of the NHPI population. The lack of concordance in identifying health disparities between different race definitions reveals the importance of standardizing race definitions (Figure 1). The UCLA CHPR race definition provides a subjective view of race by asking participants to identify the race they best identify with. While the Census race definition has been traditionally used, the aggregation of multiracial people diminishes its usefulness in health disparities research. However, the three race definitions in this study are ultimately subjective. The increasing research of health disparities genetics will elucidate the molecular and physiological basis behind health disparities and allow for a somewhat more objective definition. However, the controversy surrounding the social implications of genetic definitions is still hotly debated.[28–31]

Study limitations include the small sample size of NHPI relative to Whites and Asians. The small NHPI sample size may contribute to the large disparity seen between NHPI relative to each racial group. Often an "invisible minority" by researchers, underrepresentation of NHPI in research is a major concern for a population that experiences significant health disparities when compared to Whites and Asians.[13,15] Public health has acknowledged the lack of data regarding NHPI and current national initiatives are underway to understand the diverse NHPI population.[38] The availability of nationally representative data through the National Center of Health Statistics will only continue to uncover the story surrounding NHPI health in the United States.

The lack of analyses considering socioeconomic status and access to healthcare serves as another limitation to this study. The data and analyses acknowledge that there are disparities in chronic disease between NHPI to Whites and Asians. However, these disparities may be due to the socioeconomic and healthcare environment available.

The results of this study ultimately highlight the need for continued data disaggregation of NHPI and the importance of operationalizing racial definitions in health disparities research. Data disaggregation has led to more research surrounding the NHPI community, but it is important to acknowledge the multiethnic nature of the NHPI community. Smaller NHPI ethnic groups, such as the Chuukese and Ni-Vanauatu, have experienced significant growth since the 2000 Census.[10] Though these NHPI ethnic groups are smaller compared to Native Hawaiians, Samoans, Chamorros, Tongans, and Fijians, their rapid growth will contribute to the growing NHPI health narrative. Future studies should focus on both the multiracial and multiethnic composition of the NHPI population and continue to address these chronic health disparities within the NHPI community. Community-based participatory research provides an avenue to examine the correlates of these chronic health disparities among NHPI and should be employed as a mainstay for future interventions.[39] Moving forward, it is important that more research focus on how race is defined in health disparities research. As one of the fastest growing racial groups in the United States, it is important to continue to address health disparities within the NHPI community and increase their voice in the US health narrative.

Conflicts of Interest

None of the authors identify any conflicts of interest.

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Liaison Committee on Medical Education Accreditation, Part IX: Strengths and Challenges at the John A. Burns School of Medicine (JABSOM)

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and Kathleen Kihmm Connolly PhD

The Medical School Hotline is a monthly column from the John A. Burns School of Medicine and is edited by Satoru Izutsu PhD and Kathleen Kihmm Connolly PhD; HJMPH Contributing Editors. Dr. Izutsu is the vice-dean of the University of Hawai'i John A. Burns School of Medicine and has been the Medical School Hotline editor since 1993.

Accreditation by the Liaison Committee on Medical Education (LCME) is required for medical schools in the United States to ensure that its MD graduates are eligible to be accepted into Accreditation Council for Graduate Medical Education (ACGME)[1] accredited residency training programs and subsequently eligible for medical licensure. Accreditation is a peer-reviewed process leading to an analysis of how well a medical school is compliant with the standards of educational quality. In the accreditation process, medical schools are required to submit a completed Data Collection Instrument (DCI) report and an Institutional Self-Study Summary report. Following the school's submission of materials to the LCME there is a two and one-half (2 ½) day onsite visit by designated LCME officials.[2] Accreditation may be granted for up to eight years. During the period of accreditation the school monitors ongoing changes in the LCME educational standards to remain in compliance. JABSOM was last granted an eight year accreditation in 2009.

In the current LCME Functions and Structure of a Medical School[3] there are ninety-three (93) elements organized under twelve (12) standards. The school's LCME Workgroups spend many months to complete the DCI[4]and the Institutional Self-Study Summary Report (ISSR) for Full Accreditation. The DCI document details the medical school's administration, curriculum, student services, and resources. The ISSR, directly linked to the DCI, is a self-evaluation summary of the school's medical education program and adequacy of resources for continued quality education. The report includes a review of the areas of concern from the previous accreditation visit and analyses of the data from the DCI. It lists strengths, challenges, and items for future action.[5] Also included in the ISSR are data from the independent student analysis (ISA). The ISA is designed and developed to validate students' experiences in relation to the education standards. The medical students independently administer the ISA to their peers, analyze the data, and produce a report to the medical school administration. The medical students' opinions weigh heavily in the accreditation review.[2]

In the process of completing the ISSR, a self-study task force (SSTF) is formed, including a broad spectrum of representatives who have a vested interest in the medical school. This includes medical school faculty, administrators, students, and affiliated hospital administrators. Subcommittees of the SSTF are formed to review and provide input on specific sections of the ISSR. In addition, the SSTF meets several times to discuss and review the overall report, including discussions on the strengths and challenges of the medical school.

A summary of JABSOM's strengths from the report include: (1) a highly qualified and experienced dean; (2) an excellent problem-based learning (PBL) curriculum; (3) a well-established culture of engagement between medical students and faculty; (4) a robust medical education program evaluative process; (5) demonstrated commitment to diversity and inclusion; (6) a community-based teaching model with strong clinical affiliates; (7) strong inter-professional education and research programs; (8) expertise in health disparities; (9) well-balanced revenue base from diverse sources; (10) significant contribution of its graduates to the state workforce; and, (11) a commitment to improving the health of the people of Hawai'i and the Pacific Basin.

From the report, challenges that require ongoing monitoring due to changing circumstances include: (1) ensuring adequate resources for an enhanced medical student education program; (2) addressing the rising cost of tuition and high cost of attendance; (3) career advising in a time of substantial changes in health care delivery and financing; (4) coordinating resources for medical student education between the Office of Medical Education (OME) and the clinical departments; and, (5) assuring and assigning educational outcomes in a highly matrixed organization.

Listed below are a detailed list of the strengths, challenges and future actions from the ISSR submitted for JABSOM's reaccreditation visit in 2017.

Strengths

Leadership: In an era where the tenure of many medical school deans has been five years or less, Dean Hedges provides stability in leadership, having been in his position since 2008. He is a highly qualified and nationally recognized leader in American medicine. He has the budgetary authority to sustain the medical education program and to establish strategic programmatic and institutional goals. He has been effective in establishing new standards in education and teaching, research, patient care, and community engagement. He has guided the growth of the school's faculty practice plan to help strengthen the financial stability of the clinical departments, increase the size and diversity of the clinical faculty, and help to assure adequate numbers and types of patients for clinical teaching.

PBL Curriculum: JABSOM was a pioneer in moving from a mainly lecture-based curriculum to a PBL curriculum designed to foster self-directed and life-long learning. The PBL curriculum is frequently cited by medical school applicants as a major draw to JABSOM and named as a distinct strength of their educational experience. One measure of the strength of the curriculum is that the average score of the United States Medical Licensing Examination (USMLE) Step 1[6] taken by JABSOM medical students has matched or exceeded the national average for 10 of the last 11 years.

Student and Faculty Engagement: JABSOM has a well-established culture of engagement between medical students and faculty in a nurturing and supportive learning environment throughout the duration of their medical education, bolstered by student well-being programs. Student satisfaction of their relationship with faculty is rated highly on the ISA, the Association of American Medical Colleges (AAMC) Graduation Questionnaire (GQ), the AAMC's Year 2 Questionnaire, and on internal surveys.

Evaluation: The medical education evaluative process is mature, robust and comprehensive. It is overseen by the curriculum committee and operated through the OME. This process consists of course reviews and a number of surveys, including those of students, alumni, and residency program directors. Feedback has led to continuous quality improvement of the curriculum.

Diversity: JABSOM is one of the most ethnically diverse medical schools in the world. The school has a demonstrated commitment to diversity and inclusion, and operates a highly successful post-baccalaureate program called 'Imi Ho'ola, a long-standing program that contributes to the diversity of the student body. In addition, JABSOM has a gender and ethnically diverse faculty and complement of department chairs. The school is a leader in the United States in terms of the number of women faculty and leaders.

Community-based Medical School: JABSOM is one of the few community-based medical schools in the country. Rather than operating its own hospital(s) it has generated stable, supportive and sustainable partnerships with clinical affiliates wherein students are trained in diverse clinical settings across the State. In addition to learning in Hawai'i's major medical centers, medical students are provided the opportunity to train in rural and neighbor island communities during both the preclerkship and clerkship years. These settings provide students with access to a wide variety of patients in settings where they have abundant opportunities to participate.

Inter-professional collaborations: JABSOM provides many opportunities for inter-professional collaboration in education and research. Nurses, social workers, pharmacists, and public health faculty have participated in community-based translational research with medical school faculty members and have co-led inter-professional training programs for medical students and other health professionals for years.

Health Disparities: Many faculty members incorporate information related to the social determinants of health and the relationship to health disparities in a multi-cultural and multi-ethnic community. These faculty members provide opportunities for service learning within the framework of the medical education program.

Diverse Revenue Base: The school's revenue base is derived from diverse sources, including the State of Hawai'i, research and education grants, the faculty practice plans, and philanthropy. The budget is carefully managed. Research grants have continued to increase, and the faculty practice plan revenues have steadily increased since FY09 and substantially increased in the last three fiscal years. New specialties are being added and are anticipated to increase revenues further. The faculty practice plans include University Clinical, Education, and Research Associates (UCERA), now doing business as University Health Partners of Hawai'i (UHP) and Kapiolani Medical Specialists (KMS).

Hawai'i Workforce: JABSOM has made significant contributions to the state workforce. Half of all practicing physicians in Hawai'i are JABSOM graduates and/or faculty members. The AAMC has ranked JABSOM to be first in the nation for the retention of combined MD and residency program graduates practicing in the State.

Global Health: JABSOM has a commitment to global health, especially in contributing to the health of the people of Hawai'i and the Pacific Basin. A component of the curriculum is to train students with the skills to identify and address critical global health problems. The school is uniquely located in the pacific with strong ongoing collaboration and educational relationships within the pacific region and Asia.

Challenges

Funding: Despite a carefully managed budget and diverse revenue streams, plans to expand training opportunities to neighbor islands and rural communities are challenging, especially in finding consistent sources of funding for student transportation and housing costs. As in many other states, economic factors have impacted State investment in higher education. Increases in other revenue streams have mitigated the restricted University allocation, predominantly with revenues from the faculty practice plans and with major gifts, endowments, and scholarships. However, these have mainly supported the existing program rather than providing support for expansion. The teaching contributions of volunteer faculty members continue to be substantial in many different specialties.

Tuition: While the resident tuition is still considered a good value when compared with national averages, tuition has increased significantly over the past five years for non-residents. Tuition increases have been monitored to maintain resident tuition below or near the 50th percentile for US medical schools. The high cost of living in Hawai'i leads to additional costs of attendance. Efforts to offset these costs have included financial counseling for students and renewed emphasis on raising scholarship funds.

Career Choices: The rapidly evolving changes in the organization of health care delivery and in health care financing are contributing to the established challenges of advising medical students about career choices. There is also a continued need for career advising to assist students with the timing and selection of residency training programs. Despite these challenges, strong student match rates and feedback on the GQ suggest that the challenges have been addressed.

Collaboration: Increased collaboration between the OME and the departments is required as support for faculty time has grown in the clinical departments with the growth of the faculty practice plans and is stable in OME. The growth of the faculty in the clinical departments corresponds to the growth of the clinical activities. These activities provide a ready source of clinical experiences from which to learn but may compete for faculty time for other aspects of the curriculum. Ongoing collaboration continues to be needed to assure that adequate faculty time is available.

Coordination Among Education Sites: The community-based medical education program presents great strengths but requires extensive coordination for assurance of desired educational outcomes. Training in varied settings results in a highly matrixed organization where continuous attention and collaboration are required.

Recommendations for Future Action

Innovations in PBL Medical Education: The PBL curriculum has been a strength of the school. PBL takes place in small group settings, requiring many faculty members to spend considerable time with each class of students. Although this presents challenges with faculty time, the advantages of PBL in recruiting highly motivated students equipped for life-long learning argue for continued strong support. Efforts to safeguard sufficient resources for PBL are ongoing.

Support for Medical Students: There should be continued support for medical students by continued growth of the medical school financial diversification, generating new scholarships, enhancing financial aid services, and assisting students with debt management.

Strategic Planning: Continued strategic planning is required for medical school excellence in education and teaching, clinical healing, research and discovery, community service, support services, and capitalizing on opportunities.

Quality Improvement: Continuous quality improvement is needed to ensure effective monitoring of the medical education's compliance with accreditation standards.

JABSOM as a community-based medical school and the only medical school in Hawai'i, has strengths and challenges. JABSOM is a complex organization, where clinical training takes place in many sites that partner with JABSOM, but are not under the direct control of the school. The model has succeeded in producing outstanding physicians and world-class research and services to Hawai'i and the Pacific Basin. The school recently celebrated its 50th anniversary, marking an excellent time to take stock and to rededicate ourselves for future commitment and excellence.

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Substance Use in Pregnant Women in Hawai'i: Extending Our Capacity and Compassion

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Insights in Public Health is a monthly solicited column from the public health community and is coordinated by HJMPH Contributing Editors Tetine L. Sentell PhD from the Office of Public Health Studies at the University of Hawai'i at Manoa and Donald Hayes MD, MPH from the Hawai'i Department of Health in collaboration with HJMPH Associate Editors Ranjani R. Starr MPH and Lance K. Ching PhD, MPH from the Hawai'i Department of Health.

Abstract

Substance use can have serious consequences for the health and well-being of individuals. The problem is of particular concern when it involves pregnant women due to health risks for the mother and the fetus. In utero exposure to either legal (eg, alcohol, cigarettes, and certain prescription drugs) or illicit (eg, amphetamines, cocaine, and opioids) substances can result in potentially serious and long-lasting health problems for infants. Available data from Hawai'i indicate that substance use among pregnant women is higher than national targets, which reflect the fact that there is essentially no acceptable rate of use of these substances. Developing an effective system to support virtual elimination of substance use in pregnancy requires broad-based strategies. Progress is being made in Hawai'i to better identify and address substance use in pregnancy. These efforts are being guided by a variety of stakeholders who are dedicated to improving the healthcare and health outcomes for this population. However, significant challenges to the system remain, including provider shortages, lack of local investment, and limited capacity of appropriate, individualized treatment.

The Problem of Substance Use in Pregnancy

Substance use can have serious consequences for the health and well-being of individuals. The problem is of particular concern when it involves pregnant women due to health risks for the mother and the fetus. Both legal (eg, alcohol, cigarettes, and certain prescription drugs) and illicit (eg, amphetamines, cocaine, and opioids) substances can result in health problems for infants (see Table 1). The health outcomes of in utero exposure to substances can range in severity, but many can have long-lasting and irreversible effects.[1-2] Research also indicates maternal substance use in the post-partum period is associated with increased risk of neglect, abuse and substance use (in adolescence) for the child.[3]

Pregnancy is a point of high motivation for women using substances to quit. Research indicates that pregnant women have lower rates of substance use compared to non-pregnant women in the same age group and surveillance data in Hawai'i confirms that for all substances (smoking, alcohol, illicit drugs), use declines during pregnancy.[4,5] The cessation rates for alcohol, smoking, and illicit drugs are 87.7%, 58.2%, and 62.2% respectively according to the Hawai'i Pregnancy Risk Assessment Monitoring System (PRAMS) data.[4] This suggests that the majority of women using substances recognize that there are risks to continuing use in pregnancy and that most attempt to quit once they are aware of the pregnancy. Therefore, this is a critical time to intervene.

This article examines the problem of prenatal substance use within Hawai'i and attempts to describe the progress and challenges in addressing the problem, with a specific focus on the issue of system capacity in screening and treatment.

The 2020 National Healthy People objectives include targets for abstinence from smoking during pregnancy at 98.6%, abstinence from alcohol in pregnancy at 98.3%, and abstinence from illicit drug use during pregnancy at 100%.[6] These high national targets illustrate the general consensus of opinion among the public health and medical community that due to the significant risks to fetal development and infant health there is essentially no acceptable rate of use of these substances during pregnancy.

Accurate data on prevalence of substance use among pregnant women is hard to obtain due to the stigma around the issue and the perceived (and/or real) risk of involvement by the authorities in the case of illicit drug use. Yet, in many states, the best available data show significant gaps between the national targets and the percentage of pregnant women abstaining from substance use. The PRAMS is a population-based surveillance system funded by the Centers for Disease Control and Prevention (CDC).[7] At this time the PRAMS provides the best measure of substance use among pregnant women in Hawai'i. However, it is likely that this survey underestimates rates due to the stigma surrounding prenatal substance use and the fact that the data is collected through self-report, which may result in social desirability bias.

In 2014 there were 18,556 births in Hawai'i.[8] Based on aggregated data from the PRAMS surveys (2004-2008), 5.9% of women sampled reported drinking any alcohol in the last trimester of their latest pregnancy, 8.6% reported any cigarette smoking in the last trimester of their latest pregnancy, and 3% of pregnant women reported that they used any illicit drugs during their latest pregnancy.[4] Analysis of the data also showed that women who used illicit drugs tended to be younger (<25 years old), less educated, and were more likely to be Native Hawaiian or African American compared to women who did

Table 1. Prevalence of Substance Use Before and During Pregnancy and Evidence of Harm Related to Perinatal Substance Use			
Substance	**Evidence of harm**	**Prevalence of use during the last trimester of pregnancy[§]**	**Prevalence of use within 3 months prior to pregnancy[§]**
Smoking	Placental abruption, preterm delivery, low birth weight, sudden infant death syndrome (SIDS), childhood asthma and childhood obesity[a,b]	9%	20%
Alcohol use	Fetal alcohol spectrum disorder (FASD), which encompasses problems including; fetal alcohol syndrome (FAS), alcohol-related birth defects and neurodevelopmental disorders[c]	6%	47%
Illicit drugs (ie, methampheta-mines, cocaine, opioids)	Maternal complications, preterm birth, central nervous system abnormalities in newborns,[d,e] and neonatal abstinence syndrome (NAS)[f] – a result of in utero exposure to opioids.	3% (any point during pregnancy)	6% (within 12 months of pregnancy)

[§]Prevalence data is based on Hawaii Pregnancy Risk Assessment Monitoring System (PRAMS) from 2004-2008 as reported in: Schempf A, Hayes D, Fuddy L. Perinatal Substance Use Fact Sheet. Honolulu, HI: Hawai'i Department of Health, Family Health Services Division. Published December 2010.

[a]Department of Health and Human Services (US). The health consequences of smoking: a report of the Surgeon General. Atlanta: HHS, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health. Published 2004.

[b]Banderali G, Martelli A, Landi M, et al. Short and long term health effects of parental tobacco smoking during pregnancy and lactation: a descriptive review. Journal of Translational Medicine. 2015;13:327. doi:10.1186/s12967-015-0690-y.

[c]Terplan M, Cheng D,Chisolm MS.The relationship between pregnancy intention and alcohol behavior use: An analysis of PRAMS data. Journal of Substance Abuse Treatment, 2014;46:506-510.

[d]Wright TE, Schuetter R, Tellei J, Sauvage L. (2015). Methamphetamines and pregnancy outcomes. Journal of Addiction Medicine. 2015;9(2):111-117.

[e]Minnes S, Lang A, Singer L. Prenatal tobacco, marijuana, stimulant, and opiate exposure: outcomes and practice implications. Addict Sci Clin Pract. 2011;6(1):57-70.

[f]Stanford Children's Hospital. Neonatal Abstinence Syndrome. http://www.stanfordchildrens.org/en/topic/default?id=neonatal-abstinence-syndrome-90-P02387 Accessed Mar. 23, 2016.

not report using illicit drugs.[4] Use of alcohol during the last trimester of pregnancy was associated with higher rates of low birth weight compared to non-users.[4] Women who smoked (in the 3rd trimester) or used illicit drugs during pregnancy were also more likely to have had an unintended pregnancy, receive late or no prenatal care, and deliver a low birth weight infant compared to women who did not report using those substances.[4] Substance use during pregnancy was also associated with a greater likelihood of being on Medicaid compared to those who didn't report use of substances.[4]

A diagnosis of a substance use disorder (SUD) is based on "evidence of impaired control, social impairment, risky use and pharmacological criteria" and is defined as ranging from mild to severe.[9] For pregnant women with SUDs, treatment can be complicated.[10,11] Research conducted at an O'ahu perinatal clinic for women with SUDs (primarily methamphetamine addiction) found that over 55% of women in the sample (n = 97) had a history of child abuse and neglect and 63% had a history of domestic violence.[12] On top of potential exposure to abuse and the stigma pregnant women who are using substances face (which creates a barrier to disclosure and/or identification of the problem), there are other unique barriers to seeking treatment. For example, finding adequate childcare during treatment or being with a partner or family member who is violent and unsupportive of seeking treatment are barriers to treatment.[13]

An effective and efficient statewide system of SUD treatment needs both a strong screening program and sufficient capacity for individual-focused treatment. These efforts should involve a range of providers (eg, SUD counselors, psychologists, psychiatrists, primary care) and services (eg, appropriate residential & outpatient treatment, community-based behavioral health programs).

Capacity in Hawai'i: Screening

Work being done currently through the State of Hawai'i Healthcare Innovation Project and the Hawai'i Maternal and Infant Health Collaborative (HMIHC) promotes routine screening, brief intervention, and referral to treatment (SBIRT) as a strategy for preventing and treating prenatal substance use.[14] Plans are in place to begin training women's health care and primary care providers in Hawai'i on SBIRT.[14] This evidence-based strategy is widely promoted by other national agencies focused on substance use prevention and treatment.[15,16]

Although universal screening for substance use is already a recommendation of the American College of Obstetricians and Gynecologists (ACOG), the quality of screening and implementation is not believed to be consistent across providers.[17,18] Research on SBIRT has indicated that it can be effective at reducing smoking and alcohol use.[19-21] More research is needed to determine the impact of SBIRT for illicit drug use, but a recent review of randomized controlled trials suggests that SBIRT can have a positive impact on reducing illicit drug use among peripartum women.[3] Women identified as using illicit drugs through the screening would likely need to be referred to intensive treatment programs.[22] It is reasonable to assume that increased promotion and implementation of SBIRT among healthcare providers in Hawai'i could also increase the number of women identified with an SUD. Consequently, this would increase the demand for specialized SUD treatment services in the state.

Capacity in Hawai'i: Treatment

Unfortunately, in many parts of Hawai'i, there is already a shortage of mental health and substance abuse prevention and treatment professionals. Thirty percent of the population of

Hawai‘i resides in a county that is a designated Mental Health Professional Shortage Area (HPSA).[23] Practically the entirety of Moloka‘i, Maui, Kaua‘i, and large swaths of Hawai‘i Island were designated as HPSAs for mental health professionals in 2014.[24] Shortages of Obstetricians-Gynecologists (OB-Gyns) are also a concern. According to findings by the Hawai‘i Physician Workforce Assessment Project, statewide there is a 11.4% shortage of OB-Gyns.[25] However, this percentage varies widely by county, ranging from 64.4% in Kaua‘i to 3.1% in Maui.[25]

With regard to treatment programs, data from a report on publically funded programs by the University of Hawai‘i Center on the Family show that in 2014 there were 52 treatment sites for adults of which 28 were located on O‘ahu.[26] The report provides numbers of people who received and completed treatment, but doesn't provide data on waitlists or time from contact to entry into treatment, so there isn't a measurement of unmet need. Furthermore, while opioid addiction in Hawai‘i has not reached the proportions currently seen in some states, there is concern that it may be an increasing problem.[27,28] An increase in opioid addiction would impact the substance use treatment system in the state, particularly with regard to the need for access to medication-assisted treatment (MAT), which is an evidence-based strategy that involves the provision of medication therapies (eg, methadone or buprenorphine) to address opioid addiction.[29] ACOG recommends the use of MAT for pregnant women (administered by an addiction treatment specialist) with opioid addiction as a strategy to treat the addiction, encourage prenatal care and to reduce the risk of obstetric complications.[29]

Federal law requires that pregnant women with a SUD who seek treatment be granted priority admission to services.[30] According to the Hawai‘i Department of Health Alcohol and Drug Addiction Division (ADAD), there is "at least one contract" in each of the four counties that provides treatment and supportive services for pregnant women and women with dependent children up to 12 years of age.[30] On O‘ahu there are less than 100 residential treatment beds and only one residential treatment program (with 21 beds) that allows women to reside with their young children. There is a similar program on Maui. Hawai‘i County also has one residential facility (14 beds) that allows children to stay with their mother. There is one program in Kaua‘i County that serves pregnant women and women with dependent children, but it is an outpatient program. Residential programs are not available on Kaua‘i.

These services are insufficient for meeting the needs of Hawai‘i. Using illicit drug use in pregnancy as an example, 3% of annual births equates to roughly 556 births per year exposed to some form of illicit drug.[4,8] Even if only 50% (278) of the women who reported using lived on O‘ahu, that is over 2 times the capacity of all residential beds and 12 times the capacity of beds for pregnant women who want to keep their young children with them during treatment. Clearly, without increasing capacity to address higher level treatment needs, providers who identify substance use during pregnancy may not be able to easily refer women to necessary and appropriate treatment.

Access to services is a critical aspect, but appropriateness of available services is also vital to the effectiveness of treatment programs. As alluded to above, treatment for pregnant women must take into account the stigma of substance use in pregnancy, the demographic characteristics of pregnant women with SUDs, women's existing childcare and work responsibilities, and the co-occurrence of trauma and mental health concerns. Treatment programs tailored to meet the unique needs of women have been shown to improve retention in programs, decrease substance use, and improve access to care for women.[13] Results from a study of pregnant women who entered a comprehensive gender-specific drug treatment program in Hawai‘i showed that, in spite of their higher level of risk for experiencing preterm labor, the participants had preterm birth rates similar to averages for the state.[12] In another prospective cohort study conducted at the same facility in O‘ahu, findings suggested that efforts to decrease or stop methamphetamine use during pregnancy had a positive impact on health outcomes, including reducing preterm birth.[1] Preterm birth (defined as birth before 37 weeks gestation) is a major contributor to infant mortality and morbidity in the US, therefore efforts to decrease substance use in pregnancy align with broader efforts to reduce infant mortality.[31] The results from these two studies suggest that gender-specific treatment for substance use can positively influence birth outcomes in Hawai‘i.

Other States' Solutions for Increasing Capacity

Demand for substance abuse treatment is increasing on a national scale. One reason is because the Patient Protection and Affordable Care Act 2010 (ACA) has identified services for mental health and SUDs as "essential services" for all Marketplace plans.[32] Therefore, coverage for psychotherapy, counseling, mental and behavioral inpatient services, and SUDs is mandated.[32] Another driver of demand is the rising rates of opioid addiction (predominantly due to opioid use in the form of prescription drugs and heroin). This "epidemic" has forced states to examine and restructure their treatment systems and services.[33] In response to the increase in demand for services, several states have developed broad-based strategies to increase system capacity and attempt to address both prevention and treatment of SUDs.

California's Mental Health Planning Council recommended in 2011 that the State appropriate federal funds to incentivize individuals to complete career pathways that lead to public mental health careers.[34] In addition they recommended loan repayment programs for rural, underserved areas and urban areas where retention is an issue and training/support of existing professionals interested in pursuing mental/behavioral health professions.[34] Similar efforts have been made in Hawai‘i. The Hawai‘i State Loan Repayment program provides funds for eligible health care providers who work in HPSAs in Hawai‘i. Although a range of mental health providers are eligible for this program, the funds are not specifically designated for mental health providers.[35] Furthermore, the federal funding provided through the ACA requires matching, but these funds have yet to be

designated.[25,35] An objective outlined in the Hawai'i Healthcare Innovation Plan doesn't increase the number of mental health providers, but if implemented it could help in the prevention of SUD among pregnant women. The objective expands access to behavioral health services through training and the provision of behavioral health consultation for primary care providers. This strategy increases the capacity of primary care providers to address "mild to moderate behavioral diagnoses."[36] The early detection and identification of certain mental health issues, like depression, abuse and trauma, through contact with primary care providers could allow women to get treatment prior to getting pregnant. In addition, any effort to prevent substance use in pregnancy must also work to ensure that providers ask women about pregnancy intention and that access to acceptable and effective methods of contraception is available.[18,37] This critical measure can help women using substances avoid an unintended pregnancy.

With regard to treatment, Vermont's strategies to improve capacity have focused on a number of approaches, including: increasing SBIRT, establishing telehealth programs, and the expansion of evidence-based MAT through improved coordination of systems.[38,39] In Ohio, another state with high rates of opioid use, recommendations to improve system capacity also include increasing the number of addiction psychiatrists and addiction medicine doctors working in treatment programs.[40] Addiction medicine is a new subspecialty program for medical professionals that would require one year of additional training and a board certification exam on top of a chosen residency.[41] To the best knowledge of the authors, there are only two OB-Gyn addiction medicine specialists in Hawai'i, but there is a plan in place to implement an addiction medicine training program in the future.

Limitations

This paper focuses specifically on capacity issues, but capacity is only one aspect of a highly complex issue for governments, providers, families, and individuals. Therefore, there are a number of limitations of this discussion that are important to highlight when considering the larger question of the establishment of an effective system for treatment of pregnant women with SUDs.

Firstly, the issue of acceptance of treatment is critical. Anecdotal evidence from stakeholders in Hawai'i working on this issue, suggests that women identified as using substances are reluctant to accept referrals for behavioral health or substance use treatment services.[42] More research into the barriers to acceptance of referral to treatment for pregnant women in Hawai'i is needed.

Secondly is the question of how a referral is handled. This problem is associated with the issue of acceptance of referrals to treatment, but distinct in terms of strategies. There are a variety of models for referring women with SUDs to treatment; some of the most progressive include the integration of mental health providers or a substance abuse specialist in OB-Gyn practices. This model has been demonstrated to decrease maternal and neonatal complications when implemented into a Kaiser Permanente site.[43] It also has been found that women are four times more likely to follow-up with behavioral health treatment when services are co-located.[44] SAMHSA has put out a report that provides information on integrating substance abuse services into primary care settings.[45] Due to the costs associated with this model, it poses challenges to OB-Gyns and primary care physicians practicing independently. Changes in the payment system and coverage under the ACA may make this model more attainable for physicians in small practices.

Conclusion

The problem of substance abuse and addiction can touch anyone regardless of gender, income, race, or social status. However, research indicates that women who continue to use substances in pregnancy are particularly vulnerable. They are more likely to be young, have low levels of education, belong to a group that has faced racism and discrimination, may have a history of abuse or neglect, and may have other co-occurring behavioral or mental health issues. The consequences of substance use during pregnancy can severely impact the lives of these women, their infants, their families, and their communities for a lifetime. Therefore, a system that can efficiently identify and provide appropriate and effective services is vital for this population. Clearly, progress is being made in Hawai'i to better identify and address SUDs in pregnancy. These efforts are being guided by a variety of stakeholders who are dedicated to improving the healthcare and health outcomes for this group. The environmental scan of treatment resources sponsored by the Hawai'i Maternal and Infant Health Collaborative will provide a more extensive and systematic review of capacity than is possible within the scope of this paper.[14] It may identify other concerns in addition to the problems highlighted here; provider shortages, lack of local investment, and limited capacity of appropriate gender-specific treatment for pregnant women with SUDs. Continued focus and integrated efforts to address the problem of substance use in pregnancy are essential to meet the current demand and help to prevent substance exposed pregnancies in the future.

Conflict of Interest

None of the authors identify any conflict of interest.

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Poha Berry (*Physalis peruviana*) with Potential Anti-inflammatory and Cancer Prevention Activities

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Abstract

The Daniel K. Inouye College of Pharmacy, during a historic event in Spring 2016, graduated the first two students in the Pacific region to earn a PhD in pharmaceutical sciences at the University of Hawai'i at Hilo. The college offers PhD programs in these five disciplines: Cancer Biology, Medicinal Chemistry, Pharmaceutics, Pharmacognosy, and Pharmacology. One of the Pharmacognosy dissertations focused on plant-derived natural products with potential anti-inflammatory and cancer chemopreventive activities. Physalis peruviana *(Pp) L. originated in tropical South America. It has become naturalized and is found readily on the Island of Hawai'i. The edible fruits are commonly known as cape gooseberry or poha in Hawai'i. In part of our study, three new withanolides, physaperuvin G (***1***), physaperuvins I-J (***2-3***), along with four known withanolides, namely, 4β-hydroxywithanolide E (***4***), withaperuvin C (***5***), and physalactone (***6***), coagulin (***7***) were isolated from the aerial parts of* P. peruviana*. In addition, two known compounds, phyperunolide F (***8***), and withanolide S (***9***), were isolated and identified from the poha berry fruits. The structures and absolute stereochemistry of new compounds from poha were elucidated by several spectroscopy methods: Nuclear Magnetic Resonance (NMR) spectroscopy, X-ray diffraction, and mass spectrometry analyses. All isolated poha compounds (aerial parts and fruits) were evaluated for their anti-inflammatory activity with lipopolysaccharide (LPS)-activated murine macrophage RAW 264.7 cells, and tumor necrosis factor alpha (TNF-α)-activated nuclear factor-kappa B (NF-κB) with transfected human embryonic kidney cells 293. Most of the isolated natural compounds showed activity with these assays. Additional studies were performed with models of colon cancer. Specifically, 4β-hydroxywithanolide E (4HWE) inhibited the growth of colon cancer monolayer and spheroid cultures. The compound induced cell cycle arrest at low concentrations and apoptosis at higher concentrations. These data suggest the ingestion of poha berries may have some effect on the prevalence of colon cancer. Additionally, poha isolates compounds were evaluated for their growth inhibitory effects with U251MG glioblastoma and MDA-MB-231 breast cancer cells that harbor aberrantly-active signal transducer and activation of transcription 3 (STAT3), compared to normal NIH-3T3 mouse fibroblasts. This work has led to the filing of three provisional patents with the University of Hawai'i Office of Technology Transfer and Economic Development.*

Introduction

Although heart disease remains the leading cause of death nationwide, the death rate resulting from heart disease has significantly diminished over the years, and cancer has overtaken heart disease as the leading cause of death in 22 states in the United States.[1] The American Cancer Society estimates that 1,685,210 new cancer cases will be diagnosed this year (2016), and 595,690 Americans will die of cancer.[2] Among the types of cancers, lung and colorectal cancers account for the greatest number of deaths. Additionally, prostate and breast cancers are reported commonly in men and women, respectively.[2] In 2012, statistical data collected by the National Cancer Institute and the Centers for Disease Control and Prevention showed melanoma, oral, uterus, and pancreatic cancers affect Hawai'i residents to a greater extent than other states.[3,4] About 380 Hawai'i residents were diagnosed with melanoma in 2013.[3] The rate of new melanoma cases diagnosed among Whites in Hawai'i is almost triple the national average.[3] Oral cancer is also more common on Hawai'i Island than other areas nationwide, and this leads to higher-than-average mortality rate in Hawai'i County. However, breast and prostate cancers are still the most commonly diagnosed cancers in Hawai'i County. In particular, the Native Hawaiian population has higher-than-average cancer rates; in this regard, males had a 21% higher cancer death rate, and women had a 37% higher death rate, as compared to other groups.[3]

Conventional treatment for cancer includes radiation, surgery and chemotherapy. Often, cancer chemotherapeutic drugs are not selective and can cause toxicity and/or severe side effects, precluding effective treatment.[5] Since cancer continues to be a major public health problem and conventional cancer chemotherapy treatments have not controlled the incidence of most cancer types, new approaches for cancer treatment are critically needed. Recent detailed studies of the mechanism of action and pathogenesis of cancer has led to the discovery of new key molecular and signaling pathways amenable for targeted therapy.[5] The targeted therapy approach has shifted from using cytotoxic compounds that cause tumor regression to molecular target-based drug discovery.[6] The challenge is to identify key molecular targets that underlie the malignant behavior of a cancer cell, and to target these directly. The mutated phenotype in a cancer cell is driven by the pattern of genes expressed in the cell; therefore, much attention has focused on the abnormal activation of transcription factors that regulate genes controlling proliferation, survival, self-renewal, and invasion. Two such oncogenic transcription factors are Signal Transducer and Activator of Transcription 3 (STAT3) and Nuclear Factor-kappa B (NF-κB).[7,8]

Oncogenic Transcription Factors

NF-κB transcription factors and signaling pathways are central coordinators in innate and adaptive immune responses.[9] NF-κB regulates numerous physiological processes including cellular proliferation, development, differentiation, immunity, apoptosis, inflammation, and metabolism.[7] NF-κB proteins are present in the cytoplasm in association with inhibitory proteins (inhibitors of NF-κB).[10] NF-κB is activated rapidly in response to a wide range of stimuli, including pathogens, pro-inflammatory cytokines, such as tumor-necrosis factor (TNF-α), and interleukin-1.[7,11] Park and Hong indicated that aberrantly active NF-κB pathways may be associated with many different types of human cancers.[12]

It is generally known that normal STAT3 activation is transient in keeping with cellular requirements for proliferation, development, apoptosis, and inflammation. In contrast, aberrant STAT3 activity dysregulates growth and survival, promotes angiogenesis,[13] migration and invasion of tumor cells, and induces tumor-immune tolerance.[14] In turn, constitutive STAT3 activation is a molecular abnormality that is causally linked to cancer aggressiveness. As mentioned above, both NF-κB and STAT3 signaling pathways have integrated roles in inflammatory responses that promote cancer development and growth. Recently, the roles of NF-κB and STAT3 in a variety of cancers including breast, colon, gastric and liver cancers have been heavily studied.[12] The activation and interaction between STAT3 and NF-κB plays a vital role in control of the communication between cancer cells and inflammatory cells.[13,15] These two major transcription factors regulate the ability of pre-neoplastic and malignant cells to resist apoptosis-based tumor-surveillance and regulating tumor angiogenesis and invasiveness.[7] Thus, it is of interest to focus on specific therapies to target NF-κB and STAT3 inhibition in malignant cancers. To explore and exploit these findings for cancer therapy, we set out to search for plant-derived natural products that could simultaneously block the effects of NF-κB and STAT3. These dual STAT3/NF-κB inhibitors may lead to unique strategies for cancer therapy. The aim of this work was to identify bioactive natural products derived from *P. peruviana* as STAT3 and NF-κB inhibitors, and inhibitors of nitric oxide (NO) production via inducible nitric oxide synthase (iNOS).[16] Compounds with these activities can also serve as chemical probes to uncover STAT3-NF-κB-dependent molecular events that are important for the cancer phenotype.

Regulation of the expression of Inducible Nitric Oxide Synthase (iNOS)

Nitric oxide (NO) is a free radical that is synthesized from L-arginine in a reaction catalyzed by a family of nitric oxide synthase (NOSs) enzymes. It has beneficial antiviral, antitumor, antimicrobial, and immunomodulatory effects.[17] However, induction of aberrantly-active iNOS can lead to detrimental effects. For example, abnormal production of NO is involved in the inflammatory process and carcinogenesis.[17] Three different nitric oxide synthase enzymes are involved in NO production: endothelial NOS (eNOS), neuronal NOS (nNOS), and inducible NOS (iNOS). Among them, the iNOS gene has been found consistently associated with chronic inflammation, tumor production,[18,19] and metastasis.[20] Signal transducer and activator of transcription 1 (STAT-1α), is a transcription factor specific for the interferon (IFN) pathway and plays a vital role in mediating IFN-dependent biological responses,[17] such as tumor surveillance[21] and cell growth control.[22] Activation of the transcription factors NF-κB and STAT-1α leads to activation of the iNOS promoter and appear to be an essential step for iNOS induction in a majority of cells.[17] NO modulates different cancer-related events including angiogenesis, apoptosis, cell cycle, invasion, and metastasis.[23] Therefore, inhibition of NO production has significant therapeutic potential and numerous possibilities for cancer chemoprevention.[20] As an example, Granados-Principal and coworkers (2015)[24] revealed that L-N^G-monomethyl arginine citrate (L-NMMA), an NO inhibitor, exhibited decreasing tumor growth and enhanced survival rates in a triple-negative breast cancer (TNBC) mouse model.[24]

Solanaceae (*Physalis peruviana* L.), aka Poha Berry

Natural products obtained from plants have been the source of many useful anticancer drugs. The Department of Pharmaceutical Sciences at the Daniel K. Inouye College of Pharmacy (DKICP) has conducted research as ongoing collaboration to discover plant-derived cancer chemoprevention and anticancer agents (collaborators: Founding Dean Professor John M. Pezzuto, DKICP and Dr. James Turkson, Professor and Program Director Cancer Biology and Natural Products Program from the University of Hawai'i Cancer Center). The tropical plant *P. peruviana* L. originated in tropical South America and is a member of the Solanaceae family. We are investigating *P. peruviana* as a possible source of anti-inflammatory and anticancer agents. In Hawai'i, *P. peruviana* has become naturalized and is found and collected on the Island of Hawai'i, in Pepeekeo, in open mountain slopes at elevations between 1,500 and 4,000 feet. The plant consists of fruit, leaves, and stems. Commonly known as cape gooseberry, poha, ground cherry, and husk tomato, the fruit contains many seeds, and is juicy, sweet, and tangy, with a high content of vitamin C, carotenoids, and bioflavonoids with antioxidant properties. The berries are eaten fresh or used in making jam. Locally, the fruit is eaten fresh, preserved as jam, or prepared in pies, or ice-cream. A number of ethnic and cultural groups employ the leaves, stems, and fruits of *P. peruviana* in medicinal folkoric medicine(s) for the treatment of asthma, abdominal ailments in children, constipation, diuretic, glaucoma, headache, jaundice, reducing swelling and inflammation, postpartum pain, skin diseases, and as a vermifuge.[25-29] *P. peruviana* fruit juice has also shown reno- and hepato-protective effects against acute renal and liver injury models in rats,[30,31] with no apparent adverse effects.[32] A poultice from the leaves and stems is commonly applied over wounds and skin infections.[33]

Although other *Physalis* species have been studied, more than 30 withanolide derivatives have been isolated from *P. peruviana*.[34-37] There are only a few detailed reports on the bio-

active anti-inflammatory compounds from *P. peruviana*, and no report(s) of withanolides with NO and STAT3 inhibitory activity. Our initial study showed that extracts of the fruits, and aerial parts of *P. peruviana* decreased the activities of aberrantly-active NF-κB and STAT3, two key redox-regulated transcription factors that control cellular and disease processes. Our objective was to identify and discover compounds that specifically block either one or both of these transcriptions factors, and inhibit NO production.

Methods

Plant materials extraction, isolation, and structure determination: Collection and preparation of plant materials, extraction and isolation were performed as described previously.[16,38] The structures of new compounds and other analogues were determined by spectroscopic methods, including 1D and 2D NMR, and mass spectrometry.[16,38] The absolute configuration of compound (**1**) was confirmed using single-crystal X-ray diffraction analysis, as well as supported from NOESY experiments.[16,38] The organic extracts of *P. peruviana* aerial parts and fruits, and compounds, were evaluated using cancer chemoprevention bioassays: (a) inhibition of nitric oxide (NO) production in lipopolysaccharide (LPS)-activated murine macrophage RAW 264.7 cells; (b) tumor necrosis factor alpha (TNF-α)-induced NF-κB activity using stable transfected human embryonic kidney cells 293.[39,40]

Inhibition of TNF-α-induced NF-κB activity: This assay was performed using 293/NF-κB-Luc HEK cells (Freemont, CA, USA) as described previously.[39] All chemicals were purchased from BD Biosciences, USA. NF-κB activity was measured with a luciferase kit (Madison, WI, USA) using a LUMIstar Galaxy Luminometer (BMG Labtechnologies, Durham, NC, USA) according to the manufacturer's instructions. Data were calculated as % inhibition relatively to DMSO control. Samples which showed more than 50% inhibition at the test concentration 20 μg/mL were tested for dose-dependence to determine IC_{50} values (half-maximal inhibitory concentration). A NF-κB inhibitor was used as a positive control: *N*-tosyl-L-phenylalanylchloromethyl ketone (TPCK), IC_{50}= 5.09±0.6 μM. Sulphorhodamine B (SRB) cytotoxicity was performed in parallel to avoid false positive results.

NO inhibition assay: In this assay, potential to inhibit inducible nitric oxide synthase (iNOS) was evaluated with lipopolysaccharide (LPS)-activated murine macrophage RAW 264.7 cells as described previously.[40] Samples showing more than 50% inhibition at a concentration 20 μg/ml were tested at three-fold serial dilutions to find the IC_{50} values. L-N^G-Monomethyl arginine citrate (L-NMMA) was used as a positive control (IC_{50} = 23.5 μM, BD Biosciences, USA). The SRB assay was performed simultaneously to test the cytotoxic effect of samples.

Results and Discussion

In our study, the organic crude extracts of *P. peruviana* (aerial parts and fruits) exhibited significant inhibitory activities on both NF-κB activity and nitrite oxide generation at a concentration of 20 μg/mL, and were less cytotoxic in these anti-inflammatory assays.[16,38] Therefore, bioassay-guided fractionation of extracts of *P. peruviana* (aerial parts) were performed, and yielded three new withanolides, physaperuvins G (**1**), I (**2**), J (**3**), and four known compounds, 4β-hydroxywithanolide E (**4**), withaperuvin C (**5**), physalactone (**6**), and coagulin (**7**) (Figure 1).[16,38] In addition, two known compounds, phyperunolide F (**8**) and withanolide S (**9**), were isolated from poha fruits (Figure 2).

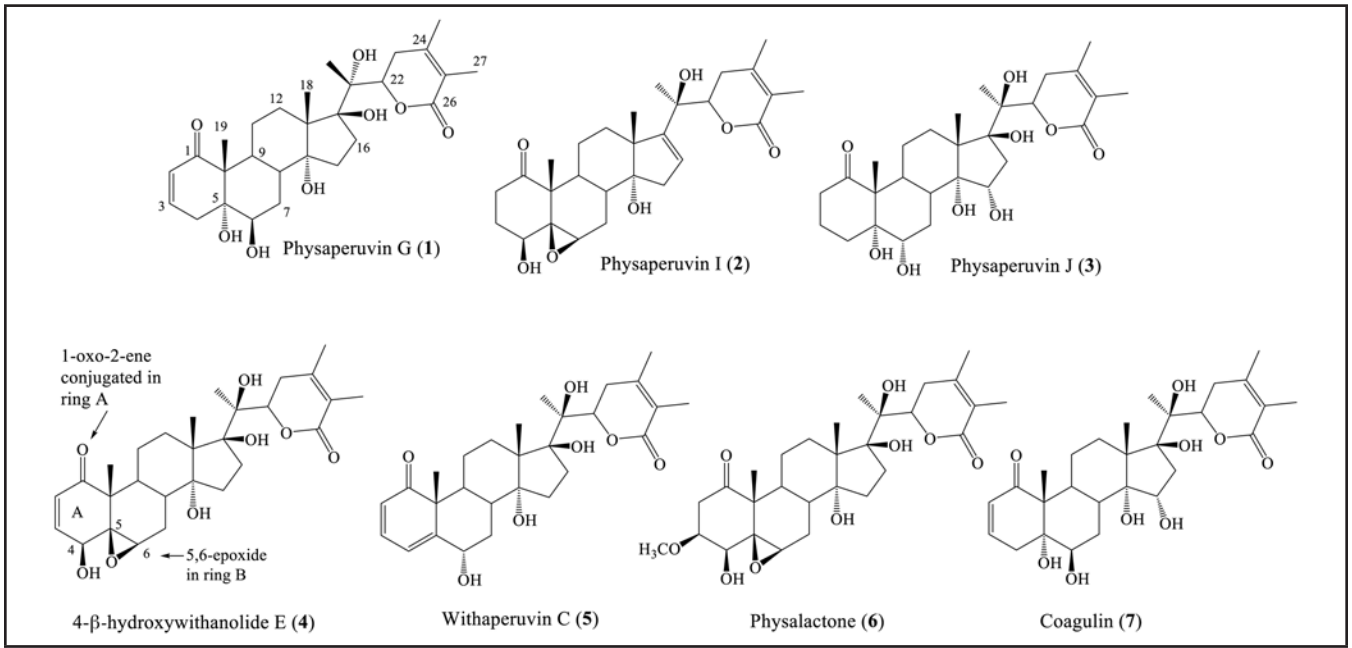


Figure 1. Structures of withanolides isolated from the aerial part of *P. peruviana*.

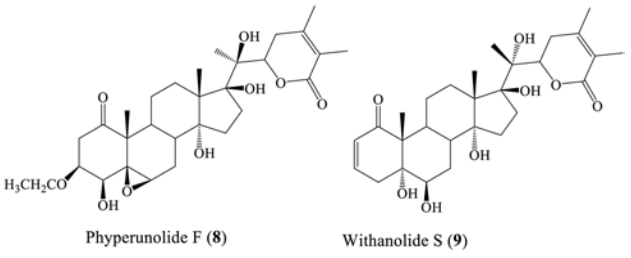


Figure 2. Structures of withanolides isolated from the fruits of *P. peruviana*.

Biological Evaluation

Anti-inflammatory Activity

The results of these assays indicate that several anti-inflammatory withanolides, namely, 4β-hydroxywithanolide E (**4**), withaperuvin C (**5**), physalactone (**6**), and phyperunolide F (**8**), purified from the aerial parts and fruits of *P. peruviana*, have potent TNF-α-induced NF-κB inhibitory activity, displaying IC_{50} values ranging of 0.04-5.6 μM (Table 1).[16,38] The remaining withanolides were either moderately active (IC_{50} 8.9–31.2 μM) or inactive. The half-maximal inhibitory concentration (IC_{50}) is reflective of the efficacy of a compound in inhibiting a specific biological function (TNF-α-induced NF-κB activity). The potency of 4β-hydroxywithanolide E (**4**) was greater than that of *N*-tosyl-L-phenylalanylchloromethyl ketone (TPCK), a positive control used for NF-κB activity (IC_{50} 5.09 μM) (Table 1).

Oh and coworkers (2008)[41] demonstrated that withaferin A (**10**) inhibits inflammation through inhibition of iNOS gene expression and NO production via inactivation of protein kinase B, also known as Akt, and subsequently down-regulating of NF-κB activity. Therefore, withanolides may have general potential for cancer chemoprevention due to their anti-inflammatory properties. Furthermore, Kleinert and coworkers (2003)[17] found that activation of the transcription factors NF-κB and STAT-1α could lead to activation of the iNOS promoter, and this appears to be an essential step for iNOS induction in most cells. Based on previous studies, inhibition of NF-κB activity correlated with inhibition of NO-production. Consequently, the anti-inflammatory effect of withanolides was tested against inhibition of NO production with LPS-treated murine macrophage RAW 264.7 cells. 4β-Hydroxywithanolide E (**4**), withaperuvin C (**5**), and physalactone (**6**) showed the highest NO-inhibitory activity against LPS-induced nitric oxide release, with IC_{50} values in the range of 0.32-2.4 μM (Table 1). In this test, cytotoxicity was observed with 4β-hydroxywithanolide E (**4**) at the 50% inhibitory concentration (Table 1). Some molecular mechanisms underlying the cytotoxic effects of 4β-hydroxywithanolide E (**4**) include the generation of damaged DNA, production of reactive oxygen species, and induction of apoptosis.[42] In contrast, withaperuvin C (**5**), physalactone (**6**), and phyperunolide F (**8**), inhibited NO production with IC_{50} values of 2.3-6.2 μM without apparent cytotoxicity to host cells (Table 1, % survival at concentration of 50 μM for **5**, **6**, and **8** were 79.3 –100.0%). Since the potency of these compounds were greater than that of L-N^G-monomethyl arginine citrate, a positive control for iNOS (IC_{50} 23.5 μM) (Table 1), withaperuvin C (**5**), physalactone (**6**), and phyperunolide F (**8**) appear to be attractive leads for further studies.

Poha fruit

Table 1. Results of anti-inflammatory activities of purified compounds from *P. peruviana*.[16,38]

Compounds	NF-κB assay			Nitrite assay		
	% Inhib.[a]	IC_{50} (μM)	% Surv.[b]	% Inhib.[c]	IC_{50} (μM)	% Surv.[d]
Physaperuvin G (**1**)	65.8 ± 4.9	31.2 ± 3.3	89.6 ± 10.1	26.4 ± 2.7	ND	84.1 ± 3.0
Physaperuvin I (**2**)	43.7 ± 4.0	ND[e]	81.9 ± 0.5	64.7 ± 4.4	14.6 ± 1.2	100.0 ± 1.3
Physaperuvin J (**3**)	60.4 ± 2.9	10.4 ± 3.6	83.9 ± 2.2	47.7 ± 2.0	ND	100.0 ± 4.0
4β-Hydroxywithanolide E (**4**)	99.5 ± 0.1	0.04 ± 0.03	88.6 ± 10.1	99.4 ± 0.1	0.32 ± 0.02	50.1 ± 13.3
Withaperuvin C (**5**)	85.0 ± 4.4	5.6 ± 2.11	100.0 ± 8.0	99.2 ± 0.7	2.4 ± 0.2	79.3 ± 1.2
Physalactone (**6**)	64.4 ± 2.9	2.1 ± 0.23	73.3 ± 7.9	97.9 ± 2.0	2.3 ± 0.2	90.7 ± 5.0
Coagulin (**7**)	70.2±8.1	8.9	82.2 ± 3.9	67.1 ± 2.2	16.7 ± 0.3	100.0 ± 6.3
Phyperunolide F (**8**)	86.8±1.8	0.06	100 ± 8.0	88.4 ± 0.8	6.2± 1.6	100.0 ± 0.7
Withanolide S (**9**)	41.7± 3.8	ND		9.4 ± 2.6	ND	100.0 ± 2.3
TPCK[f]		5.09				
L-NMMA[g]					23.5	

[a]% Inhibition of NF-κB at 50 μM. [b]% Survival at concentration of 50 μM. [c]% Inhibition of NO production at 50 μM. [d]% Survival at concentration of 50 μM. [e]ND, Not determined. [f]Positive control for NF-κB. [g]Positive control for NO.

Anti-cancer Activity

Of cancers affecting both men and women, colorectal cancer is the second leading cause of cancer deaths in the United States. Although a number of studies have been reported concerning the potential anti-cancer activity of withanolides, investigations with models of colon cancer are scarce. Using a small panel of colon cancer cell lines, we observed promising growth inhibitory effects following treatment with 4β-hydroxywithanolide E (**4**).[42] In addition to demonstrating activity with cells cultured as monolayers, the compound was found to mediate a significant response with three-dimensional spheroid cultures. Based on these data, we became interested in the mechanism by which (**4**) blocked colon cancer cell growth, and more detailed investigations were performed with HT-29 cells in culture (Figure 3).[42]

The mode of action facilitated by (**4**) was found to be dose-dependent. At higher concentrations, the cells underwent apoptosis. At lower doses, those considered a greater interest since the concentration required to inhibit growth of cultured cells is ~0.1 μM, a complex array of responses were observed. First, the level of $p21^{Waf1/Cip1}$, a cyclin-dependent kinase inhibitor, was enhanced, and simultaneously, the levels of several cell cycle-related proteins were reduced. In addition, the levels of Hsp90 client proteins were downregulated, nuclear sirtuin 1 (SIRT1) was increased, and histone H3 acetylated at lysine 9 was decreased. The expression of 21 genes was altered based on analysis of an array of cell cycle-related genes. Of particular note, the level of *PTGS2* (prostaglandin-endoperoxide synthase 2), which is known to be associated with poor prognosis, was decreased, and this correlated with reduced protein levels of cyclooxygenase-2 (COX-2). In sum, these data indicate that 4β-hydroxywithanolide E (**4**) functions by a unique multimodal mechanism of action and advanced testing would be worthwhile.

Withaferin A (**10**) (Figure 4) is a withanolide derivative which is very closely related to 4β-hydroxywithanolide E.[43] Withaferin A (**10**) is isolated from *Withania somnifera* which is a popular Ayuverdic herb that has the ability to reduce tumor cell proliferation while increasing overall animal survival time.[43] In addition, it has been shown to enhance the effectiveness of radiation therapy while potentially mitigating undesirable side effects.[43] Withaferin A (**10**) has been shown to have preclinical effects on human breast cancer *in vitro* and *in vivo*.[44] A report showed that withaferin A inhibited interleukin-6 (IL-6)-inducible activation of STAT3 in breast cancer cells.[45] It triggers apoptosis, which largely inhibits cell migration/invasion of breast cancer cells, even after IL-6-induced activation of STAT3.

Cysteine proteases are important proteins for therapeutic targeting of tumors and inflammatory disease.[51,52] It is known that Michael-acceptor reactions form covalent bonds with the active site of cysteine proteases to elicit a biological effect.[49,50] This Michael-reaction is the nucleophilic addition of a carbanion or another nucleophile such as a sulfhydryl group to an α,β-unsaturated carbonyl compound. Structure-activity relationship also revealed that both 4β-hydroxywithanolide E (**4**) (Figure 1) and withaferin A (**10**) (Figure 4) contain Michael-acceptor moieties, such as present in 4β-hydroxy-5β,6β-epoxy-

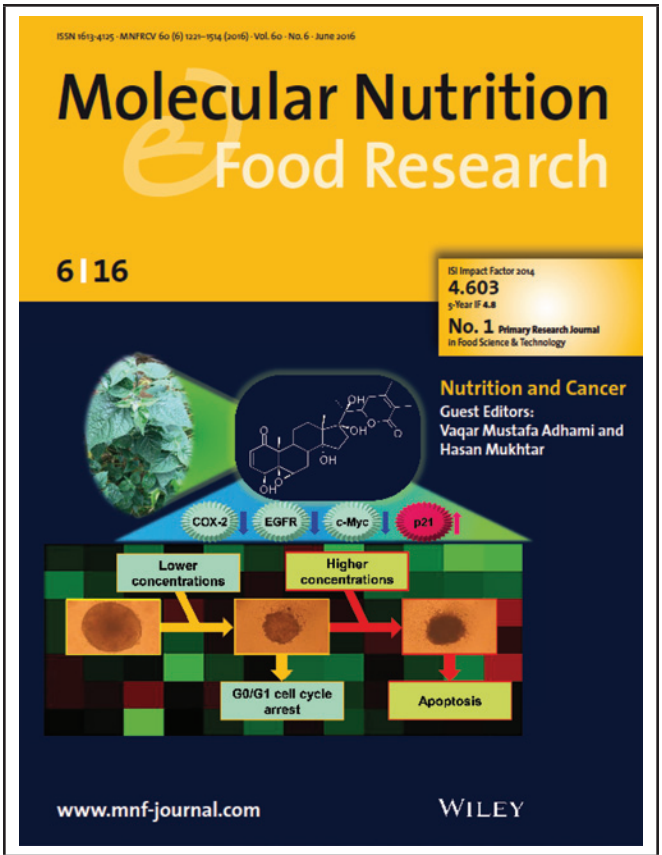
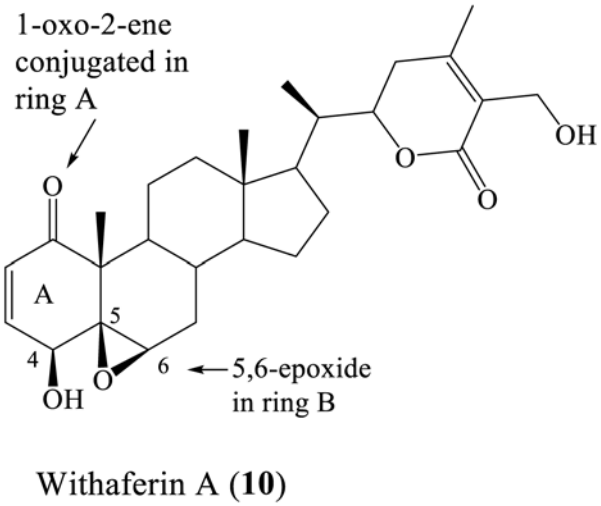


Figure 3. Journal cover featuring 4β-hydroxywithanolide E (4): Park EJ, Sang-ngern M, Chang LC, Pezzuto JM. Induction of cell cycle arrest and apoptosis with downregulation of Hsp90 client proteins and histone modification by 4β-hydroxywithanolide E isolated from *Physalis peruviana*. Mol. Nutr. Food Res. 2016; 60: 1482-1500. Copyright Wiley-VCH Verlag GmbH & Co. KGaA. Reproduced with permission.



Withaferin A (**10**)

Figure 4. Structure of withaferin A isolated from *Withania somnifera*.

2-en-1-one that are attributable to cytotoxic activity.[46-48] The α,β-unsaturated ketone moiety in withaferin A (**10**) that could exhibit Michael-acceptor reaction, may bind directly to various cellular nucleophiles and thereby lead to a loss in selectivity.

Physalactone (**6**) contains an α,β-unsaturated enoate moiety (a *δ*-lactone ring substituent at the C-17 position) and therefore may be capable of a Michael-acceptor reaction. However, in our study, the thiol-reactivity of physalactone (**6**) in NMR trapping experiments with cysteamine showed that the side chain enoate signal remained unchanged after the cysteamine addition. Furthermore, our data (Table 1) demonstrated lack of cytotoxic effects of certain withanolides. Therefore, withanolides such as physalactone (**6**) and phyperunolide F (**8**) derivatives from poha berries, deserve further studies to determine the mechanism of action.

Conclusions

As modern medicine continues to expand, so do the uses of botanical medicines. Tropical plants continue to yield new and interesting lead agents with potential for future drug development or as herbal remedies. The phytochemical and biological evaluation of *P. peruviana* collected in Pepeekeo, Hawai'i, has provided several new lead active compounds that could be developed further as new cancer chemoprevention and cancer chemotherapeutic agents. Through this research effort, we have identified withanolide derivatives as the main components in the aerial parts and poha berries of *P. peruviana*. Among the isolates, compounds 4β-hydroxywithanolide E (**4**), withaperuvin C (**5**), physalactone (**6**) from aerial parts, and phyperunolide F (**8**) from poha berries, block NF-κB transcription factor and inhibit NO production. Specifically, physalactone (**6**) and phyperunolide F (**8**) appeared to be the most promising leads. These compounds are more potent than a positive control, L-N^G-monomethyl arginine citrate (IC_{50} 23.5 μM), with less or no cytotoxicity at 50 μM. This lead could be useful for development of novel anti-inflammatory and cancer chemoprevention agents. 4β-Hydroxywithanolide E (**4**) exhibited potent antiproliferative activity with the HT-29 human colorectal cancer cell line.[42] The compound showed G0/G1 cell cycle arrest at lower concentration and induced apoptosis at higher concentrations. Furthermore, 4β-hydroxywithanolide E (**4**) modulated oncogenic proteins by downregulating Hsp90 client proteins and exerted epigenetic modification by decreasing acetylation of histone H3. In sum, our studies may help to elucidate potential mechanisms facilitated by the traditional use of *P. peruviana* as anti-inflammatory and anticancer herbs.

Future Directions

Future studies with these bioactive withanolides are needed to define the effects of the various structural features on anti-inflammatory and anticancer activities. For example, the re-isolation of sufficient quantities of promising compounds [4β-hydroxywithanolide E (**4**), physalactone (**6**), phyperunolide F (**8**)] for more advanced mechanistic studies as well as antitumor studies with animal models would be of interest. Work of this type may also lead to a better understanding of the molecular mechanisms of the cooperative roles of NO and NF-κB in cancer etiology and offer greater opportunities for the design of new chemopreventive and chemotherapeutic approaches. In addition, the potential beneficial effects of using *P. peruviana* as whole herbs should be explored.

Translational research is needed to determine if *P. peruviana* can mediate any beneficial responses in humans, and to determine an optimal dosage range for achieving these effects. As an herb, *P. peruviana* might be used in conjunction with radiation therapy or chemotherapy to ameliorate toxicity, which speaks to its potential role in integrative oncologic care. Model systems for the evaluation of health claims made for herbal remedies derived from poha berries including cancer chemoprevention, anti-inflammatory, antioxidant, and reduction of oxidative stress may be explored. The identification of bioactive and less cytotoxic constituents in poha berry will promote the use of the plant in Hawai'i as an herbal remedy in anticancer and cancer chemoprevention regimens. Finally, improving and promoting local products in the State of Hawai'i could be particularly important in enhancing the economic well-being of Hawai'i, and possibly leading to sustainable drug development or as an herbal remedy.

Conflict of Interest

None of the authors identify any conflict of interest.

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THE WEATHERVANE

RUSSELL T. STODD MD; CONTRIBUTING EDITOR

RE-EXAMINING THE LIMITS OF PATIENT CONFIDENTIALITY.

Two weeks before a Germanwings co-pilot deliberately crashed the Airbus 320 into the French Alps in March 2015, a doctor recommended psychiatric hospitalization for the flight officer. Sadly for the 150 people onboard and their families, he did not take action out of fear of breaching Germany's privacy laws. The twin engine Airbus was enroute from Barcelona to Dusseldorf when the captain left his seat to go to the bathroom. 30 seconds later, Andreas Lubitz, the 27 year-old co-pilot, put the aircraft into a steep dive and steered into a remote mountain range. The report details how Mr. Lubitz's private physician, who worried that his patient was psychotic, and a psychiatrist who also treated the pilot "were probably aware" of his occupation. Yet the health care providers failed to inform any aviation authority or government agency about the co-pilot's mental state. German health care people operate under some of the most stringent patient privacy laws carrying stiff criminal penalties, but they are allowed to breach confidentiality in cases of "imminent danger" to the public. Investigators are expected to pursue changes in privacy laws in Germany and across Europe in the 87- page report.

IN ANY OTHER BUSINESS THEY'D BE CALLED PUSHERS.

Always on the lookout for opportunities to push their best-selling brand, Newport cigarettes, R.J. Reynolds American Inc. is marketing a package of 20 for one dollar. Workers will hand out vouchers at bars, convenience stores, festivals, and ball games that customers take to the Newport Pleasure Lounge, a mobile air-conditioned trailer. There the voucher will provide a pack of Newports for a mere dollar. Quite a bargain, since in New York tax alone is $4.35 per pack. This cigarette accounts for almost all of Lorillard's (company marketing Newports) $7 billion in sales for 2014 and is the only major brand consistently gaining share of the shrinking tobacco market over the past decade. Two 18-wheelers take Newport lounges to events popular with 21 to 30 year-olds such as Las Vegas, fairs, or music festivals. Representatives check ID and refuse to sell to non-smokers. The appeal of mentholated cigarettes mirrors the milennials' desire for more flavorful foods and beverages.

MANY PEOPLE CLAP, A FEW EVEN CRY AND ALMOST ALL SMILE.

On August 21, 2017, millions of people will know something is wrong when a total eclipse of the sun sweeps across the country. Astronomer Jay Paschoff of Williams College, Massachusetts says, "You don't know what's going on, but you know something is wrong." The first eclipse to move coast to coast in almost a century, the darkness will come ashore at 10:16 A.M. Pacific time at Lincoln City and Depoe Bay, Oregon, and proceed eastward to darken Oregon, Idaho, Wyoming, Nebraska, Kansas, Illinois, Missouri, Kentucky, Tennessee, North Carolina, Georgia, and South Carolina. It will pass over 5 state capitols, Salem, OR, Lincoln NE, Jefferson City Mo, Nashville TN, and Columbia, S.C. it will cut a path of totality about 150 kilometers wide (90 miles) and move at 2,700 kilometers per hour (1,650 mph) so don't try to keep up with it in your Mustang Cobra. Just east of St. Louis at a spot in the Shawnee National Park, it will show the longest duration of totality at 2 minutes and 42 seconds. Cape Island, South Carolina, is the final stop as the eclipse departs at 2:49 P.M. Eastern time, just about an hour and a half after landfall on the Oregon coast. Based on a typical weather pattern for mid-August the western half of the path is more likely to cooperate with clear skies. Eclipse enthusiasts will travel from all over the world to experience almost 3 minutes of twilight and glimpse the seldom seen solar corona, a halo of light from plasma that will frame the blocked out sun. This is a once-in-a-lifetime astronomy treat. Try to be there.

A TREAT YES, BUT DON'T LET IT BECOME A TRICK.

It is an almost magical event. Still, remember that damaging radiation can burn the retina. You can look at the sun briefly during eclipse totality as it passes over you. Beyond totality looking directly at the sun can burn the retina and no eye medication nor eye surgeon can replace a cooked retina. One percent of the remaining sun shadow is 10,000 times more powerful than the full moon's light.

IS THE FDA OWNED BY BIG PHARMA TOO?

After the media revelation about the dangers of the morcellator, an internal medicine team reporting in the Journal of the American Medical Association (JAMA) found that 42 out of 50 selected medical devices cleared by the Food and Drug Administration (FDA) over 5 years lacked supporting data. In 1990 the Safe Medical Devices Act was passed calling for sufficient data to justify FDA clearance of new or modified devices. "If wonderful studies are being done, there is no evidence of this, and no way for the public to see it," according to Dr. Diana Zuckerman, study author and president of the National Center for Health Research. She found it shocking that very little information is available despite an FDA claim of transparency. At issue is a type of medical device approval where nearly 400 implanted devices annually are cleared by the FDA. The system is called 501 (K) and the company can get clearance simply by showing that the product is roughly equivalent to a similar one already on the market. Wow. You could throw a cat through that loophole.

IT'S ONLY A DEATH BED CONFESSION IF YOU DIE.

In 1995 in Nashville, Tennessee, James Washington committed murder but escaped prosecution. Fourteen years later in 2009 while incarcerated on an unrelated charge, he suffered a severe heart attack and believed he was about to die. While in mortal extremis he called an officer to his side and said he wanted to confess the murder and get it off his conscience before he died. Miraculously he recovered and tried to recant his confession. The Nashville prosecuting attorney combined the confession with sparse evidence from 1995 and obtained a murder conviction. Washington was sentenced to 51 years in prison.

ONE MORE USE FOR YOUR IPHONE.

Do you ever wonder what is happening with that rumbling gas in your gut? If you want to know, an Australian research team has designed an encapsulated device that can be swallowed and will detect hydrogen, methane, and fiber content. About the size of a brazil nut, the capsule was tested in pigs fed varying amounts of fiber. Impulses can be transmitted to an iPhone and theoretically could assist in diagnosing irritable bowel syndrome, among other GI disorders. It might also be used to liven up a dull party.

ADDENDA

- A regulation hole in golf must be 4.25 inches in diameter and no less than 4 inches deep.
- No matter how much you push the envelope, it is still stationery.
- Love is an exploding cigar we willingly smoke.
- In every fat book there is a thin book trying to get out.
- When I get mad, it makes me want to do yard work, so my wife spends most of the day following me around trying to piss me off.
- I don't like to admit I'm old and worn out, but I stay away from the curb on garbage day.

ALOHA AND KEEP THE FAITH rts

(Editorial comment is strictly that of the writer.)

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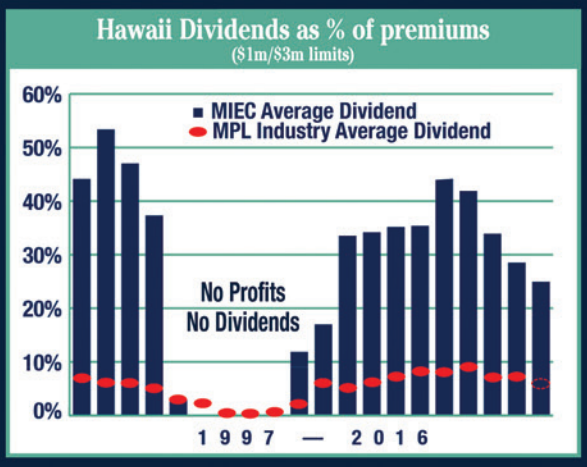

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