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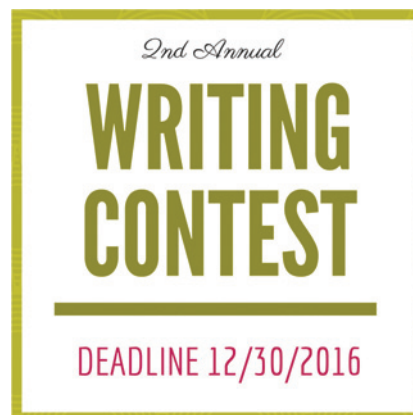
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A 23-year-old Man with Leptospirosis and Acute Abdominal Pain

Momal Mazhar MD; Janet J. Kao MD; and Dennis Thomas Bolger Jr. MD, MPH

Abstract

*Leptospirosis is a zoonosis caused by the spirochete *Leptospira interrogans*. Most cases of leptospirosis are mild to moderate, and self-limited. The course of disease, however, may be complicated by multiorgan dysfunction such as in Weil's disease. We present a case of Weil's disease with pancreatitis in a young Caucasian man residing in Hawai'i. Although leptospirosis is common in Hawai'i, few patients present with pancreatitis. This report of leptospirosis-induced pancreatitis should help raise awareness of clinicians to assess for pancreatitis when evaluating a patient with leptospirosis and acute abdominal pain.*

Keywords

Leptospirosis, Weil's disease, pancreatitis, multiorgan dysfunction, hyperbilirubinemia, acute abdominal pain

Introduction

Leptospirosis is a zoonosis caused by the spirochete *Leptospira interrogans*. Compared to temperate regions, the incidence of this disease is significantly higher in tropical and subtropical regions.¹ In the United States, an estimated 100-200 leptospirosis cases are identified annually, of which 50% occur in Hawai'i.² The infection is primarily transmitted to humans through direct contact with water, mud, or soil contaminated with the urine of chronically infected mammals and rodents.³ An incubation period of 5-14 days is typical. During this time, the spirochetes proliferate in the bloodstream and then disseminate hematogenously. The clinical manifestations of leptospirosis in humans vary from a subclinical infection to severe illness with multiorgan dysfunction. Usual disease presentation includes a flu-like illness with mild hepatic and renal impairment, whereas severe disease forms are characterized by hepatorenal failure, encephalopathy, and pulmonary hemorrhage.⁴⁻⁶ The illness itself has a biphasic nature: an initial septicemia phase and consequent immune phase. During septicemia, patients will present with fever, headache, myalgia, conjunctival suffusion, and various non-specific findings such as mild cough, rash, lymphadenopathy, nausea, and vomiting.⁷ Subsequently, patients may have a brief afebrile period of variable duration whereafter they develop organ derangements, most commonly of the liver and kidneys. In rare cases, it is reported to directly affect other organs such as the eye, bone marrow, and pancreas. Weil's disease, the most severe form of illness, is characterized by jaundice, renal failure, and hemorrhage with a variable clinical course.⁴ Infected patients with acute renal failure may demonstrate elevated serum amylase levels, however, clinical symptoms of pancreatitis are uncommon.⁴ We present a case of Weil's disease accompanied by pancreatitis.

Case Report

A 23-year-old Caucasian man from the continental United States residing in Hawai'i presented to the emergency department (ED) three days prior to admission with a two-day history of fever (104F/40C), chills, headache, neck stiffness, productive cough, nausea, and diffuse myalgias. At that time, he denied photophobia, rash, abdominal pain, and diarrhea. On exam, he was found to be tachycardic (119 beats per minute [bpm]) and febrile (101.4F/38.5C). He received 2 L normal saline. He was reassessed and found to be hemodynamically stable. He was discharged by the ED physician with prescriptions for acetaminophen and ondansetron. The patient reported that his fever was controlled with acetaminophen, however, his nausea was unremitting.

Two days after his first ED visit, the patient developed symptoms of photophobia, non-bloody, watery stools, non-bloody, non-bilious emesis up to seven times per day, bloody sputum, and dark tea-colored urine. On the night prior to his second ED visit, the patient also noticed yellowing of his eyes and face and onset of abdominal pain prompting him to return to the ED. The patient reported swimming in freshwater 2 weeks prior to admission, but denied skin abrasions and water ingestion. He further denied history of recent travel, sick contacts, eating uncooked foods, animal bites, and positive purified protein derivative (PPD) status. Upon questioning, the patient admitted to recreational alcohol consumption, his last episode being consumption of 4 beers (48 fluid ounces) twelve days prior to onset of illness.

Abbreviations

ALT: alanine aminotransferase
AST: aspartate aminotransferase
bpm: beats per minute
CDC: Center for Disease Control
CT: Computerized tomography
ED: Emergency Department
ICU: Intensive Care Unit
IgM: Immunoglobulin M
INR: International Normalized Ratio
PPD: Purified Protein Derivative
PT: Prothrombin Time
PTT: Partial Thromboplastin Time

Upon admission, the patient's vital signs were significant for hypertension (149/81 mmHg), tachycardia (120 bpm), pyrexia (101.1F/38.4C), and tachypnea (24 breaths per minute); he also demonstrated pulse oximetry of 94% on room air, and BMI 22 kg/m². In addition, he was icteric, with conjunctival injection but no suffusion. He had decreased breath sounds bilaterally, abdominal rigidity, and arthralgias of his hips, knees, and ankles, but no effusions. Kernig's and Brudzinski's signs were absent. On abdominal exam, bowel sounds were hyperactive. Abdominal organomegaly could not be assessed because the patient had severe rigidity and tenderness to palpation and percussion. There was no rebound tenderness.

Laboratory studies demonstrated leukocytosis (approximately 18,000/mm³) with neutrophil predominance (83%), thrombocytopenia (42,000/mm³), hyponatremia (132 mEq/L), hypokalemia (3.0 mEq/L), respiratory acidosis, metabolic alkalosis, and wide anion gap acidosis, as well as acute kidney injury (creatinine levels 4.4 mg/dL). Total creatine kinase was elevated (1162 IU/ml), alanine aminotransferase (ALT) and aspartate amino-

transferase (AST) were elevated (184 mEq/L and 144 mEq/L, respectively), and there was significant hyperbilirubinemia (total 13.0 mEq/L, direct 9.9 mEq/L, indirect 3.1 mEq/L). Coagulation studies demonstrated prothrombin time (PT) 13.2 seconds, partial thromboplastin time (PTT) 28.9 seconds, and international normalized ratio (INR) of 1.0. Urinalysis revealed large amounts of blood and bilirubin. Troponin I was not elevated. Computed tomography (CT) scan of the chest (Figure 1) revealed diffuse, bilateral peribronchial thickening and consolidation with extensive bud nodular opacities. Abdominal ultrasound was performed and did not demonstrate gallbladder inflammation, common bile duct dilatation, or evidence of gallstones. CT scan of the abdomen was performed without oral or intravenous contrast, due to the patient's acute kidney injury, and demonstrated hepatosplenomegaly without biliary dilatation and an unremarkable pancreas.

The patient was admitted for systemic inflammatory response syndrome with suspicion for infection or inflammation in the hepatobiliary system. Differential diagnoses included chol-



Figure 1. Computed tomography (CT) scan of the chest demonstrating diffuse, bilateral peribronchial thickening and consolidation with extensive bud nodular opacities.

angitis, pancreatitis, hepatitis (viral, autoimmune, drug- or toxin-associated), leptospirosis, dengue, murine typhus, and typhoid fever. As such, he was started on empiric intravenous antibiotics (doxycycline, ceftriaxone, and metronidazole) while awaiting blood/sputum/urine/stool cultures, gram stains, and serological test results.

Shortly after admission to the medical floor, the patient developed respiratory distress. He was found to have oxygen saturation of 80% on room air. He was tachycardic, tachypneic, and expectorated a large volume of blood. The patient quickly became less responsive to verbal stimuli. Given his acute respiratory failure, the patient was transferred to the intensive care unit (ICU) where he was supported with supplemental high flow oxygen via Venturi mask and close monitoring. At this time, the patient's serum lipase was found to be 1750 Units/Liter (normal range 13-60 U/L). The patient became increasingly lethargic and he was unable to tolerate oral intake. The patient's condition slowly improved with intravenous fluids and empiric triple antibiotic therapy. He was weaned to supplemental oxygen via nasal cannula and had no further respiratory distress or evidence of recurrent pulmonary hemorrhage.

Back on the hospitalist ward team, the patient demonstrated jaundice, decreased abdominal rigidity, and tenderness to palpation predominantly in the right upper quadrant and epigastric region. Laboratory values demonstrated down-trending hepatic transaminases, serum creatinine, and creatine kinase. However, serum bilirubin levels were increased (total 18.7 mEq/L, direct 16.5 mEq/L, indirect 2.2 mEq/L). Abdominal ultrasound was repeated and showed an unremarkable pancreas and gallbladder, but demonstrated hepatomegaly without evidence of biliary dilatation or ascites. The patient was started on a clear liquid diet and continued to demonstrate nausea and epigastric pain without emesis. Serological tests returned significant only for leptospira immunoglobulin M (IgM). The Center for Disease Control (CDC) would define a positive leptospira IgM as a probable case. The patient's antibiotics were narrowed to intravenous doxycycline. The patient was discharged after demonstrating clinical improvement on completion of seven-days of intravenous doxycycline. At the time of discharge, the patient was able to tolerate a regular diet without nausea. The patient was educated that his illness was likely related to freshwater exposure to the infectious agent and counseled on methods for decreasing risk.

Discussion

Leptospirosis is a disease with a variable grade of severity and organ involvement. Neurologic injury is seen in up to 25% of all cases and is most commonly associated with aseptic meningitis; however, intracranial hemorrhages, cerebellitis, and myelitis have been reported as well.^{4,8} Hepatic injury is associated with disruption of cellular cohesion, plugging of bile canaliculi, and occasional acute inflammatory infiltrates.⁴ This pathophysiology is consistent with the laboratory findings of hypertransaminemia, and direct hyperbilirubinemia. Pulmonary injury often presents with hemorrhage, as in our patient, and

has been related to toll-like receptor (TLR) activation from *Leptospira* lipoproteins.^{4,5} Cardiac involvement may present with non-specific electrocardiogram abnormalities or findings consisting with pericarditis or myocarditis (PR interval prolongation, T-wave inversion, first degree atrioventricular block).⁴ Acute renal failure, also associated with TLR activation, is reported in 16%-40% of cases where oliguria is a significant predictor of death.^{4,9}

Although acute pancreatitis has been recognized as a rare involvement of the multiorgan dysfunction of leptospirosis, most reported cases are of patients who developed hemorrhagic or necrotizing pancreatitis several days after the onset of disease. Furthermore, most reports deal with leptospirosis cases occurring in under-developed countries and involving mainly elderly patients.¹⁰⁻¹³ The case presented herein adds to the body of knowledge in that leptospirosis-induced pancreatitis occurred in a young patient and at the early onset of disease. This patient developed acute abdominal pain and rigidity coupled with high lipase level and inadequate pancreatic imaging. He became critically ill from a combination of acute kidney injury, acute respiratory failure, pancreatitis, acute cholestatic hepatitis, and immune dysfunction. In the context of this report, it is important to consider alcohol consumption as a possible cause of pancreatitis. However, the patient reported last ingestion 12 days prior to disease onset, decreasing the likelihood of alcohol-induced pancreatitis. Also, patients often minimize the amount consumed. Animal studies suggest alcohol consumption is usually not associated with pancreatitis unless 5 drinks or more per day (60 g of ethanol) are consumed.¹⁴ Nonetheless, such results suggest that ethanol could sensitize the pancreas to injury while additional factors may trigger the development of overt pancreatitis. In the setting of leptospirosis, this may be *Leptospira* antigen-associated vascular endothelial damage, which has been associated with the various other organ dysfunctions of leptospirosis.⁴ Vascular injury most likely causes ischemic effects on the pancreas such as through decreased removal of reactive oxygen species, intracellular enzymes and toxins, and increased stasis of injurious elements that, together, may manifest as acute pancreatitis. *Leptospira interrogans*-induced acute pancreatitis seems rare. However, because of the high mortality rate associated with pancreatitis, clinicians should keep in mind the possibility of *Leptospira*-induced pancreatitis when confronted with leptospirosis.¹⁵

Conclusions

Leptospirosis is a frequently encountered infectious disease in Hawai'i and certain other parts of the world. Weil's disease represents the most severe form of leptospirosis. While multi-organ dysfunction is common, pancreatitis is rare. Furthermore, significant alcohol consumption may predispose leptospirosis patients to pancreatitis. Acute pancreatitis is associated with significant morbidity and mortality, resulting in the death of 20% of patients.¹⁶ Thus, it is essential to assess risk factors for pancreatitis, such as alcohol consumption and gallstones, in patients presenting with leptospirosis.

Conflict of Interest

None of the authors identify any conflict of interest.

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E-cigarette Use Related to Demographic Factors in Hawai'i

Jason C. Seto; James W. Davis PhD; and Deborah A. Taira ScD

Abstract

E-cigarette use is rapidly expanding in the United States and is projected to be a \$3 billion industry by the end of this year. E-cigarette use in Hawai'i is significantly higher than national averages. The goal of this study was to examine the relationship in Hawai'i between demographic characteristics and several aspects of e-cigarette use including percentage of residents trying e-cigarettes, reasons for use, and perceived effects on health. Survey data were collected from a random sample of Hawai'i residents via the telephone in the summer of 2015, using methodology similar to that of the Hawai'i Health Survey. Chi-squared tests found e-cigarette use to be significantly associated with age ($P=.001$), gender ($P=.03$), ethnicity ($P<.001$), and education ($P<.001$). Among e-cigarette users, 12% said they started smoking regular cigarettes after starting e-cigarettes, 21% said their use of regular cigarettes did not change, 6% said they reduced use of regular cigarettes, and 20% said they completely stopped smoking regular cigarettes. Multivariable logistic regression results suggest Native Hawaiians ($OR=29.1$, $P=.01$) and Filipinos ($OR=24.3$, $P=.01$) were significantly more likely to report perceived improved health due to e-cigarette use compared to Caucasians. Given existing health disparities for Native Hawaiians and Filipinos, the fact that these groups are significantly more likely than other ethnic/racial groups to report that e-cigarettes improved their health bears notice and highlights the need for additional research in this area.

Keywords

Electronic cigarettes, smoking, health disparities, Hawai'i

Introduction

E-cigarettes are small, battery powered devices that heat a liquid into an aerosol that is then inhaled to simulate smoking.¹ Sales in the United States were estimated at \$1 billion in 2013 and are expected to climb to \$3 billion by 2015 as a number of tobacco manufacturers are launching products.²

Despite high use rates, e-cigarettes have not been rigorously studied and there is a great deal of uncertainty as to their effects on health. One hotly debated issue is the relationship between e-cigarettes and conventional cigarettes. Proponents of e-cigarettes cite studies showing that e-cigarettes are often used to aid efforts to stop smoking conventional cigarettes, which are known to cause cancer and lead to premature death.³⁻⁵ Others, however, believe the opposite—that e-cigarettes lead to increased use of other tobacco products.⁶ Potential risks of e-cigarettes are also poorly understood.^{7,8} With e-cigarettes, the quantity of nicotine or other potentially harmful chemicals being inhaled is unclear, as is whether e-cigarette use is associated with both acute and long-term cardiopulmonary and other adverse events.

There is great concern about the prevalence of e-cigarette use among adolescents as e-cigarettes are sometimes sold in flavors (eg, bubblegum, chocolate, cotton candy) that may be appealing to teens.⁹ Marketing is currently unregulated, and e-cigarette companies have heavily invested in television advertisements attempting to make e-cigarette use seem “cool.”

A recent CDC study reports that e-cigarette use among high school students rose from 1.5% to 13.4% from 2011 to 2014.⁹ The largest increase over a one-year period occurred from 2013 to 2014 when e-cigarette use nearly tripled from 4.5% to 13.4%.⁹ In 2014, e-cigarette use surpassed the use of every tobacco product, including conventional cigarettes.

E-cigarette use in Hawai'i exceeds national averages, with use among adolescents estimated to be three times the national rate.¹⁰ An estimated 13% of smokers in Hawai'i have tried e-cigarettes as a means of stopping smoking.¹¹ Moreover, from 2011 to 2015, e-cigarette use increased six-fold from 2% to 12% among middle school students and more than quadrupled from 5% to 22% among high school students.¹² The goal of the current study was to examine the association between demographic factors and various aspects of e-cigarette use in Hawai'i, including reasons for trying, utilization per week, and perceived impact on health.

Methods

The study population ($N=937$) included English-speaking adult respondents to a representative statewide telephone survey in Hawai'i administered by SMS Research Inc, in the spring and summer of 2015. Survey question content was based on information we had obtained from qualitative interviews with e-cigarette users (unpublished). Survey methodology was similar to that of the Hawai'i Health Survey and the survey included all of the demographic questions that are part of that survey.¹³ Cell phones as well as landline phones were included in the sample. Sampling of households was stratified by island and randomized within island. Neighbor islands were oversampled in comparison to O'ahu.

E-cigarette Questions

Four questions regarding e-cigarettes were included in the health survey by the investigators (Table 1). One was whether the respondent had ever tried e-cigarettes. If they responded yes, they were asked their primary reason for use, relation to regular cigarette use, and perceived impact on their health.

Questions related to demographic variables were the same as those administered as part of the Hawai'i Health Survey and included age, gender, education level, chronic diseases, self-reported health status, and birthplace.¹³

For chronic conditions, respondents were asked about each household member: Has anyone in the household been told by a physician or medical professional that they have arthritis? Similar questions relating to diagnosis with asthma, diabetes, high blood cholesterol, and hypertension were also asked. The respondents also gave information on the educational status of each household member who was 18 years and older.

Table 1. E-cigarette survey questions	
Question	Response set
1. Have you ever tried e-cigarettes?	<ul style="list-style-type: none"> • Yes, I have tried and continue to use them; • Yes, I have tried them but I don't use them now; • No I have never tried e-cigarettes
2. Which best describes your main reason for starting to use e-cigarettes?	<ul style="list-style-type: none"> a. To quit smoking conventional cigarettes b. To cut down on use of conventional cigarettes c. More acceptable than smoking regular cigarettes d. Reduce smoking exposure to family members e. Saw friends using them f. For fun or pleasure g. Saw advertisement
3. How would you describe your use of regular cigarettes after beginning use of e-cigarettes?	<ul style="list-style-type: none"> a. I have never smoked regular cigarettes b. I currently smoke both regular cigarettes and e-cigarettes and have not changed my use of regular cigarettes c. I have reduced my use of regular cigarettes since I started using e-cigarettes d. I have completely stopped using regular cigarettes since I started using e-cigarettes e. I have started smoking regular cigarettes since I started using e-cigarettes
4. Overall, what do you believe to be the effect on your health of e-cigarettes?	<ul style="list-style-type: none"> a. Improved my health b. No effect c. Worsened my health

Respondents listed up to four ethnicities for both their mother and their father. The choices were Caucasian, Hawaiian, Chinese, Filipino, Japanese, Korean, Samoan/Tongan, Black/African American, Native American/Aleut/ Eskimo/Inuit, Vietnamese, Asian Indian, Portuguese, and Guamanian/Chamorro, or other race/ethnicity. These were categorized into a single race/ethnicity as follows: If Hawaiian was listed for the mother or father, the person's ethnicity was coded as being Native Hawaiian. Otherwise, the person was categorized according to the first ethnicity listed (other than Caucasian or unknown) for the father. If the father's responses were Caucasian and/or unknown, the person's ethnicity was coded to the first ethnicity listed (other than Caucasian or unknown) for the mother. If there were no other responses other than Caucasian or unknown, the person was categorized as Caucasian. Otherwise, the person's ethnicity was coded as "do not know, refused, or missing."

Statistical Analyses

Descriptive statistics are presented as means for continuous variables and frequencies for categorical variables. Chi-squared tests were used to examine differences in trying e-cigarettes, and reasons for trying them related to demographic characteristics. A logistic regression model was used to examine perceptions of the impact of e-cigarettes on health (better, same, worse) related to demographic characteristics. We included individuals who reported ever using e-cigarettes or currently use e-cigarettes in this model. Independent variables examined were those with *P*-values of at least 0.2 in bivariate analyses. These included age, island, gender, self-reported health status, ethnicity, education, birthplace, and chronic disease. For each independent variable, the largest subgroup was used as the reference group (age 35-64, living on O'ahu, male, Caucasian, high school education, born in Hawai'i, and no chronic disease).

All analyses were completed in SAS. Sample weights were included in the analyses to account for the complex survey design. These weights reflect the probability of household selection, household non-response, a factor for crude completion adjustment, and post-stratification by age-sex-strata. This study was granted exempt status by the University of Hawai'i Institutional Review Board.

Results

Characteristics of the Study Population

The final survey sample included 937 individuals. Our study population consisted of slightly more males than females (53.7% to 46.3%, Table 2). A disproportionate number of participants were over the age of 65 (35.2%). Also, 61% lived on O'ahu. As is consistent with the multiethnic nature of the population in Hawai'i, no one race or ethnicity made up a majority of the sample. The three largest groups by race and ethnicity were Caucasian (35.7%), Japanese (21.4%), and Native Hawaiian (15.5%). Approximately half (46.8%) had a college education or higher, and 40.4% reported having a chronic disease condition.

Tried E-cigarettes

Figure 1 displays the percent of respondents who: (1) tried e-cigarettes and still use them (6.5%); (2) tried but do not currently use (12.9%); and 3) never tried e-cigarettes (80.6%). The proportion of respondents trying e-cigarettes differed significantly by age ($P=.001$), ethnicity ($P<.001$), education level ($P<.001$) and gender ($P=.03$).

Overall, approximately 30% of participants under the age of 24 had ever tried e-cigarettes. The majority (83%) of those who ever tried e-cigarettes said that they did not continue their use. In the subsequent age groups 25-34, 35-54, and 55-64, the percentage of those who tried e-cigarettes gradually decreased.

Table 2. Demographic Characteristics of the Study Population (N=937)		
Factor	Characteristic	Weighted %
Age	Age 18-24	10.1%
	Age 25-34	11.7%
	Age 35-64	43.0%
	Age 65+	35.2%
Island	O'ahu	61.0%
	Other island	39.0%
Gender	Female	46.3%
Self-reported health	Excellent health	28.8%
	Poor, fair, or good health	61.2%
Ethnicity	Caucasian	35.7%
	Filipino	8.9%
	Japanese	21.4%
	Native Hawaiian	15.5%
	Other race/ethnicity	18.5%
Education	College or higher	46.8%
	Junior college	25.2%
	High school or less	27.8%
Birthplace	Hawai'i	53.6%
	Mainland or other country	46.2%
Chronic disease	No	59.6%
	Yes	40.4%

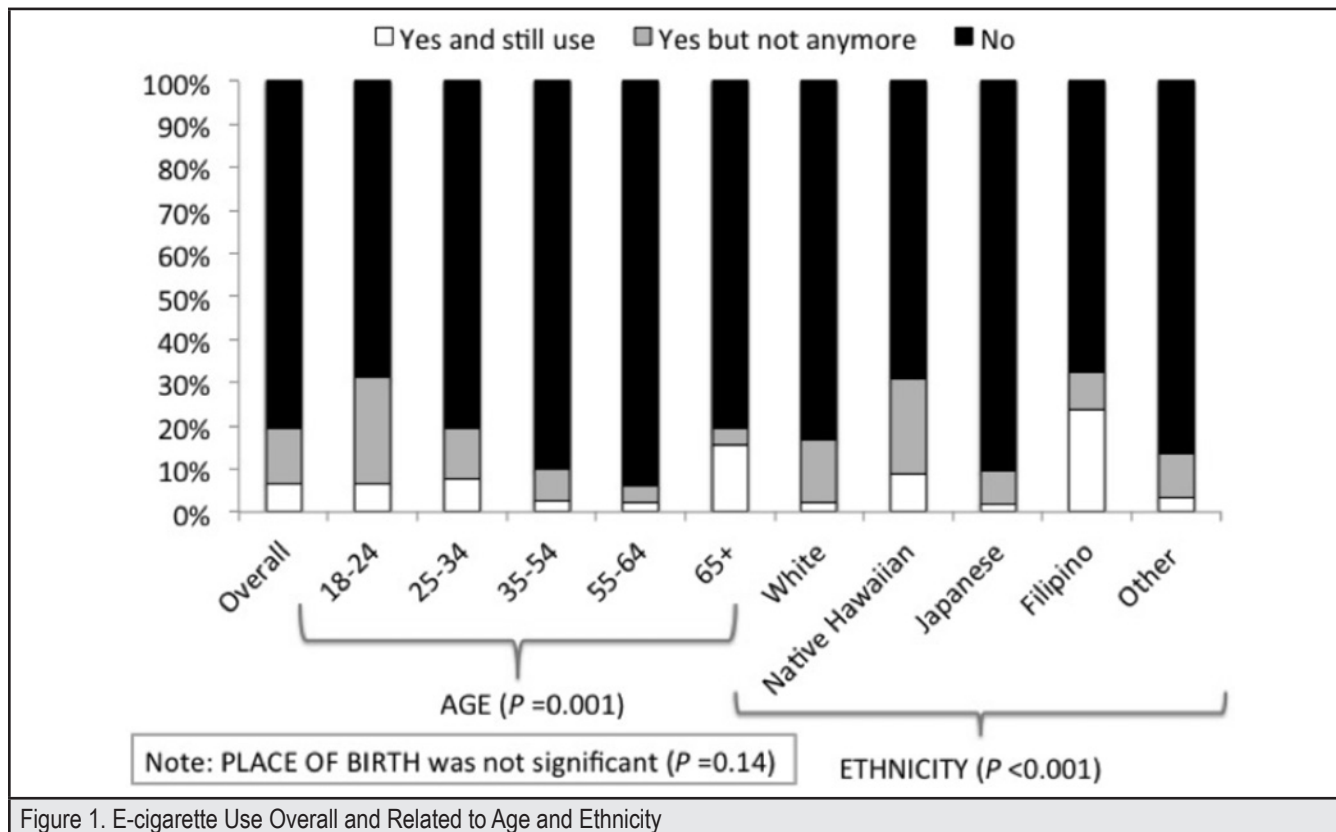


Figure 1. E-cigarette Use Overall and Related to Age and Ethnicity

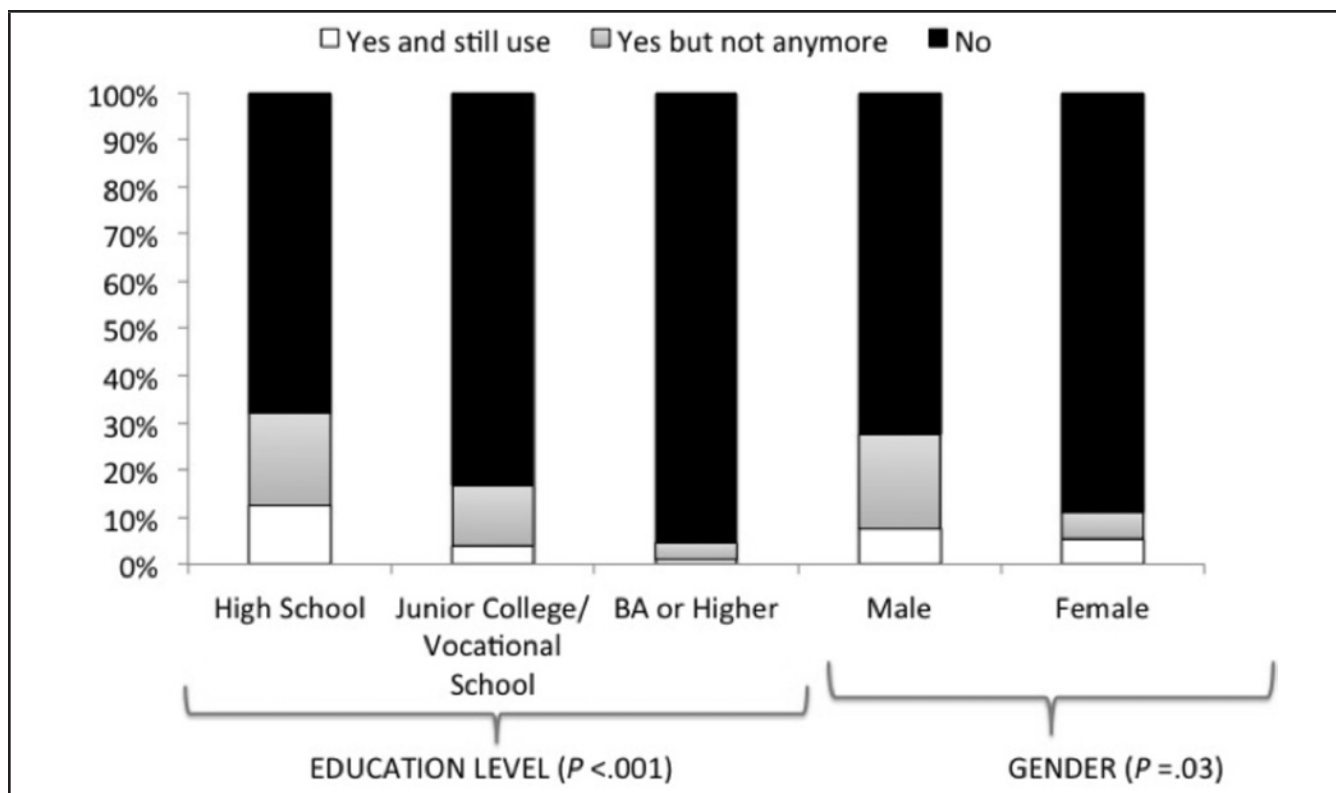


Figure 2. E-cigarette Use Related to Educational Level and Gender

However, for the 65-74 age group, more than 35% of respondents had ever tried e-cigarettes, and the majority of respondents in this age group said that they continued to use e-cigarettes.

E-cigarette use was most prevalent in Filipinos (32%) and Native Hawaiians (31%) followed by Caucasians (17%), other (14%), and Japanese (9%) (Figure 1). With regard to gender, about 28% of males reported having ever used e-cigarettes compared to about 12% of females; a larger percentage of males also reported being former e-cigarettes users (Figure 2, $P=.03$). Our data also shows a striking and significant downward trend, with those at higher levels of education being less likely to have ever tried e-cigarettes ($P<.001$).

Reasons for Using E-cigarettes

Reasons for starting e-cigarettes varied significantly by demographic characteristics. In general, respondents tended to either start using e-cigarettes for recreational use or to quit the use of traditional cigarettes (Table 3). Over half of those under the age of 24 started using e-cigarettes for fun/pleasure while over 90% of those in the 65-74 age group started in an attempt to quit smoking conventional cigarettes ($P<.001$). About 19.2% of those ages 25-34 started e-cigarettes to reduce regular tobacco exposure to family members as opposed to less than 7% across the other age groups.

The reasons for starting e-cigarettes varied significantly by race and ethnicity (Table 3, $P=.003$). Approximately 65% of

Caucasians started e-cigarettes for recreational purposes and about the same percentage of Filipinos started to quit smoking conventional cigarettes. Close to half of Japanese, other Asian/Pacific Islanders, and Native Hawaiians started using e-cigarettes for recreational purposes and the other half reported using them as a replacement for conventional cigarettes.

Over 60% of males started using e-cigarettes either for fun or pleasure or because they saw their friends using, while around 75% of females started e-cigarettes to quit smoking conventional cigarettes ($P<.001$; Table 3). Education level ($P>.05$) and birthplace ($P=.15$) were not significantly associated with reasons for use.

Relation of E-cigarette Use on Use of Regular Cigarettes

When describing use of regular cigarettes after beginning e-cigarettes, 40% said they never smoked regular cigarettes, 21% said their use of regular cigarettes has not changed, 6% said they reduced use of regular cigarettes, and 20% said they completely stopped smoking regular cigarettes, whereas 12% said they started smoking regular cigarettes (Figure 3).

Perceived Health Effects

In the unadjusted logistic regression model, age, island, self-reported health and ethnicity were significantly associated with the perception that e-cigarette use improved health (Table 4). Those older than 65 years ($OR=18.0$; $P=.03$) were more likely

Table 3. Reason for Starting E-cigarettes Related to Age, Gender, Ethnicity, and Place of Birth (Weighted Percent).							
	Quit cigarettes (%)	Cut down on cigarettes (%)	More acceptable (%)	Reduce family member exposure (%)	Saw friends using (%)	Fun or pleasure (%)	P-value
Age							
18-24	12.4	4.9	0.0	6.3	26.0	50.5	<.001
25-34	42.7	7.9	4.5	19.2	8.5	17.1	
35-54	55.0	2.4	6.4	1.2	3.5	21.1	
55-64	46.3	22.5	0.0	0.0	19.4	11.8	
65-74	92.7	3.6	0.2	1.0	0.7	0.6	
75+	42.2	57.8	0.0	0.0	0.0	0.0	
Gender							
Male	22.3	5.1	1.5	8.6	19.0	40.7	<.001
Female	73.8	7.1	2.2	0.4	7.2	9.2	
Birthplace							
Hawai'i, Urban	26.3	11.2	1.4	12.9	16.5	31.3	.15
Hawai'i, Rural	18.4	0.0	0.6	0.8	43.3	25.6	
Other US State	36.1	0.6	4.7	0.3	3.5	54.8	
Overseas	87.3	2.4	0.0	0.0	2.0	8.3	
Race/ Ethnicity							
Caucasian	23.8	1.9	3.6	0.3	3.3	67.1	.003
Native Hawaiian	23.4	12.7	2.6	10.1	28.2	16.7	
Japanese	37.8	8.8	0.0	0.0	34.2	19.3	
Filipino	73.3	2.7	0.0	15.9	5.0	2.7	
Other Asian/ Pacific Islander	41.8	1.9	0.0	0.0	17.9	37.5	
Education Level							
College or higher	32.9	5.6	16.3	0	9.1	34.0	<.001
Junior college	31.6	4.6	2.1	19.7	7.6	28.3	
High school	40.9	6.2	0.16	0.43	19.8	32.5	

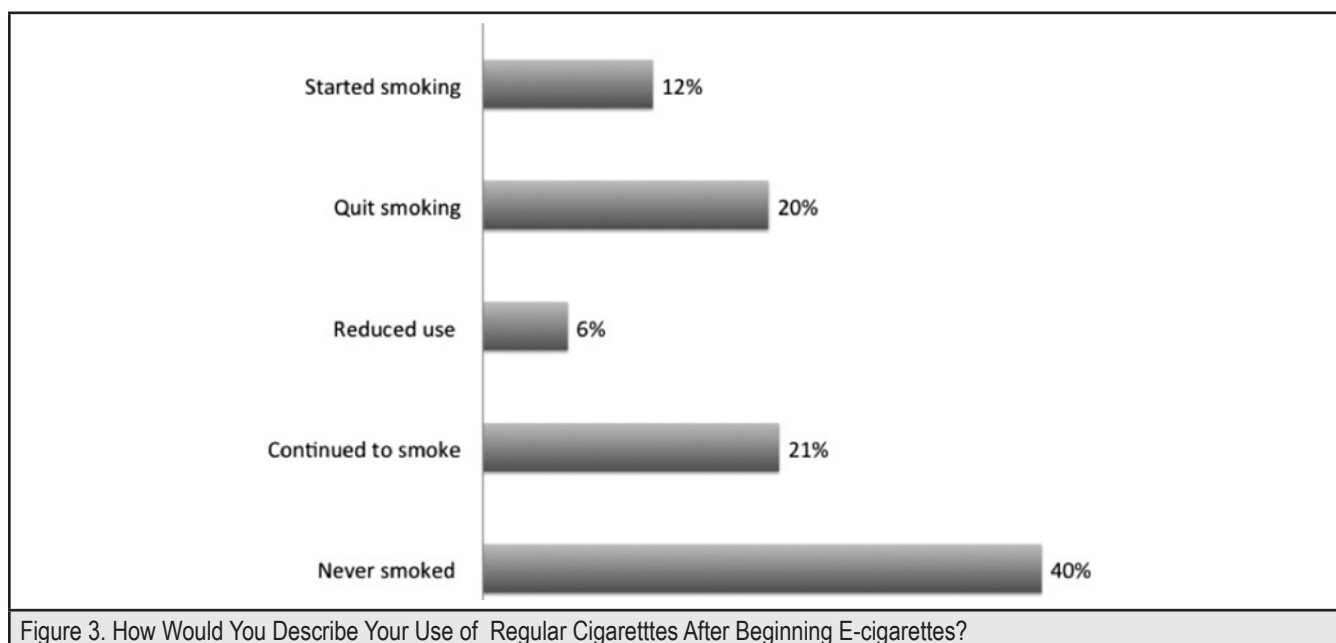


Table 4. Factors related to perceived effect on health relative to no effect, unadjusted.			
Factor		Improved my health	Worsened my health
Age	Age Less than 25	0.71 [0.12, 4.1]	3.2 [0.76, 13.3]
	Age 25-34	1.5 [0.13, 18.1]	3.0 [0.65, 13.9]
	Age 35-64	1	1
	Age 65+	18.0 [1.5, 222.7]	0.48 [0.074, 3.1]
Island	O'ahu	1	1
	Other island	0.12 [0.019, 0.78]	2.5 [0.51, 12.0]
Gender	Female	5.7 [0.66, 48.6]	1.3 [0.36, 5.0]
	Male	1	1
Self-reported health	Excellent health	1	1
	Poor, fair, or good health	0.11 [0.016, 0.82]	0.68 [0.11, 4.2]
Ethnicity	Caucasian	1	1
	Filipino	18.9 [1.8, 204.9]	0.21 [0.024, 1.8]
	Japanese	2.3 [0.17, 31.7]	0.83 [0.10, 6.8]
	Native Hawaiian	2.6 [0.36, 19.3]	0.30 [0.046, 2.0]
	Other race/ethnicity	0.17 [0.019, 1.4]	0.053 [0.008, 0.37]
Education	College or higher	1.7 [0.16, 18.8]	1.3 [0.25, 7.3]
	Junior college	0.64 [0.071, 5.9]	0.23 [0.055, 1.00]
	High school	1	1
Birthplace	Hawai'i	1	1
	Mainland or other country	2.2 [0.25, 19.2]	0.63 [0.93, 4.3]

Table 5. Factors Affecting Perception of Impact of E-cigarettes on Perceived Health Improvement: Multivariate Results.				
Health Better (Reference group: health same or worse)	Odds Ratio	Lower CL	Upper CL	P-value
Age 25 or under	0.17	0.03	1.2	.07
Age 25-34	1.1	0.07	15.5	.96
Age 35-64	1			
Age 65+	5.7	0.28	114.3	.26
Oahu (vs neighbor islands)	0.09	0.01	1.1	.058
Female	0.53	0.08	3.5	.51
Health excellent (vs poor, fair, good, very good)	0.11	0.02	0.64	.013
Filipino (vs Caucasians)	24.3	2.2	272.1	.01
Japanese (vs Caucasians)	7.4	0.24	228.6	.25
Native Hawaiian (vs Caucasians)	29.1	2.1	411.0	.01

than middle-aged respondents to report that e-cigarette use had improved their health. Respondents living on an island other than Oahu (OR=0.12; $P=.03$) were less likely to report health improvements. Those in less than poor health (OR=0.11; $P=.03$) were also less likely to report that e-cigarette use had a positive impact on their health. Filipino respondents (OR=18.9; $P=.02$) were more likely than Caucasians to report that e-cigarettes had improved their health.

Table 4 also reveals results of bivariate analyses related to perceptions that e-cigarette use led to worse health. Those of “other” ethnicity (OR=0.053; $P=.003$) were less likely than Caucasians to report that their health had gotten worse because of e-cigarettes.

Finally, in our multivariable analyses (Table 5), having poor self-reported health [OR=0.11, 95% CI (0.02, 0.64)] was significantly associated with reduced odds of reporting that e-cigarettes improved health, while being Filipino [OR=24.3, 95% CI (2.2, 272.1)] or Native Hawaiian [OR=29.1, 95% CI (2.1, 411.0)] was associated with a significant increase in reporting that e-cigarette use improved health.

Discussion

The goal of this study was to examine the association between demographic factors and use of e-cigarettes, reasons for use, and perceived effects on health through a statewide telephone survey. Consistent with the literature, younger people were more likely than older people to have ever tried e-cigarettes and males were more likely than females.¹⁴⁻¹⁶

The groups most likely to continue using e-cigarettes were those over age 65, Filipinos, and those with less than a high school education. Among these groups, the most common reason for starting was to quit regular cigarettes.

Approximately 20% of respondents said they completely quit regular cigarettes after beginning e-cigarette use and another 6% said they reduced regular cigarette use. E-cigarettes have been shown to be more effective than placebo devices for smoking cessation.¹⁷⁻²⁰ They may also aid in smoking reduction, but the quality of available evidence is low. Hence, more research is needed.

Moreover, 12% of e-cigarette users said they started smoking regular cigarettes after beginning e-cigarettes. Although we do not know how many of these smokers would have begun smoking cigarettes without exposure to e-cigarettes, it is still concerning and further research is needed in this area as well.

One of the most striking findings was in the relation between gender and reasons for use. Females were considerably more likely than males to use e-cigarettes in order to quit smoking traditional cigarettes, while males were more likely to report using them for fun, pleasure, or social reasons. These results are particularly unexpected given the fact that males are nearly five times more likely to smoke regular cigarettes than females.²¹

Native Hawaiians and Filipinos were significantly more likely to report that they perceived that their health had improved due to e-cigarette use. Interestingly, these are also the two ethnicities with the highest proportion of participants who have ever used e-cigarettes. It is possible that e-cigarette use is more prevalent in communities in which the perceived health effects tend to be more positive. Also, further research is needed in this area as Native Hawaiians and Filipinos have existing health disparities in cancer and cardiovascular disease.²²

There are several limitations to our study. First, the data are from only one state and are self-reported. Moreover, the sample is potentially biased as it includes only those who are willing to participate in a telephone survey. Another limitation is the small sample size, particularly for sub-groups.

Conclusions

In conclusion, our study of e-cigarette use in Hawai‘i reveals that there are vast differences in use, reasons for trying, and perceived health benefits that vary by age, gender, ethnicity, health status, and education level. Understanding the reasons for use, patterns of use, and perceived health benefits will help physicians, nurses, pharmacists, and other health care providers in counseling patients. To inform these discussions, more research is clearly needed regarding the potential health benefits and risks of e-cigarettes.²³ Moreover, policy makers need to consider carefully what types of regulation might be warranted to discourage use among adolescents and those who have never smoked, but also to allow use among current smokers if e-cigarettes are determined to facilitate cessation of tobacco smoking.²⁴

Conflict of Interest

None of the authors identify any conflict of interest.

Disclosure Statement

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Hospital-Acquired Methicillin-resistant *Staphylococcus aureus* Bacteremia Related to Medicare Antibiotic Prescriptions: A State-Level Analysis

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Abstract

Methicillin-resistant *Staphylococcus aureus* (MRSA) results in almost half of all deaths caused by antibiotic resistant organisms. Current evidence suggests that MRSA infections are associated with antibiotic use. This study examined state-level data to determine whether outpatient antibiotic use was associated with hospital-acquired MRSA (HA-MRSA) infections. The 2013 Centers for Disease Control and Prevention (CDC) Healthcare-Associated Infections Progress Report was used to obtain HA-MRSA infection rates. Data on the number of antibiotic prescriptions with activity towards methicillin-sensitive *Staphylococcus aureus* (MSSA) at the state level were obtained from the 2013 Medicare Provider Utilization and Payment Data: Part D Prescriber Public Use File. Pearson's correlation coefficient was used to analyze the relationship between the number of antibiotic prescriptions and HA-MRSA infection rates. The average number of HA-MRSA infections was 0.026 per 1000 persons with the highest rates concentrated in Southeastern and Northeastern states. The average number of outpatient prescriptions per capita was 0.74 with the highest rates in Southeastern states. A significant correlation ($\rho = 0.64$, $P < .001$) between infections and prescriptions was observed, even after adjusting for non-reporting hospitals. This association provides evidence of the importance of appropriate antibiotic prescribing. Prescriber and heat map data may be useful for targeting antimicrobial stewardship programs in an effort to manage appropriate antibiotic use to help stop antibiotic resistance.

Keywords

Antibiotic resistance, Antimicrobial stewardship, Medicare, Methicillin-resistant *Staphylococcus aureus*, Methicillin-sensitive *Staphylococcus aureus*

Introduction

Infectious disease is the second leading cause of death worldwide and the third leading cause of death in developed countries.¹ Over the past 70 years, the use of antibiotics and other antimicrobial agents has greatly reduced morbidity and mortality from infectious diseases.² However, as these drugs have been some of the most commonly prescribed medications over a long period of time, some bacteria have found ways to develop resistance towards antibiotics that are designed to kill them, rendering the drugs less effective.² The economic cost of antibiotic resistance in the United States is estimated to be as high as \$55 billion per year for both direct healthcare costs and additional costs to society associated with lost productivity.³⁻⁵ In the United States, more than 2 million people each year have an infection that is resistant to an antibiotic, leading to 23,000 deaths.⁴ Methicillin-resistant *Staphylococcus aureus* (MRSA) alone results in almost half of all deaths caused by antibiotic resistant organisms.⁴ Antibiotic resistance is a global problem putting current and future populations at substantial risk of injury, loss, and death and has been declared a substantial threat

to public health and national security by the Infectious Diseases Society of America and Institute of Medicine.^{2,3}

Antibiotic use is the single most important factor leading to antibiotic resistance.⁴ The problem of antibiotic resistance could be reduced if antibiotics were prescribed more appropriately.⁴ Up to 50% of antibiotics are not needed or are not optimally prescribed.^{4,6} There are trillions of microorganisms in the human body made up of both beneficial and potentially harmful bacteria.^{4,7} Among these microorganisms, antibiotic resistant bacteria may be present but in small enough numbers that infection does not develop.⁴ An example is nasal colonization or carriage of MRSA.⁸ Beneficial bacteria play a role in keeping harmful bacteria numbers low.⁴ When antibiotics are given, harmful as well as beneficial bacteria that protect the body from infection are killed.⁴ The few antibiotic resistant bacteria that are present are then allowed to multiply and infect the body causing an antibiotic resistant infection.⁴ This infection can ultimately spread to healthcare and community settings.^{4,9,10}

Staphylococcus aureus (*S. aureus*) infections are among the most common and problematic.¹¹ Penicillin resistance among *S. aureus* was detected within a decade after its introduction worldwide in the 1940s.² In response, new antibiotics were developed but within a decade, MRSA was identified.² This pattern of resistance continues to occur at an increasing rate with each new antibiotic developed.² Recently, economic concerns have driven pharmaceutical companies away from new antibiotic approvals and developments, leaving few options left to treat antibiotic resistant *S. aureus*.^{1,2} Adding to the problem is *S. aureus*'s ability to colonize and form biofilms on biomaterials in hospitals.¹⁰ Certain strains of MRSA form biofilms contributing to the spread of hospital-acquired (HA-MRSA), which is generally defined as a MRSA infection detected by a positive culture taken more than 48 hours after hospital admission and treated in the inpatient setting.^{10,12,13}

This continual trend toward increased antibiotic resistance highlights the urgency of ensuring that inappropriate antibiotic use be decreased. A possible solution to antibiotic resistance is antimicrobial stewardship.^{14,15} Antimicrobial stewardship refers to a coordinated effort designed to improve the appropriate use of antimicrobials by promoting the selection of the optimal antimicrobial drug regimen, dose, duration of therapy, and route of administration. These efforts can ultimately reduce the cost of healthcare infections and can reduce the potential for developing antimicrobial resistant organisms.¹⁶ While prior

studies have examined inappropriate inpatient antibiotic use, to our knowledge, the relationship between the use of outpatient antibiotics to treat methicillin-sensitive *Staphylococcus aureus* (MSSA) and the incidence of HA-MRSA has not been studied.

The goal of the study was to examine the association between Medicare Part D antibiotic prescriptions with bactericidal or bacteriostatic activity towards MSSA and HA-MRSA bacteremia infection rates (incidence of infections that were reported by healthcare facilities) by state. Our hypothesis was that states with heavy antibiotic use would also have high rates of HA-MRSA infections.

Methods

The study involved comparing per capita antibiotic prescriptions for Medicare beneficiaries to the number of HA-MRSA infections reported by hospitals at the state level. HA-MRSA infection data were obtained from the 2013 Centers for Disease Control and Prevention (CDC) Healthcare-Associated Infections (HAI) Progress Report which included the number of laboratory-confirmed HA-MRSA infections and the number of hospitals reporting for each state.¹⁷ Because all states had non-reporting hospitals, infection rates for each state were adjusted to estimate infection rates as if each state had 100% hospital reporting by dividing the infection rate by the percent of hospitals reporting.

Inclusion criteria for the numerator for antibiotic use were being enrolled in a Medicare Part D prescription drug plan and being prescribed systemic antibiotics with bactericidal or

bacteriostatic activity towards MSSA according to the 2014 Sanford Guide to Antimicrobial Therapy.¹⁸

The 2013 Medicare Provider Utilization and Payment Data: Part D Prescriber Public Use File (PUF) identified providers using their National Provider Identifier (NPI) and the specific prescriptions that were dispensed on their behalf, listed by brand and generic name.¹⁹ For each prescriber and drug, the dataset includes the total number of prescriptions that were dispensed (original and refills), days supply, the total drug cost, and the provider's address.

Claims data for all providers who prescribed antibiotic medications with MSSA coverage were downloaded and summarized at the state level. The antibiotics included are listed in Figure 1. The metric of interest was antibiotic prescriptions per 1000 persons aged 65 and over per state, which was obtained by dividing number of prescriptions by the state's population aged 65 and over. We examined the correlation between the number of prescriptions per 1000 persons aged 65 and over, and the number of HA-MRSA infections per 1000 persons in the general population at the state level in the United States (US) in 2013 using the Pearson's correlation coefficient. Scatterplots were used to detect outliers visually and the correlation coefficient was re-calculated after removing any outliers. Statistical analyses were conducted in Stata v.11 (College Station, TX). Following the guidance of the University of Hawai'i Office of Research Compliance, we did not seek Institutional Review Board approval, as all of the data were de-identified and publicly available.

Amikacin	Cephalexin	Minocycline
Amoxicillin/clavulanate	Ciprofloxacin	Moxifloxacin
Ampicillin/sulbactam	Clarithromycin	Nafcillin
Azithromycin	Clindamycin	Nitrofurantoin
Cefaclor	Daptomycin	Norfloxacin
Cefadroxil	Demeclocycline	Ofloxacin
Cefazolin	Dicloxacillin	Oxacillin
Cefdinir	Doripenem	Piperacillin/tazobactam
Cefditoren	Doxycycline	Quinupristin/dalfopristin
Cefepime	Ertapenem	Rifampin
Cefotaxime	Erythromycin	Sulfamethoxazole/trimethoprim
Cefotetan	Fosfomycin	Telithromycin
Cefoxitin	Gatifloxacin	Tetracycline
Cefpodoxime	Imipenem/cilastatin	Ticarcillin/clavulanate
Cefprozil	Levofloxacin	Tigecycline
Ceftaroline	Lincomycin	Tobramycin
Ceftazidime	Linezolid	Trimethoprim
Ceftriaxone	Meropenem	Vancomycin
Cefuroxime		

Figure 1. Antibiotics and Activity Against MSSA by Generic Name.
Antibiotics included in this study by generic name with systemic bactericidal or bacteriostatic activity towards Methicillin-sensitive *Staphylococcus aureus* according to The Sanford Guide to Antimicrobial Therapy 2014.

Results

In 2013, the average percentage of hospitals reporting HA-MRSA in the US was 61.5%. Reporting by individual states varied from a high of 88.4% of hospitals reporting in Illinois to a low of 22.0% of hospitals reporting in Maryland (Figure 2).

The US average of reported number of HA-MRSA infections per 1000 persons in the general population was 0.026 in 2013. The highest number of infections per 1000 persons were in Alabama (0.06) and the lowest in Alaska (0.003). Figure 3 displays a heat map of the infection rates by state. The states with the highest infection rates were primarily in Southeastern and Northeastern regions.

In 2013, over 33 million Medicare Part D MSSA covering antibiotics were prescribed. The average number of Medicare Part D MSSA covering antibiotic prescriptions per 1000 persons in those aged 65 and over in the US in 2013 was 0.74. The highest prescribing state was Kentucky (1.25) and the lowest prescribing state was Alaska (0.22). A heat map for the number of prescriptions in each state shows the highest prescribing states primarily in the Southeastern region (Figure 4).

Less than half (48%) of facilities in Hawai'i reported HA-MRSA infections. The HA-MRSA infection rate was 0.014 and the adjusted rate was 0.03, resulting in a state ranking of 15th and 16th, respectively, out of 50 in terms of lowest unadjusted and adjusted infection rate respectively. The Medicare Part D MSSA antibiotic prescribing rate was 0.5, resulting in a state

ranking of 9th out of 50 in terms of lowest prescribing rate.

There was a positive, statistically significant correlation between the rate of HA-MRSA infections and the MSSA antibiotic prescription rate for each state ($\rho = 0.72$, $P < .001$, Figure 5). Because a varying proportion of hospitals reported infections in each state, a secondary analysis was performed using an infection rate adjusted for hospital non-reporting (Figure 6). The adjusted analysis resulted in a positive and statistically significant correlation ($\rho = 0.64$, $P < .001$) that was less positive than the original correlation and also resulted in an outlier (North Dakota). The HA-MRSA rate for North Dakota increased from 0.038 to 0.169 after adjustment for hospital non-reporting. When the outlier was removed, this correlation increased considerably and became greater than that for the unadjusted results ($\rho = 0.78$, $P < .001$).

Eighty-four percent of all MSSA covering antibiotics (or 28.8 million) were prescribed by physicians and other providers in 10 specialty areas (Figure 7). Family practice and internal medicine were the top two prescribers, together prescribing more than half of all MSSA covering antibiotics. Family practice prescribed 25.8% and internal medicine prescribed 25.7%. The third highest prescribing specialty was urology that prescribed 6.1% of the total, followed by ophthalmology (6.1%), nurse practitioner (5.9%), physician assistant (4.5%), emergency medicine (3.7%), dermatology (2.1%), pulmonary disease (2.1%), and general practice (1.7%).

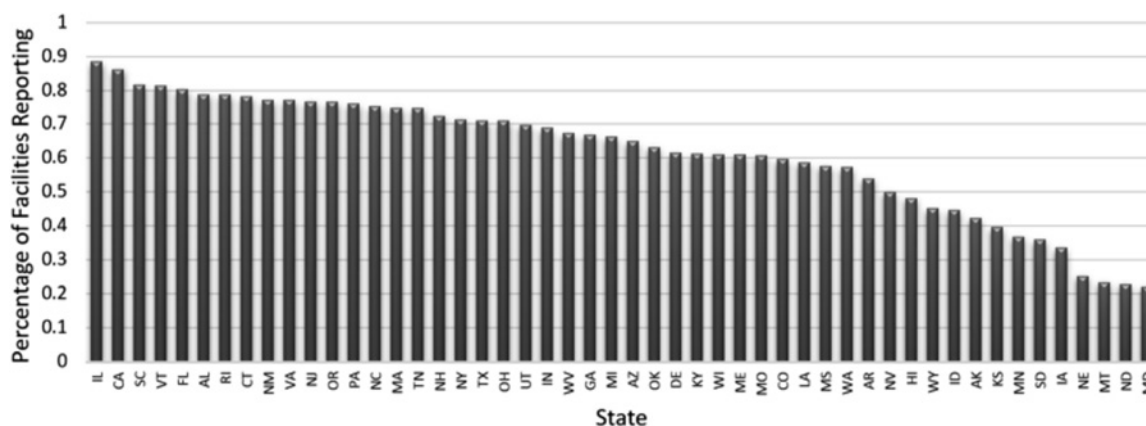


Figure 2. Percentage of Hospitals Reporting HA-MRSA Bacteremia Infections by State.

The 2013 percentage of each State's hospitals reporting the number of HA-MRSA infections in order from highest (left) to lowest (right). The average percentage in the United States of hospitals reporting these infections was 61.5%.

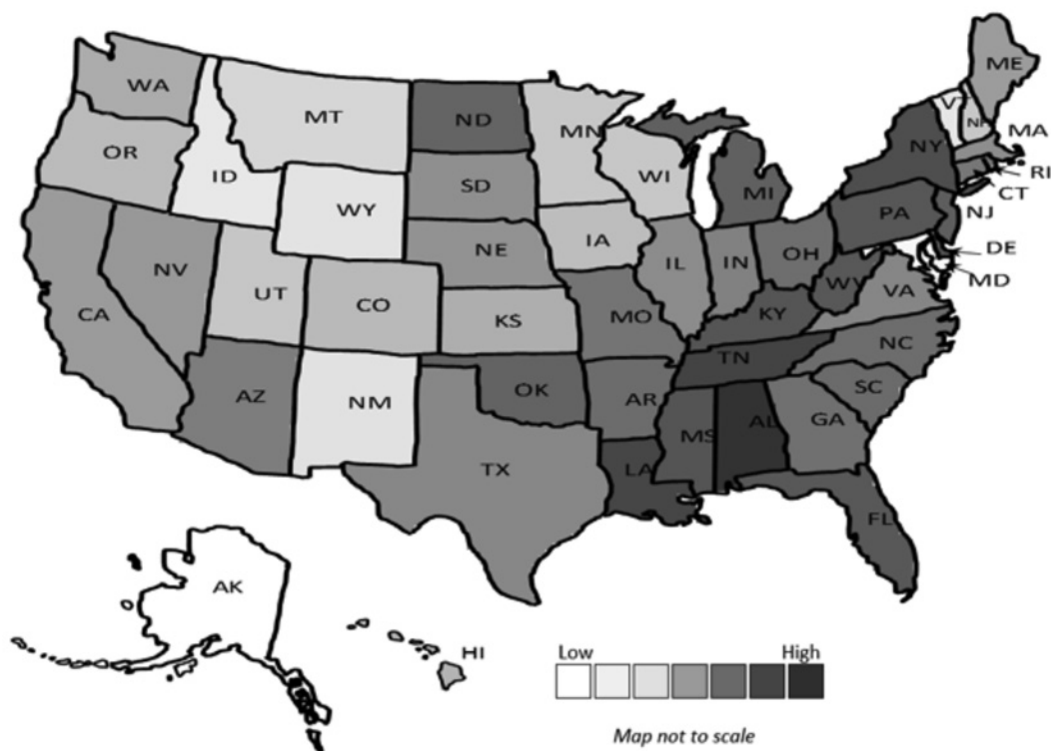


Figure 3. HA-MRSA Bacteremia Infections per 1000 Persons.

The 2013 United States heat map of the number of HA-MRSA infections per 1000 persons with the lowest numbers in white and highest in dark gray.

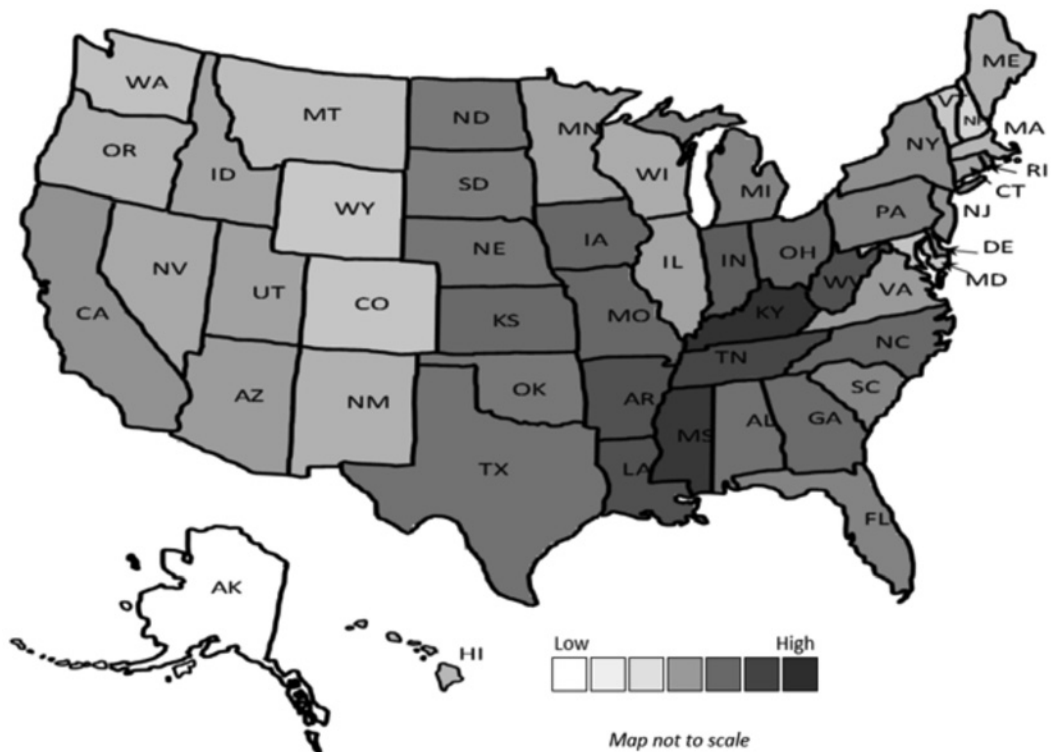


Figure 4. MSSA Antibiotic Prescriptions per 1000 Persons.

The 2013 United States heat map of the number of Medicare Part D MSSA antibiotic prescriptions per 1000 persons with the lowest numbers in white and highest in dark gray.

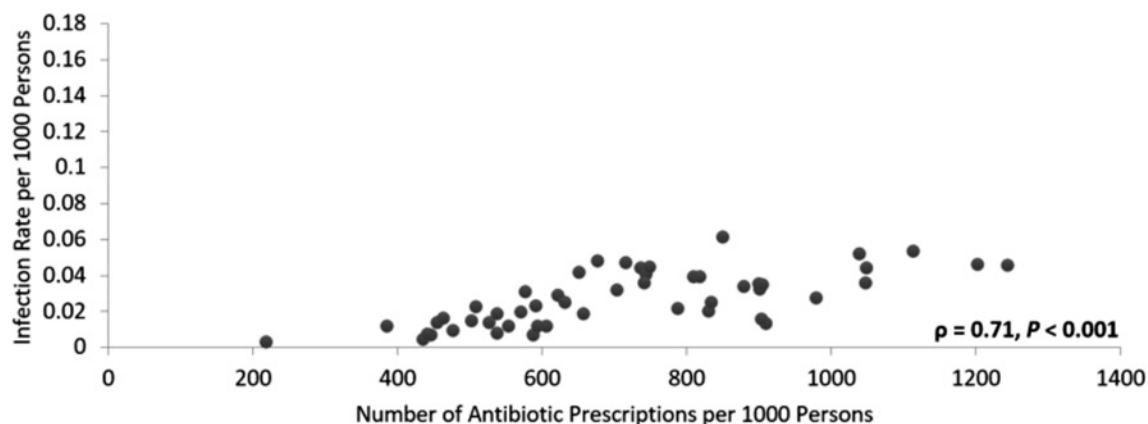


Figure 5. HA-MRSA Infection Rate Related to Number of Antibiotic Prescriptions by State, 2013.

The 2013 relationship between the HA-MRSA infection rate and the number of Medicare Part D MSSA covering antibiotic prescriptions in each state. Each state's value is represented as a single point on the figure. The relationship was examined using the Pearson's correlation coefficient which resulted in $p = 0.71$ with $P < .001$.

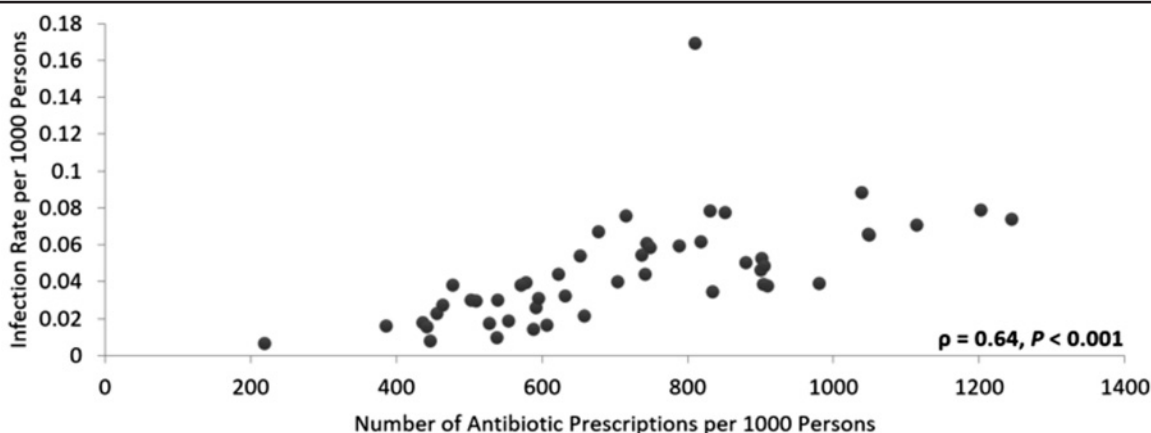


Figure 6. HA-MRSA Infection Rate Related to Number of Antibiotic Prescriptions by State, 2013, Adjusted for Hospital Non-reporting.

The 2013 relationship between the HA-MRSA infection rate and the number of Medicare Part D MSSA covering antibiotic prescriptions in each state with adjusted values. The infection rates were recalculated after adjusting for non-reporting hospitals. The adjusted relationship was examined using the Pearson's correlation coefficient which resulted in $p = 0.64$ with $P < .001$.

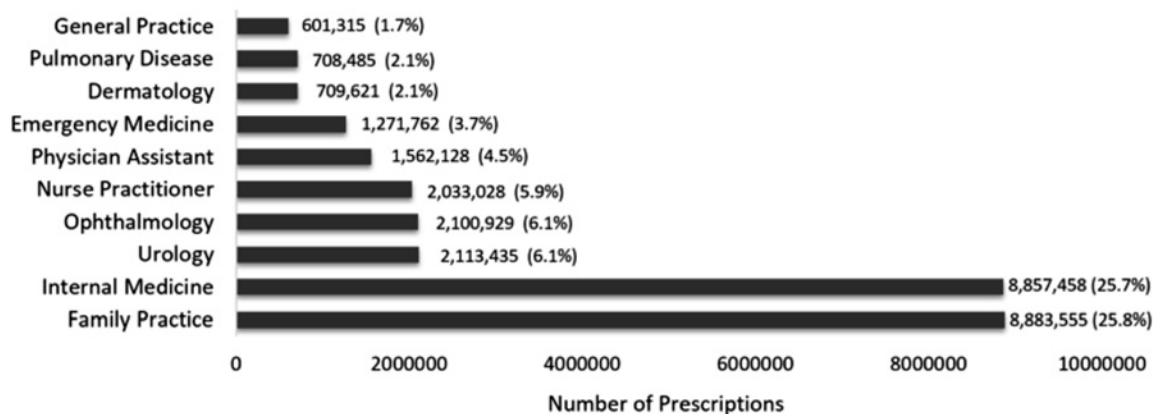


Figure 7. Number of MSSA Antibiotic Prescriptions for Top 10 Specialties.

The 2013 top 10 specialties who prescribed Medicare Part D MSSA covering antibiotics in order from lowest (top) to highest (bottom) including the number of prescriptions and percentage of antibiotics prescribed out of the total number of prescribed MSSA antibiotics.

Discussion

In this study comparing HA-MRSA infection rates to Medicare Part D antibiotic prescriptions at the state level, we found a significant correlation between the presence of HA-MRSA and the number of outpatient antibiotic prescriptions with activity towards MSSA.

Both unadjusted HA-MRSA infection rates and those adjusted for hospital non-reporting were significantly correlated with MSSA antibiotic prescription rates. However, after adjusting for non-reporting hospitals, the correlation was weaker. The adjustment for non-reporting hospitals created an outlier value for North Dakota. North Dakota had a relatively high unadjusted infection rate and a very small percentage of hospitals reporting. One limitation of our adjustment is that we corrected for the number of hospitals reporting without regard to hospital size. It may be that in North Dakota, a large hospital reported their data and many small ones with a small number of cases did not report. In this case, we would have over-adjusted for non-reporting.

Previous research has shown an association between prior antibiotic use and MRSA colonization and infection at the population- and individual-level with an increased risk of morbidity and mortality.^{2,8,20,25} An association between primary care outpatient antibiotic prescribing and community-acquired MRSA (CA-MRSA) has also been shown.^{20,26} State level antibiotic prescriptions and MRSA wound infections have been studied.²⁷ Research has been done on the decrease of MSSA susceptibility over the past decade, and hospital-acquired MRSA resistance rates have been compared with MSSA resistance rates.^{28,30} The spread of certain MRSA strains have been tracked across the United States.¹¹ There have been studies showing an association between antibiotic use and HA-MRSA; however, these studies focused on a few antibiotics prescribed mainly from an inpatient setting.^{9,31,33} This study adds to the existing literature by examining the relation between outpatient antibiotic use and HA-MRSA infections.

Although antimicrobial stewardship programs are beneficial for reducing antimicrobial resistance, they are difficult to initiate. It takes coordination, economic resources, and in many cases, it adds to healthcare professionals' time and workload. Initiating these programs may not be feasible, especially at the national level. This study provides a possible way to help focus the initiation of antimicrobial stewardship programs in specific states or in specific healthcare specialties. States with high antibiotic prescribing rates or high infection rates may benefit from these programs more than states with low prescribing or low infection rates. More benefits could also be seen in specialties with higher antibiotic prescribing rates over those with lower prescribing rates.

In Hawai'i, efforts have been made to initiate antimicrobial stewardship programs throughout the state, especially at the health system level. Hawai'i ranked in the top third in terms of

lowest infection rates in the US and in the top fifth in terms of the lowest prescribing rates. If the study's hypothesis is correct and higher prescribing rates means more antibiotic resistant infections, then since Hawai'i has both relatively low prescribing rates and infection rates, Hawai'i seems to be contributing to the development of HA-MRSA to a lesser extent than most other states. This relatively low contribution combined with efforts to initiate antimicrobial stewardship programs makes Hawai'i appear to be a relatively safe state in terms of developing HA-MRSA.

There are several limitations to our study. First, only one year of data (2013) on antibiotic prescriptions was included, and data was only available for Medicare Part D subscribers. Hence, antibiotic use was only representative of disabled and/or elderly with Medicare Part D coverage, whereas the infection rates were representative of the entire state population. Although it would have been ideal to include antibiotic use for the general US population, we were limited by the availability of publicly available data. On the other hand, our analysis includes all patients with Medicare Part D coverage across the US, which provides a broad sampling of patients at risk for HA-MRSA. Second, we only had data on outpatient (not inpatient) antibiotic use. Third, our HA-MRSA data was hospital reported and not all hospitals submitted data. While we tried to adjust for non-reporting, we may have some measurement error in HA-MRSA rates. Moreover, we do not have information on HA-MRSA infections in people who did not go to the hospital. Also, we did not correct for spacial proximity so the significance of our correlations may be exaggerated. Finally, data were aggregated at the state level, not at the individual level, so we do not know whether the patients actually taking the antibiotics were the ones with HA-MRSA infections.

Conclusion

In summary, this study shows a significant correlation between outpatient Medicare Part D antibiotics with MSSA coverage and hospital-onset MRSA infections in the US. Although cause and effect cannot be established, this study supports the theory that the indiscriminate use of antibiotics is "pushing" MSSA towards developing into its drug-resistant counterpart, MRSA. This study, along with results from previous studies, suggests that antibiotic use in any setting may lead to MRSA infections in healthcare settings. This study also highlights how publicly available data aggregated at the prescriber level and heat map data may be able to help focus antimicrobial stewardship programs to specific specialties or states in order to reduce inappropriate antibiotic use. Antibiotic resistance is a dangerous problem. Our study helps to justify the need for immediate national action to avoid a post-antibiotic world.

Conflict of Interest

None of the authors identify any conflict of interest.

Disclosure Statement

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MEDICAL SCHOOL HOTLINE

Leonard Tow Humanism in Medicine Address: “Death Was Never Enemy of Ours.”

Bill Haning MD

The Medical School Hotline is a monthly column from the John A. Burns School of Medicine and is edited by Satoru Izutsu PhD; HJMPH Contributing Editor. 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.

The object of any discussion of humanism in medicine should be to emphasize those qualities of the art that extend beyond the administration of medications, the wielding of a knife, the manipulating of damaged limbs or spine. That would seem clear enough, but there actually is some variation in the definition of humanism. The criteria from the Arnold P. Gold foundation for this award emphasize compassion and respect. The original definition, dating back to the 18th century, emphasizes the value of reason over religious belief, and thus acclaims the dignity and the capability of humankind, magnificent and grand concepts. They are not quite the same; so I will go with “compassion & respect.” It's smaller and more manageable; and paraphrasing A.A. Milne, I am increasingly “...a bear of little brain.”

So what am I to do with this subject? And how have I come to earn the award? Quite possibly, I do not deserve the award, except for the happy fact that there are such loose criteria. Was it because I got a degree in philosophy long before I became eligible to treat patients? Is it because my lectures in neuroscience emphasize the connection between illness and the healing effects of simple compassion and willingness to listen? There are many physicians far more accomplished than I am in creating that connection, and in carrying it through to the point of benefit to the patient. So I think a compromise conclusion is in order: physicians are innately humanists. You have to have a rational view of the world and of the human body and spirit or there's no point in all of the scientific preparation. Whatever else we are in addition, we are at least scientists. Everybody in this profession who has made a commitment to the Oath of Hippocrates is inherently humanistic. While an oath commits the physician to respect for the patient in a variety of ways, it is entirely voluntary; and yet I have heard very few who objected to it, or to taking it, other than to quibble over certain words that are used and ultimately to accept the basic premises. So I think it's simply a matter of my being visible — target of opportunity, and all that. If I get an award for being a humanist, it is simply that I am a representational object, one among the many physicians who should be receiving an award for humanism, because that's inherent in the job; or possibly should not be receiving an award: a lot of the folks I have served with in several military services, including Navy and Marines, performed acts of effort and loyalty that went well beyond normal expectations of

human endurance, but were not rewarded with awards. It was part of the job. The folks up on the stage who are committing to this job, medical students, understand that it's going to be a bit tougher than some of the other choices they had, and will require considerable fidelity. If anything, over the years, I have watched the job get harder, not because of sleep deprivation or greater intellectual demands; but because of exactly those winds which distract us from our essential humanistic ambitions.

One wind, more than any other, appears to be a gale rather than a zephyr: the commercialization of medical practice in this country. The application of a profit motive to pharmaceutical dispensing and to health care coverage has unfortunately driven much of this. You will be weary of hearing how the electronic health record has depersonalized interactions with the patients, but it is documentation and coding and reimbursement requirements which drive the electronic health records demands. It is demand and possibly avarice associated with the market model that cause the prices of the medications to go up; at the same time that the overhead for management of physicians through insurance providers has ensured that prescribing a medication is still cheaper than actually talking with the patient. Many human endeavors and articles of production work well within a market system. But medical practice does not; it is more like a utility, in that it is a necessity. And we have long ago learned to regulate necessities with the entire public in mind: water, power, and even to some extent food, the provision of which although not yet a utility is at least subsidized. Among other examples, it is this commercial model which is the motivator for the availability of and the over-prescription of addictive, opioid analgesic medications in the United States.

Why, then, did you pick this title, Haning? The title — *Death Was Never Enemy of Ours* — is taken from *The Next War*, a poem by Wilfred Owen, a British Army lieutenant and poet who was killed in the trenches on the Western front, a week before the Armistice, in which he describes familiarity with the inevitable. In an environment in which death seemed certain, to him and to his fellows, there came at some point a resolution to accept it. There was no putting it off. And in so doing, death could be seen less as an enemy, perhaps not so much as a friend, but certainly as a reliable companion.

Many physicians do not have a daily acquaintance with death. But it is inherent in the earliest part of our training, we are confronted with it at the moment we walk into the prosecution lab, with its bodies having been donated to assist us in developing competence in caring for the living. They lie there, still, arrayed with what dignity we can manage, the life spirit having abandoned them. They are nonetheless representative of the history populated by one soul, whether for three decades or for ten. So we are instructed early to become familiar with this companion, death, and to answer some questions that follow.

Doctors haven't been able to do much throughout history. In fact, to be colloquially blunt, we haven't done squat, certainly not in the sense of curing illness. Inarguably, a great deal of the pharmacopeia that existed prior to this past 20th century was injurious if not actually lethal. Physicians were rightly mocked for their reliance upon nostrums and toxic substances that produced violent reactions, in the name of expelling evil humors. Our predecessors were trying to find their way, they were really hoping that they could identify the philosopher's stone that would turn lead into gold, metaphorically: illness back into health. A lot of people learned to throw away the medications that the doctors gave them, but they came to doctors anyway. They wanted answers to certain questions: what is this, what can I do, what will happen, when will it happen, will it hurt, will it be ugly? Finally, will this kill me? And if we were doing our job right, we gave them.

Obviously, not all about medicine is in staving off or dealing with those questions about death. But questions about death are at the root of every other medical question people ask. Don't kid yourself. When you go to the dermatologist with that funny mark on your skin, you want to know that it's not melanoma. When you've had that cough for three weeks straight, you want to know if the Big Crab has arrived to make a meal of you, if you should blame those cigarettes that you used to smoke, or those pakalolo doobies that you were toking for 20 years. When you come to the psychiatrist or the neurologist confused or sad, you want to know if this moment will turn into madness, into the death of your mind.

We may have an appropriate and proportionate sense of the basis for seeking help. When we take our small child to the pediatrician with a fever and an earache, we generally have "ear infection?" superficially in mind. We expect it is that problem or something similarly treatable which will be found and managed. I agree, we don't go into the waiting-room with death at the forefront of our conscious thoughts. But it is our child, and she is in pain. And even if she does not understand or fear the risks that illness may presage, at some level, we do.

An honored friend, now deceased, at one time a high school classmate and for many years a colleague at Tripler Army Medical Center, was a pediatric oncologist, coincidentally named Bill. His office was at the exact antipode of my own in that massive hospital. And from time to time, when exasperated by my alcoholic patients, who would seem so promisingly to be doing well only to fall drunk, I would plonk myself in one of his office chairs and bemoan my outcast state. He would sit, placidly, with a benign half smile on his face—he had a disarming resemblance to a Bassett hound—and listen to me. And on one occasion, when I was through ranting, he asked if he could tell me about one of his small patients. He proceeded to describe a child of six, with leukemia, for whom with great diligence and skill he had procured another six months of life, he hoped. And this achievement clearly gave him such joy that I could only congratulate him enthusiastically. Cynically, I was thinking, "Six months? What is that? How much effort and energy to purchase 100 or 200 days!" It was only later that I realized that he reveled in this achievement not so much for what it provided the child, as for what it provided the parents: six months more of memory of their son.

An element of humanism not often mentioned is realism. It is the acknowledgment of truth. Everybody dies. We are engaged in that act from the moment of our birth, if not nine months before. And what physicians don't do is prevent death. We may delay the appointment of its arrival; sometimes it is argued that we protract its presence needlessly, and other times it is argued that we are too peremptory in hastening it. But it is very much our companion, and it is the thing our patients always ask us to address: will this kill me? If so, when? How will it do so? Will it be painful? Will it be ugly, to those around me?

And finally, the most important question for us as physicians, will you help me through this?

Thank you for this opportunity.

Dr. William Haning is the Director of MD Programs for the University of Hawai'i John A. Burns School of Medicine, and is a tenured Professor in the Department of Psychiatry who concentrates in the field of addictions. This presentation was given upon his receipt of the 2016 Leonard Tow Humanism in Medicine Award, of the Arnold P. Gold Foundation; White Coat Ceremony, Honolulu, Hawai'i, 15 July 2016.

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INSIGHTS IN PUBLIC HEALTH

Improving Health for Mothers, Infants, and Families with the Hawai'i Maternal and Infant Health Collaborative

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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

The Hawai'i Maternal and Infant Health Collaborative, founded in 2013, is a public-private partnership committed to improving birth outcomes and reducing infant mortality. The Collaborative was developed in partnership with the Executive Office on Early Learning Action Strategy with help from the Department of Health and National Governor's Association. The Action Strategy provides Hawai'i with a roadmap for an integrated and comprehensive early childhood system, spanning preconception to third grade. The Collaborative helps advance goals within the Action Strategy by focusing on ensuring that children have the best start in life by being healthy and welcomed. The Collaborative has completed a strategic plan and accompanying Logic Model, The First 1,000 Days, aimed at achieving the outcomes of 8% reduction in preterm births and 4% reduction in infant mortality. To date over 120 people across Hawai'i have been involved in the Collaborative. These members include physicians and clinicians, public health planners and providers, insurance providers and health care administrators. The work is divided into three primary areas and coordinated by a cross sector leadership team. Work is specific, outcome driven, informed by data and primarily accomplished in small work groups.

Background

Infant mortality (eg, death of an infant in the first year of life) and preterm birth (eg, delivery prior to 37 completed weeks of gestation) are major indicators of population health. A previous Public Health Insights article highlighted disparities in infant mortality and described the need for a collaborative approach to reduce infant mortality.¹ The Hawai'i Maternal and Infant Health Collaborative (HMIHC) was founded in 2013 as a public-private partnership committed to improving birth outcomes and reducing infant mortality. The formation of the HMIHC built upon several activities in the state including the March of Dimes and Association of State and Territorial Officers (ASTHO) 2012 President's Challenge pledge to improve birth outcomes by reducing infant mortality and prematurity and to decrease Hawai'i's prematurity rate by 8% and infant mortality by 4% over a 5-year time period from 2009 to 2014.² Additionally, an overarching effort in 2012 was the establishment of the Executive Office on Early Learning (EOEL) to coordinate a collaborative effort to improve learning outcomes for Hawai'i's children from the prenatal period to age eight. With a change in Governor in 2014 the Action Strategy continues its coordinating efforts as

a not for profit providing backbone support to the subject area teams of which the HMIHC is one. The Maternal and Child Health Branch through the Family Health Services Division (FHSD), Department of Health partnered with others on this initiative that identified six goals. The work of Team 1, Healthy and Welcomed Starts, formed the foundation for an application to participate in a learning network with the National Governor's Association (NGA). In May 2013, the Hawai'i Department of Health was selected to participate as one of four states in the NGA learning network on Improving Birth Outcomes.³

The NGA learning network included peer learning from other states and national experts, and included a state planning session in July 2013, bringing together stakeholders. A broad group of approximately 60 perinatal, child, and women's health stakeholders, including public health workers, advocates, consumers, health care providers, and policy makers was an essential step toward developing, aligning and implementing key policies and initiatives to improve birth outcomes as measured by the incidence of pre-term births and infant mortality. The Planning Session was convened and facilitated by the Hawai'i Department of Health and the National Governor's Association. Information was presented on the Early Childhood Action Strategy; Hawai'i data on infant deaths particularly for those in higher risk disparate groups; and national initiatives to improve birth outcomes including the Collaborative Improvement and Innovation Network (CoIIN) framework to reduce infant mortality. Four breakout sessions were conducted to consider policy and program options for state planning. Participants emphasized the need to have a life course approach; a collaborative to address the improvement of birth outcomes including a clinical component; access to relevant data for ongoing assessment on improvement of birth outcomes; and that discussions and development of strategies and approaches must continue. Some of the next steps identified from the session were the need to continue with an interactive dialogue with partners to improve birth outcomes in our State and to establish a structured collaborative that can serve as the lead entity for multiple actions to improve birth outcomes.

Mission/Roles

HMIHC is a public-private collaborative effort with a mission to reduce infant mortality and improve birth outcomes in Hawai'i with a multi-pronged approach including policy, the delivery system, clinical practice and professional development, consumer education, and the payer system (eg, insurance and financing). Examples of HMIHC activities over the last year in these areas are:

1. Policy – working toward passage of the Maternal Mortality and Child Death Review Bill
2. Improvements in the delivery system – working with hospitals and insurance providers to clarify reimbursement mechanisms
3. Clinical Practice – white papers and training for physicians on long acting reversible contraception
4. Payer system – clarification of Medicaid reimbursement coding for contraception

All work is informed by data, addresses disparities and social determinants of health, addresses the needs of all islands, and provides opportunities for all interested stakeholders to participate. A Core Team of public and private partners provides coordination of efforts, establishes shared goals, establishes and supports key relationships, ensures stakeholder engagement, identifies emerging issues, and assesses project outcomes. The intent of the Collaborative is to identify barriers to achieving the outcomes of improving birth outcomes and reducing infant mortality. Once barriers are identified the next step is to develop strategies to address them. From there the Collaborative identifies and engages key partner(s) who could implement the strategies and then evaluates the implementation.

Using this pathway we can look at the Collaborative work on Screening, Brief Intervention, and Referral to Treatment (SBIRT). SBIRT is an evidence-based practice used to identify, reduce, and prevent problematic use, abuse, and dependence on alcohol and illicit drugs.^{4,6} SBIRT emphasizes screening individuals by professionals for risky substance use behaviors using a standardized screening tool. This is followed by a brief intervention for those identified at risk by screening which can include a short conversation that provides feedback and advice at the time of screening. The professional provides a referral for brief therapy or additional treatment for those who need additional services.

1. HMIHC identified prenatal substance use as a major barrier to healthy birth outcomes based on review of the data and conversations with stakeholders.
2. Universal prenatal SBIRT was identified as a best practice strategy to address the problem.
3. HMIHC sponsored a statewide planning process to develop a plan for how this strategy could be implemented and had key leadership commitment to implementation; Department of Health took the lead, Department of Human Services-MedQUEST division, and the Aloha United Way signed on as key supporters. In follow up to the planning meeting, HMIHC assisted the Department of Health to secure funding to hire a contractor to help with further planning, implementation, and evaluation. At that point HMIHC role was accomplished. Planning for transition

of SBIRT from a standing committee of HMIHC was done as the implementation and process was well established.

4. The HMIHC will continue to be available to facilitate as barriers are identified as well as to help in reviewing the metrics of implementation.

Activities and Measures of Success

Since the initial work in 2013, the HMIHC has hosted several large group meetings to share information and bring together stakeholders around infant mortality and prematurity reduction. The structure for the HMIHC includes a core group and individual workgroups spread across the three time periods (pre/interconception, pregnancy and delivery, and infant health and safety) and an overarching workgroup related to policy and advocacy. Several diverse partners participate both in the core group and the workgroups representing private organizations including the March of Dimes Hawai'i Chapter and Healthy Mothers Healthy Babies Coalition of Hawai'i; professional organizations such as American Congress of Obstetricians and Gynecologists, American Academy of Pediatrics, and American Academy of Family Physicians; major health insurers in the state; the Hospital Association of Hawai'i; and state agencies including the Hawai'i Department of Health and the Hawai'i Department of Human Services. The HMIHC hosts large group meetings of stakeholders at least once a year. Additionally, regular meetings of core members of HMIHC are held to provide updates from the work groups and provide long term guidance and planning for the collaborative. Communication with partners includes regular newsletters highlighting progress and activities (<http://hawaii.actionstrategy.org/teams/team1>).

One of the initial markers of success was the development of an overarching plan to reduce infant mortality and prematurity that brought together multiple stakeholders to identify ongoing activities and gaps. The HMIHC developed a logic model to help inform the process based on evidence informed strategies around particular topics to fill in the gaps and augment existing activities (Figure 1). The logic model has been instrumental in assisting the Collaborative to look at the complex and multifaceted issue of preterm births and infant mortality. It has been very helpful in setting priorities for the workgroups by presenting the activities and the various short, medium, and long range outcomes. Additionally, it serves as a tool to share with stakeholders to highlight the work being done while providing a framework to ensure that different audiences are included in the activities (eg, public payers, community, clinicians, etc). The logic model also provides a road map and is a key component in the regular assessment and discussion of activities of the HMIHC.

The HMIHC has worked on several activities including developing an approach to impact health issues identified through a review of data and raising awareness of its importance to stakeholders. This approach includes: (1) policy and advocacy; (2) the delivery system; (3) consumer education; and (4) the payment system. Some of the accomplishments from 2015 reflect work group activities involved in the pre/interconception period (eg, Promoting access to long acting reversible contraception and

Hawaii Maternal and Infant Health Collaborative; The First 1,000 Days Logic Model 2014-2020

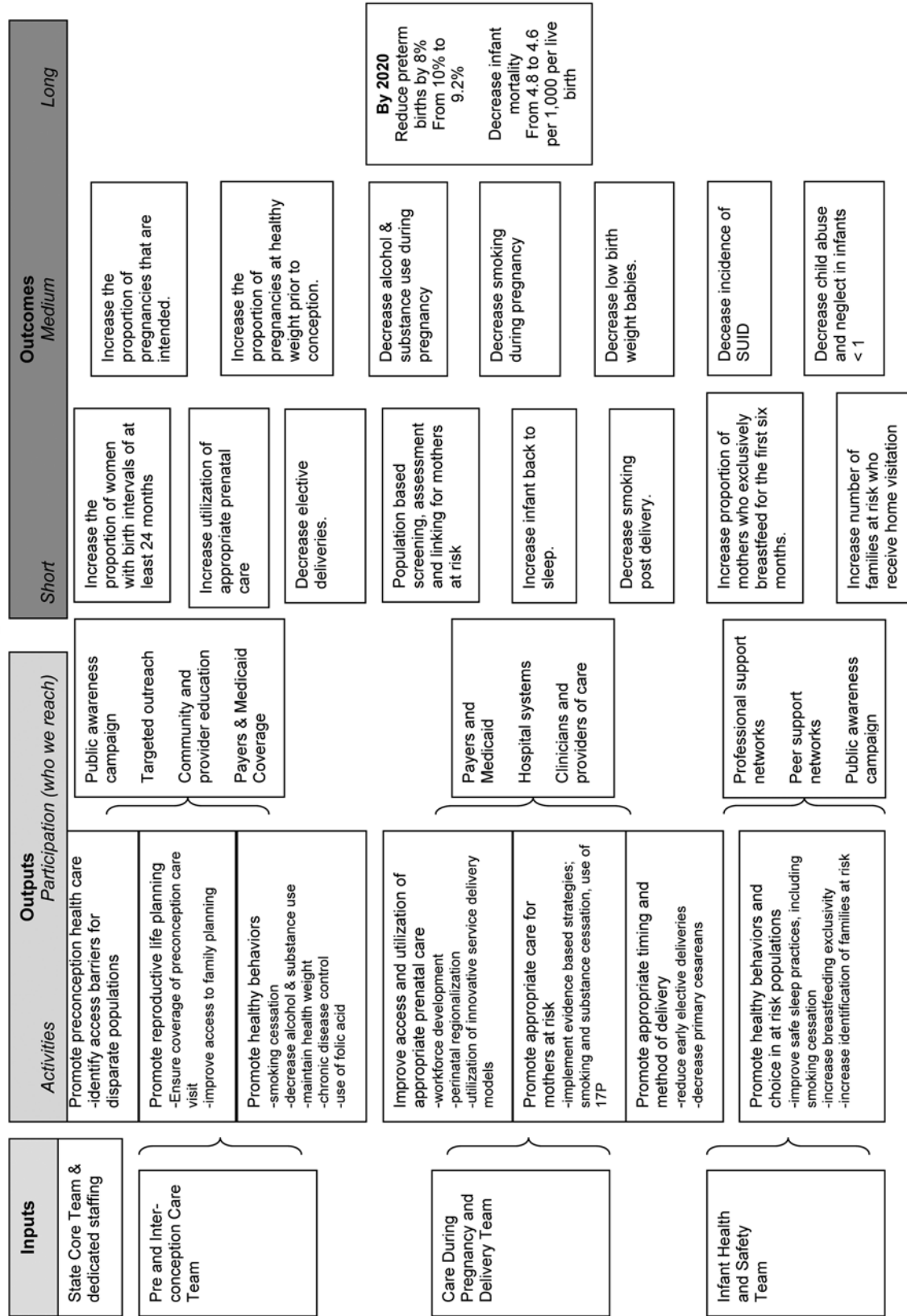


Figure 1. 2014-2020 HMIHC Logic Model

introducing One Key Question®); the pregnancy and delivery period (eg, Prenatal SBIRT for smoking and substance use cessation, and Utilization of 17-Alpha-Hydroxyprogesterone caproate (17P)); the infant health and safety period (eg, safe sleep promotion, and supporting breastfeeding); and the policy and advocacy work that focused on reinstating the State child death review and establishing a maternal mortality review (Table 1).

There is a lot of momentum for the work of HMIHC in 2016 across all workgroups: the pre/interconception period (eg, expanding the use of One Key Question®); the pregnancy and delivery period (eg, facilitation of efforts to establish the system for Prenatal Screening and Brief Intervention for smoking and substance use cessation); the infant health and safety period (eg, continuing support of Safe Sleep Hawai'i and expanding their focus to improving breastfeeding exclusivity) (Table 2).

Other Factors for Success

There are several factors that have come together to ensure the continued effectiveness for the collaborative work. Having an experienced facilitator is critical to ensure several aspects of the collaborative are functional including communicating with members and ensuring the HMIHC is documenting and continually reassessing its progress. Other things that support

the HMIHC include a physical space for the regular meetings, annual retreat to reflect and reassess direction, and providing regular updates to partners. Emphasizing the public and private partnerships by having both public and private co-leads for the collaborative as well as for the individual workgroups has helped foster collaborative efforts to strengthen and develop new partnerships. Critical to the collaborative success to date has been the ongoing commitment by individuals in the collaborative and the partners, continued work with the Action Strategy, and coordination with other national and state efforts including the Title V Maternal and Child Health Block grant,⁷ Hawai'i Home Visiting Network,⁸ Governor's Office of Health Care Transformation, Alcohol and Drug Abuse Division of the Department of Health and the national participation in the CoIIN learning network to reduce infant mortality.⁹

Recently, the Hawai'i DOH released a strategic plan, which emphasizes the life course approach.¹⁰ In particular, some of the workgroup efforts of the HMIHC (eg, SBIRT, Reducing Unintended pregnancy, Establishment of Maternal Mortality and Child Death Reviews) are included prominently in this Department Strategic Plan. The adoption of these activities into the Hawai'i DOH strategic plan recognizes the accomplishment of the HMIHC and helps raise the importance of leadership and partnerships to address these complex issues.

Table 1. 2015 HMIHC Workgroup Priorities and Accomplishments			
Time Period	Outcome	Work Group Priorities	Accomplishments
Pre and inter-conception care	Increase the rate of intended pregnancies Increase use of highly effective contraception	Improved access to long acting reversible contraception (LARC) Improve reproductive life planning	<ul style="list-style-type: none"> Clarified MedQuest coverage of post-delivery LARC Developed and distributed a chart of coverage and coding for providers Developed and distributed a white paper Sponsored training on post-delivery LARC for providers at the annual ACOG Hawai'i Section Conference Secured partnership with Oregon Reproductive Health Foundation to bring One Key Question® to Hawai'i Training and presentation to HMIHC membership and commitment to implement
Pregnancy and Delivery	Increase full term births Increase infants born substance-free	Improve access and utilization of 17P Universal prenatal screening, brief intervention and referral to treatment	<ul style="list-style-type: none"> Surveyed clinicians on the utilization, attitude, and barriers to 17P Completed SBIRT Implementation plan Secured grant funding for contractor to implement provider training for prenatal SBIRT Contractor retained for assessment of substance abuse treatment resource capacity
The first year of life	Decrease infant mortality	Increase safe sleep practices Reinstatement of child and maternal mortality review teams	<ul style="list-style-type: none"> Expansion of Crib for Kids Developed White paper for the importance of maternal and child death reviews Advocated for introduction and support of legislation

Table 2. 2016 HMIHC Priorities and Work in Progress			
Time Period	Outcome	Work Group Priorities	Work in Progress
Pre and inter-conception care	Increase the rate of intended pregnancies Increase use of highly effective contraception Improve birth spacing	Improved access to long acting reversible contraception (LARC) Improve reproductive life planning	<ul style="list-style-type: none"> Design and conduct public and provider education Encourage hospital in-patient stocking Clarify FQHC reimbursement Clarify private health insurance coverage Determine metrics and data tracking Establish HMIHC One Key Question® (OKQ) team Develop implementation plan for OKQ Support pilot site implementation Conduct contraceptive training for WIC and home visiting staff Conduct OKQ train-the-trainer session Conduct OKQ session for WIC and home visiting Determine OKQ metrics and data tracking
Pregnancy and Delivery	Increase full term births Increase infants born substance-free	Improve access and utilization of 17P Universal prenatal screening, brief intervention and referral to treatment	<ul style="list-style-type: none"> Targeted patient education and outreach <ul style="list-style-type: none"> NICU families Home visiting families WIC participants Increase access Clarification of insurance coverage Contractor retained for system design and implementation <ul style="list-style-type: none"> Payment reform Health plan relations Development & promotion of guidelines Grant Advisory Committee established <ul style="list-style-type: none"> Relations with current and potential funders Oversight, partnership and coordination of effort Monitor grant deliverables Review contractors progress and approve payment
The first year of life	Decrease infant mortality	Increase safe sleep practices Reinstatement of child and maternal mortality review teams Increase infants exclusively breastfed	<ul style="list-style-type: none"> Continue coordination with Safe Sleep Hawai'i Review hospital discharge procedures Private partners provided testimony and language to support passage of SB 2317 to re-establish CDR and establish MMR teams Promote breastfeeding exclusivity Promote lactation counseling and clarify insurance coverage Provide consumer education on hormonal contraceptives and breastfeeding Explore/encourage Baby Friendly designation for hospitals Develop metrics and data tracking

This will help the HMIHC as it continues to assess and identify new areas to address. At times there will be a shift in roles for oversight and implementation of priorities. The HMIHC will still be kept aware of these particular issues and available to assist as needs arise because of its capability for strong public and private partnerships and commitment to decreasing infant mortality and preterm births.

Conclusion

Much of the HMIHC work to date has been driven by assessment of needs from the partnerships, state data, and best practice knowledge gained from leveraging community-based and nationally driven efforts to improve outcomes in maternal and infant health. The HMIHC will continue to base its future directions using this same process to keep partners engaged and committed to this work. The HMIHC is always looking for partner engagement. Clinicians, public health professionals and the general public are welcome to visit the HMIHC website (<http://hawaiiactionstrategy.org/teams/team1>) to learn more about the collaborative work and how to join. The HMIHC was established in 2013 to address the complex issues related to infant mortality and preterm birth and has worked as a true collaborative to improve health of children and families in the State of Hawai'i.

Disclaimer

The findings and conclusions in this article are those of the authors and do not necessarily represent the official position of the Hawai'i Department of Health, March of Dimes Hawai'i Chapter, or the Hawai'i Maternal and Infant Health Collaborative.

Conflict of Interest

None of the authors identify a conflict of interest.

Acknowledgment

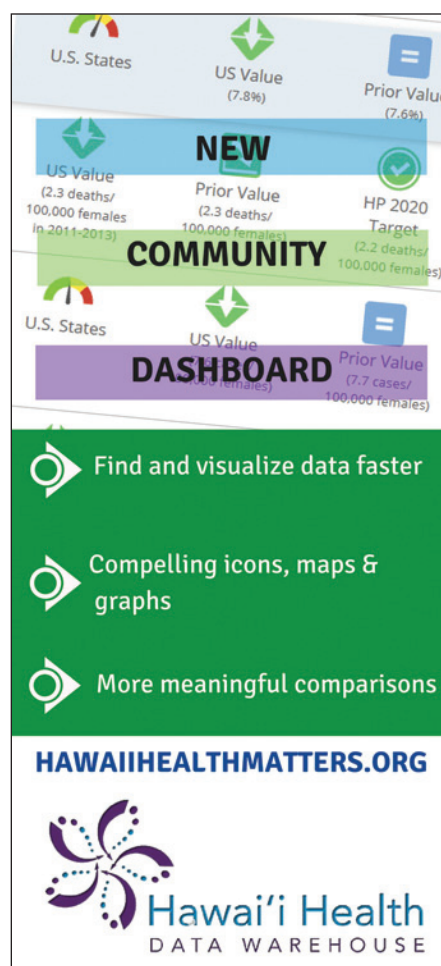
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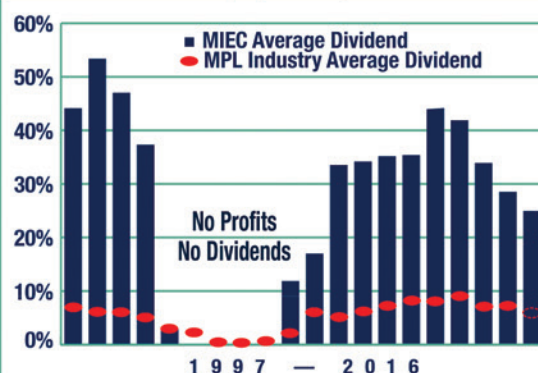
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