

# Risk factors associated with methamphetamine use and heart failure among Native Hawaiians and other Pacific Island peoples

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**Objective:** Heart failure (HF), a long term outcome of chronic methamphetamine use (MU), occurs more frequently in racial and ethnic minority populations at high risk for cardiovascular disparities. This study examined the association of socio-demographic and clinical risk factors with MU among heart failure patients who are Native Hawaiians (NH) or other Pacific Island peoples (PIP).

**Design/Setting/Patient population:** Cross-sectional study of NHs and PIPs with advanced heart failure enrolled in the Malama Pu'uwai Study, a randomized control trial to test an educational intervention to reduce re-hospitalization and/or death. A total of 82 participants were enrolled between 6/1/06 to 12/31/07 and met the following eligibility criteria: 1) self-identified NH or PIP, 2) Left ventricular systolic ejection fraction  $\leq 45\%$ , 3) Age of 21 years or older. Data were analyzed by odds ratios (OR), 95% confidence intervals (CI), and multiple logistic regression analysis.

**Main outcome measure:** Methamphetamine use.

**Results:** Twenty-two percent of HF participants were identified as being current or prior methamphetamine users. Younger age and non-married status (combined never married or divorced/separated) were independently associated with MU after adjustment for sex, education, and other co-morbidities associated with HF (ie, age  $> 50$  years, OR = 0.16, 95% CI, 0.03–0.84; non-married status combined as never married OR = 8.5, CI, 1.5–47; divorced/separated OR = 11, CI 1.8–75).

**Conclusions:** Risk factors associated with MU in NH and PIPs with heart failure include: younger age and being divorced/separated or never married. Health care providers should be aware of MU as a contributing factor in the approach and treatment of HF in NHs and PIPs.

**Keywords:** Native Hawaiian and other Pacific Islander, ethnic minority, methamphetamine use, heart failure

## Introduction

Methamphetamine use (MU), initially recognized as a health problem limited to Hawai'i and the western region of the US, has continued to spread eastward and has increasingly affected both rural and urban areas throughout the US.<sup>1</sup> According to a 2005 national survey, an estimated 10.4 million people age 12 years or older have tried the highly addictive drug in the US.<sup>2</sup> Minority populations are at higher risk, particularly racial/ethnic groups such as Native Hawaiians (NHs) and Pacific Island Peoples (eg, Samoan, Tongan, Micronesian) who are concentrated in the western regions of the US. Native Hawaiians experienced a 10-fold increase in methamphetamine use between 1995–1998.<sup>3,4</sup> In parallel with this upward trend, 5.6% of all Native Hawaiian 12th graders in the state of Hawai'i have used methamphetamine at least

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once in their lifetime compared with 4.8% among high school seniors nationally.<sup>1,5</sup> In the wake of the growing epidemic of MU, health care providers and acute care hospitals are seeing long term health effects of methamphetamine use.<sup>6-9</sup> Between 2004 and 2005, estimated emergency department visits for methamphetamine abuse rose by almost 50% to 108,905 visits per year.<sup>10,11</sup> In addition, treatment admissions for methamphetamine abuse also have increased to 150,000 admissions per year in 2004 and the number of states reporting high rates of admissions (defined as >24 per 100,000 population) increased from 5 states in 1992 to 21 states in 2002.<sup>1</sup>

Despite the growing and persistent problem of MU, few studies have examined long term health problems attributable to chronic MU. Although behavioral and neurological effects of chronic MU have been reported, an emerging literature on the impact of chronic MU on the cardiovascular system has resulted in a growing recognition of methamphetamine-associated cardiomyopathy and heart failure.<sup>6-9,12</sup> Heart failure is a major public health problem in the US with an estimated prevalence of 5.2 million and direct and indirect costs totaling \$33.2 billion.<sup>13</sup> In addition to being one of the leading causes of hospitalization, disparities in the burden of heart failure have been identified, with studies reporting poorer quality of life, more frequent hospitalizations, and decreased survival among African-Americans and Hispanics relative to Caucasians.<sup>14-16</sup>

Recent studies have found that a growing number of HF cases are being reported in patients with current or prior use of methamphetamine. Methamphetamine-induced cardiomyopathy or HF seems to strike younger patients, racial/ethnic minorities and in some case reports, were found to be reversible.<sup>6, 8, 9, 12,17-19</sup> Yeo and colleagues conducted a case-control study (N = 221) on heart failure patients admitted to a tertiary care hospital in Hawai'i and found that methamphetamine users (n = 107) had a 3.7-fold higher odds ratio for cardiomyopathy after adjustment for age, BMI, and renal failure.<sup>9</sup> Other basic science studies also have suggested that methamphetamine exposure is associated with structural and functional changes of myocytes resulting in cardiomyopathy and the clinical syndrome of congestive heart failure.<sup>6,8,12,18,20-28</sup>

NHs and other PIPs are known to be at overall increased risk for heart disease as well as a number of risk factors for heart failure including diabetes, hypertension, tobacco use, and obesity<sup>13,14</sup> and this population continues to experience disparities despite improvements in heart disease mortality experienced in the general US population.<sup>13,29</sup> The purpose

of this study is to examine socio-demographic and clinical risk factors associated with methamphetamine use in NHs and PIPs with moderate to severe heart failure.

## Methods

Participants included in this study were enrolled in the Malama Pu'uwai (Heart Health Care) Study after informed consent was obtained. The Malama Pu'uwai Study (MPS) is a randomized controlled trial that is testing whether a culturally tailored educational program delivered post-discharge from the hospital will reduce re-hospitalization and/or mortality in NH and PIP patients with moderate to severe heart failure. All participants included in this study met the following eligibility criteria: 1) Self-identified as Native Hawaiian and/or Pacific Island racial/ethnic background (including Samoan, Tongan, Micronesian); 2) Age  $\geq 21$  years; 3) Recently discharged from a single tertiary care hospital with a primary or secondary diagnosis of heart failure (index hospitalization); 4) moderate to severe heart failure defined as a left ventricular systolic ejection fraction (EF)  $\leq 45\%$  by echocardiography or similar cardiovascular imaging technique (eg, nuclear imaging, cardiac catheterization).

All participants underwent a baseline visit that included clinical assessment and a personal interview. Use of methamphetamine was determined by medical record review of the index hospitalization using a standardized protocol performed by a single trained reviewer or by a personal interview using standardized questionnaires at study entry. Positive methamphetamine use (MU) was defined as written documentation by a health care professional (eg, nurse, physician, social worker) or positive toxicology screen or if patient reported a history of methamphetamine use by interview. Participants without documentation of MU were categorized as non-methamphetamine users (non-MU) and served as the comparison group.

A total of 82 participants were enrolled between June 1, 2006 and December 31, 2007 in the MPS and were included in this study. All participants were interviewed and evaluated per the MPS protocol for: 1) demographics (ie, age, race/ethnicity – participants were allowed to self-identify multiple race/ethnicity groups and then asked to select the group they identified the most with, marital status and education); 2) assessment of alcohol consumption in the past 12 months (yes or no); and 3) smoked 100 or more cigarettes in their lifetime (yes or no); 4) Medication use, including prescription and/or non-prescription; 5) Clinical assessment of blood pressure, pulse, weight and measured height using standardized protocols. Medical records

from the index hospitalization also were reviewed for the following co-morbid conditions: 1) hypertension – defined as blood pressure  $\geq 140/90$  mmHg or known history of hypertension; 2) diabetes – defined as known history of diabetes by a medical professional; 3) atherosclerotic heart disease – defined as history of myocardial infarction, coronary bypass surgery or angioplasty or other percutaneous revascularization procedure; 4) history of cerebrovascular disease or stroke.

## Statistics

Odds ratios were used to measure the association of risk factors between MU and non-MU and were computed using unconditional logistic regression.<sup>15</sup> The 95% confidence intervals for the OR estimates were determined using normal theory approximation. Significance testing of regression coefficients was based on Wald's statistic. Any univariate factors associated with methamphetamine use was included into subsequent logistic regression modeling if the score statistic for that variable was statistically significant after adjustment for multiplicity using the Hochberg procedure.<sup>16</sup> The Fisher's exact test was used for comparison of categorical variables and Student's t-test for continuous variables. A p-value of  $<0.05$  was considered to be statistically significant. Statistical analysis was performed using SAS statistical software version 9.1.3 (SAS Institute, Cary, NC).

## Results

Current or prior history of MU occurred in 22% of Native Hawaiians (NHs) and Pacific Island Peoples (PIPs) with moderate to severe heart failure. MUs were significantly younger (mean age MU 43 years vs non-MU 58 years.;  $p = <0.0001$ ), more likely to be NHs than PIPs and were more likely to be non-married (never married OR = 13, 95% CI, 2.6–68; divorced/separated OR = 10, 95% CI, 1.7–62). MU was associated with higher BMI (BMI  $\geq 30$ –39 kg/m<sup>2</sup>, OR 4.9; BMI  $\geq 39$  kg/m<sup>2</sup>, OR 3.9), higher pulse (OR 2.3–3.4), being a smoker (OR 2.9), an alcohol user (OR 2.2), or having a college degree (OR 2.8). However, none of these trends reached statistical significance. No significant differences (all odds ratios  $\leq 1.9$ ) were observed between MU and non-MU with regard to sex, or systolic or diastolic blood pressure (Tables 1 and 2).

Table 2 shows that the distribution of co-morbid conditions was similar between MU and non-MU. The most frequent co-morbid condition was hypertension (68%), followed by atherosclerotic heart disease (ASHD) at 62% and

diabetes at 45%. The occurrence of ASHD was more frequent in the non-MU (67%) participants compared with the MU (44%), but was not statistically significant. Overall, both the MU and the non-MU had an equal frequency of underlying co-morbid conditions despite the fact that the MU group was significantly younger.

Using multiple logistic regression adjusting for all relevant variables, we found that older age ( $\geq 50$  years old) was a 'protective' risk factor for MU (OR = 0.16, 95% CI, 0.03–0.84) compared with non-MU. Non-married status (never married or divorced/separated) also was independently associated with an increased risk for MU (never married OR = 8.5, 95% CI, 1.5–47; divorced or separated OR = 11, 95% CI, 1.8–75) (Table 3). After adjustment for multiplicity, race/ethnicity was no longer a statistically significant predictor of MU and consequently was not included in the multiple logistic regression model. Subsequent regression models were analyzed sequentially adding the following covariates: race/ethnicity, sex, education, alcohol use, smoking, atherosclerotic heart disease, hypertension, diabetes, and stroke. However, none of these models changed the independent association of age and marital status with MU. Thus, we report in Table 3 the independent association of younger age and non-married status with positive MU compared with non-MUs in a population of NHs and PIPs with moderate to severe HF.

## Discussion

Methamphetamine use occurs frequently (22%) among NH and PIP patients with moderate to severe (LVEF  $\leq 45\%$ ) heart failure. This finding adds to the growing clinical recognition of methamphetamine use in heart failure patients and in particular among high risk populations with cardiovascular disparities.<sup>30</sup> In a study by Yeo et al 43% of patients with cardiomyopathy were found to be MUs (prior or current users) and the majority of patients with cardiomyopathy and MU were NHs and PIPs (54%).<sup>9</sup> Studies among primarily Caucasian patients also have reported nearly 20% of HF patients having a prior history of alcohol and/or substance abuse in addition to other co-morbid conditions, such as hypertension and diabetes.<sup>31</sup> Our study is consistent with these findings of more than 20% of patients with heart failure having MU as a contributing cause. In this high risk patient population, we found that methamphetamine users were significantly more likely to be NHs compared with PIPs. Thus, although hypertension, ASHD, and diabetes are frequent underlying causes of HF, other potential cardiac insults such as methamphetamine use may pose additional cardiotoxicity.<sup>30</sup>

**Table 1** Demographic characteristics of Native Hawaiian and Pacific Island people with moderate to severe heart failure by methamphetamine use (N = 82)

Variable	Positive methamphetamine use (n = 18) n (%)	Negative methamphetamine use (n = 64) n (%)	Odds ratio (95% CI)
Age			
<40 years	6 (33)	6 (9)	1.0 Referent
40–49 years	6 (33)	10 (16)	0.60 (0.13–2.7)
≥50 years	6 (33)	48 (75)	0.13 (0.03–0.51)
Sex			
Female	4 (22)	22 (34)	1.0 Referent
Male	14 (78)	42 (66)	1.8 (0.54–6.2)
Marital status			
Currently married	2 (11)	37 (58)	1.0 Referent
Never	10 (56)	14 (22)	13 (2.6–68)
Divorced or separated	5 (28)	9 (14)	10 (1.7–62)
Widow or widower	1 (6)	4 (6)	4.6 (0.34–63)
Education level			
Less than high school	4 (22)	10 (16)	1.0 Referent
High school diploma/GED	9 (50)	32 (51)	0.77 (0.20–3.0)
Some college/technical training	2 (11)	18 (29)	0.31 (0.05–2.0)
College degree	3 (17)	3 (5)	2.8 (0.39–20)
Race/Ethnicity			
Native Hawaiian	16 (89)	40 (63)	1.0 Referent
Pacific Island people	2 (11)	24 (38)	0.21 (0.04–.99)
Smoked 100 cigarettes in lifetime (%)			
No	2 (11)	17 (27)	1.0 Referent
Yes	16 (89)	47 (73)	2.9 (0.60–14)
Alcohol consumed in past 12 months			
No	5 (28)	29 (45)	1.0 Referent
Yes	13 (72)	35 (55)	2.2 (0.68–8)

Our results also suggest that among racial/ethnic populations at high risk for cardiovascular disparities, such as heart failure, consideration of alterNative causes of HF may be important contributors to the manifestation of CVD disparities. Racial/ethnic differences in HF risk factors also was examined by Deswal et al in Black patients with advanced HF in a VA system.<sup>32</sup> The authors found that uncontrolled hypertension and hospitalization for any cause accounted for a significant difference in health disparities when compared with their White counterparts.<sup>32</sup> Similarly, our results suggest that the frequency or severity of known underlying causes of HF, such as MU in addition to a background of hypertension, ASHD and diabetes, may have a significant additive effect on the development of CVD outcomes especially among NHs and PIPs. Surprisingly little is known about the prevalence of methamphetamine use in patients with heart failure. Yet it is well known that

racial and ethnic minority patients have persistent disparities on the severity and treatment of heart failure that may contribute to differences in health outcomes. Miller recently highlighted the gap in our fund of knowledge between heart failure patients that have been included in clinical trials that guide practice guidelines and heart failure patients that are racially and demographically more diverse and for whom the treatment guidelines may not be optimal treatment. Thus, our studies provides new insight to the clinical and demographic characteristics of NHs and PIPs who are at increased risk for heart failure and for poor health outcomes.<sup>33</sup>

Our study is the first to identify not only the increased frequency of MU among NH and PIP HF patients but also to examine the potential risk factors associated with MU in this distinct population. Although MU has been recognized as a growing health problem in the US since the early 1990s, little is available in the literature about its long term impact on

**Table 2** Clinical characteristics among Native Hawaiian and Pacific Island peoples with moderate – severe heart failure by methamphetamine use (N = 82)

Clinical characteristic	Positive methamphetamine use (n = 18) n (%)	Negative methamphetamine use (n = 64) n (%)	Odds ratio (95% CI)
Blood pressure			
Systolic blood pressure*			
< 140 mmHg	16 (89)	60 (94)	1.0 Referent
≥ 140 mmHg	2 (11)	4 (6)	1.9 (0.32–11)
Diastolic blood pressure*			
< 90 mmHg	16 (89)	59 (92)	1.0 Referent
≥ 90 mmHg	2 (11)	5 (8)	1.5 (0.26–8.3)
Pulse*			
< 65 beats per minute	3 (17)	22 (34)	1.0 Referent
> 65 to 85 beats per minute	9 (50)	29 (45)	2.3 (0.55–9.4)
≥ 85 beats per minute	6 (33)	13 (20)	3.4 (0.72–16)
Body mass index			
< 30 kg/m <sup>2</sup>	2 (11)	22 (34)	1.0 Referent
≥ 30 to 39 kg/m <sup>2</sup>	8 (44)	18 (28)	4.9 (0.92–26)
≥ 39 kg/m <sup>2</sup>	6 (33)	17 (27)	3.9 (0.70–22)
Unknown	2 (11)	7 (11)	3.1 (0.37–27)
Systolic Ejection Fraction, %			
Severe (<30)	11 (61)	36 (56)	1.0 Referent
Moderate-severe (30–34)	1 (6)	7 (11)	0.47 (0.05–4.2)
Moderate (35–39)	6 (33)	11 (17)	1.8 (0.54–5.9)
Mild-Moderate (40–44)	0 (0)	10 (16)	0.16 (0.0088–3.0) <sup>†</sup>
Atherosclerotic Heart Disease			
No	10 (56)	21 (33)	1.0 Referent
Yes	8 (44)	43 (67)	0.39 (0.14–1.1)
Stroke*			
No	16 (89)	58 (91)	1.0 Referent
Yes	2 (11)	6 (9)	1.2 (.22–6.6)
Diabetes mellitus*			
No	10 (56)	35 (55)	1.0 Referent
Yes	8 (44)	29 (45)	0.97 (0.34–2.8)
Hypertension*			
No	5 (28)	21 (33)	1.0 Referent
Yes	13 (72)	43 (67)	1.3 (0.40–4.0)

\*Missing values (≤2) were absorbed into the referent groups.

<sup>†</sup>Missing cell imputed with 0.5 in order to compute OR and CI.

heart failure specifically and/or its impact on the development of cardiovascular disease in general.

A few studies have examined the differences in patient related factors among minority patients with heart failure compared with their white counterparts. Deswal et al found in a VA population that non-marital status was higher in Black patients with HF compared with Whites.<sup>32</sup> Our study, in another high risk minority population, is in agreement with

this study and others that suggests that greater awareness of psychosocial factors and MU in HF patients is needed and may have important implications for successful chronic disease management. In particular, programs aimed at treating and/or preventing HF hospitalizations and death in health disparate populations should consider the possibility of psychosocial issues (eg, marital status, social support) in patients with heart failure and a prior or current history of

**Table 3** Multivariate analysis of factors associated with methamphetamine use in Native Hawaiians and Pacific Island peoples with moderate to severe heart failure (N = 82)\*

Factors	Odds ratio (95% CI)
Age (years)	
<40	1.0 Referent
≥40 to 50	0.70 (0.13–3.9)
>50	0.16 (0.03–0.84)
Marital status	
Currently married	1.0 Referent
Never married	8.5 (1.5–47)
Divorced or separated	11 (1.8–75)
Widow or widower	5.7 (0.38–87)

\*Adjustment for race/ethnicity, sex, education, alcohol use, smoking, atherosclerotic heart disease, stroke, hypertension, and diabetes were not significant confounders to the model.

MU as they relate to successful heart failure management. Specifically, patients with HF that have a prior history of MU may be younger than the typical HF patient and may have a need for alterNative approaches to ensure adherence to the treatment regimen.

Other studies have examined the role of marital status on health outcomes in HF patients. One study found that among HF patients that were married, the quality of this relationship independently predicted survival, especially among women HF patients.<sup>34</sup> Another study found that high social networking, irrespective of marital status, reduced re-hospitalization in HF patients.<sup>35</sup> Our results support the ‘protective’ role of being married on the association of MU in HF patients. The mechanism for how being married may ‘protect’ against MU has been proposed to be via social support that may mitigate the risk for illicit drug use. This proposed mechanism is supported by other studies in which patients with heart failure who were unmarried had a lower level of self-care knowledge and adherence than those who were married, indicating that marriage improves the ability to care for one’s self.<sup>36</sup> The long term benefits of social support in HF patients is consistent with a wealth of literature that has reported that improved health status and social support are associated with decreased hospitalizations or all cause death.<sup>37</sup>

Unfortunately, the cross sectional design of our study does not allow for determining cause and effect relationships between marital status and MU in HF patients. However, recognition of MU in HF patients is important not only for diagnostic purposes but also for long term treatment and prevention of HF in patients from minority or

health disparate populations. Further delineation of which factors (ie, hypertension, diabetes, methamphetamine, etc.) either collectively or individually can be attributed to the development of heart failure in this population will aid our understanding in developing appropriate treatments to reverse these trends. Our study also highlights an opportunity to intervene early to prevent advanced heart failure in NH and PIP patients with a prior history of MU who may benefit from programs that can provide a supportive context to prevent relapse of MU as well as HF disease management. Further understanding as to the underlying risk factors leading to HF are needed in health disparity populations. Innovative approaches to reduce and/or prevent the development of advanced HF in these populations has important social and economic implications for the health burden of HF in the US since HF is one of the most costly disease hospitalizations in the US.<sup>38,39</sup>

Several limitations should be considered when interpreting the results of this study. The cross-sectional design precludes making any causal inferences between the model risk factors and MU. While the limited sample size may be contributing to the lack of statistical significance observed for some of the risk factors examined. Medical record review of methamphetamine use may also underestimate the actual number of methamphetamine users and other illicit drugs such as cocaine were not assessed in this study. Despite these limitations, this study provides initial findings to a growing body of literature that is recognizing with greater frequency the role of methamphetamine use as a significant contributor to the development of HF. Because MU and heart failure tends to occur more frequently in racial and ethnic minority populations and originally became manifest in the western regions of the US where the majority of NHs and PIPs reside. This may be, just the beginning of a larger, but as of yet unrecognized, problem that contributes to the management of heart failure and cardiomyopathy especially in high risk minority or ethnic populations.

Our study suggests that MU in NHs and PIPs with moderate to severe heart failure occurs at a frequency of more than 1 in 5 cases (22%). Factors independently associated with MU in heart failure patients of NHs and PIP ancestry were non-marital status and younger age. Intervention efforts to reduce persistent cardiovascular health disparities, specifically heart failure, may want to consider strategies to also reduce MU in this and other high risk patients. Further studies are needed to identify key modifiable risk factors that may enable better health outcomes in health disparate populations (eg, NHs and other PIPs) if we hope to reverse and eventually eliminate heart failure disparities.

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## Disclosures

None of the authors have conflicts of interest to disclose.

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