Hawai‘i Journal of Medicine & Public Health

A Journal of Asia Pacific Medicine & Public Health

April 2013, Volume 72, No. 4, ISSN 2165-8218

HELPING CANCER PATIENTS ACROSS THE CARE CONTINUUM: THE NAVIGATION PROGRAM AT THE QUEEN'S MEDICAL CENTER 116
Amanda L. Allison MA; Debra D. M. Ishihara-Wong RN, APRN, MN; Jermy B. Domingo MPH; Jocelyn Nishioka; Andrea Wilburn BA; JoAnn U.Tsark MPH; and Kathryn L. Braun DrPH

THE EFFECTS OF EXTENDED RELEASE NIACIN ON LIPOPROTEIN SUB-PARTICLE CONCENTRATIONS IN HIV-INFECTED PATIENTS 123
Chunrong Lin MD; Andrew Grandinetti PhD; Cecilia Shikuma MD; Scott Souza PharmD; Nisha Parikh MD, MPH; Beau Nakamoto MD, PhD, MBA, MS; Kalpana J. Kallianpur PhD; and Dominic Chow MD, PhD, MPH

FAVORABLE OUTCOMES FOR NATIVE HAWAIIANS AND OTHER PACIFIC ISLANDERS WITH SEVERE TRAUMATIC BRAIN INJURY 129
Kazuma Nakagawa MD; Reid R. Hoshide MPH; Susan M. Asai BSN; Katherine G. Johnson MS; Juliet G. Beniga BSN; Melanie C. Albano BSN; Johnna L. del Castillo BS, BA; Daniel J. Donovan MD; Cherylee W. Chang MD; and Matthew A. Koenig MD

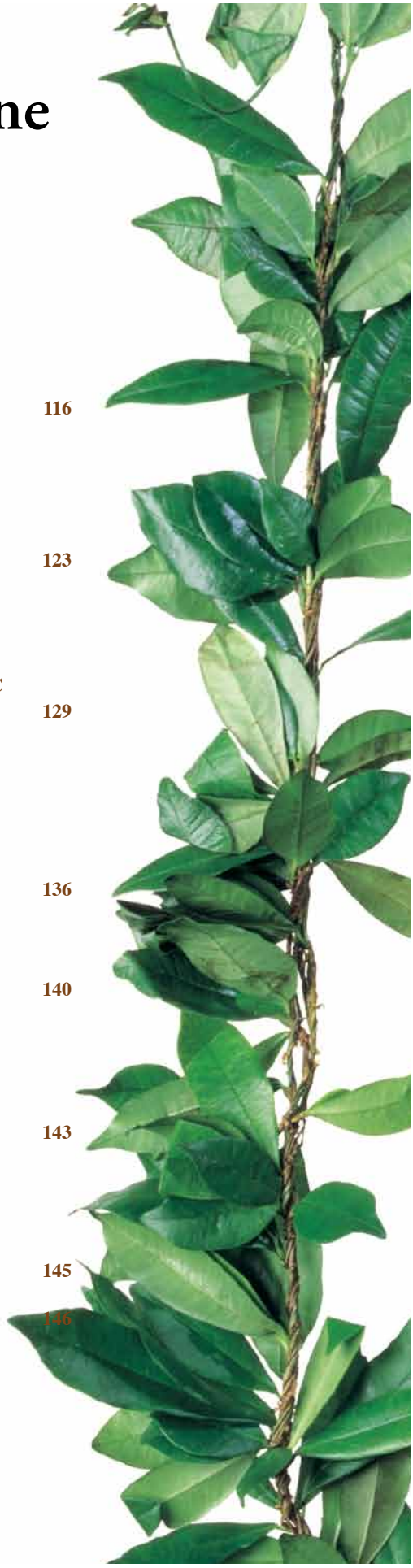
CREUTZFELDT-JAKOB DISEASE: A CASE REPORT AND DIFFERENTIAL DIAGNOSES 136
Gotaro Kojima MD; Brent K. Tatsuno MD; Michiko Inaba MD; Stephanie Velligas BSc; Kamal Masaki MD; and Kore K. Liow MD

MEDICAL SCHOOL HOTLINE 140
Teen Health Camp Hawai‘i: Inspiring Hawai‘i's Youth to be Healthcare Leaders of Tomorrow
Brandyn S. Dunn MPH, MSI; Eduardo Duquez MSIV; Teresa Schiff MSIII, Nem Lau; Agnes R. Malate; and Kelley Withy MD, PhD

INSIGHTS IN PUBLIC HEALTH 143
A New and Innovative Public Health Specialization Founded on Traditional Knowledge and Social Justice: Native Hawaiian and Indigenous Health
Maile Taualii PhD, MPH; Treena Delormier PhD, PDt; and Jay Maddock PhD

CME LISTING 145

THE WEATHERVANE 146
Russell T. Stodd MD



EFFICENCY COMES ALIVE

Who says you can't roar responsibly? The 2013 Jaguar XF is available with new, more efficient engines: the turbocharged Jaguar i4, and the supercharged Jaguar V6 with the intelligent stop/start technology. Both with fuel-saving 8-speed transmissions. Let efficiency come alive for you.

HOW ALIVE ARE YOU?

2013 Jaguar XF
[J00063]

$497 PER MONTH
5 TO CHOOSE FROM

42-MONTH LEASE
$4,210 + TAX TITLE AND FEES DUE AT SIGNING
$0 SECURITY DEPOSIT
$47,850 MSRP

DEMO SALE ALSO GOING ON NOW

JAGUAR

Jaguar Honolulu
744 Ala Moana Boulevard
(808) 592-5100
jaguarhonolulu@fjha waii.com
www.jaguarhonolulu.com

*On approved credit for well-qualified lessees as determined by approved lender. Prices and payments may vary slightly due to options & added equipment. Vehicle may not be exactly as shown. All prices plus 4.712% tax, title, documentation and registration fees. 2013 Jaguar XF #J00063, total due at signing $5,993.89 includes $0 security deposit, $795 acquisition fee and first month's payment; purchase option at lease end $22,968. Lease terms are based on 10,000 miles per year. Must take delivery by APRIL 30, 2013.

Hawai‘i Journal of Medicine & Public Health

A Journal of Asia Pacific Medicine & Public Health

ISSN 2165-8218 (Print), ISSN 2165-8242 (Online)

The Journal’s aim is to provide new scientific information in a scholarly manner, with a focus on the unique, multicultural, and environmental aspects of the Hawaiian Islands and Pacific Rim region.

Published by University Clinical, Education & Research Associates (UCERA)

Hawai‘i Journal of Medicine & Public Health
677 Ala Moana Blvd., Suite 1016B
Honolulu, Hawai‘i 96813
http://www.hjmph.org
Email: info@hjmph.org

The Hawai‘i Journal of Medicine & Public Health was formerly two separate journals: The Hawai‘i Medical Journal and the Hawai‘i Journal of Public Health. The Hawai‘i Medical Journal was founded in 1941 by the Hawai‘i Medical Association (HMA), which was incorporated in 1856 under the Hawaiian monarchy. In 2009 the journal was transferred by HMA to University Clinical, Education & Research Associates (UCERA). The Hawai‘i Journal of Public Health was a collaborative effort between the Hawai‘i State Department of Health and the Office of Public Health Studies at the John A. Burns School of Medicine established in 2008.

Full text articles available on PubMed Central

The Hawai‘i Journal of Medicine & Public Health (ISSN 2165-8218) is a monthly peer-reviewed journal published by University Clinical, Education & Research Associates (UCERA). The Journal cannot be held responsible for opinions expressed in papers, discussion, communications, or advertisements. The right is reserved to reject material submitted for editorial or advertising columns. Print subscriptions are available for an annual fee of $165; single copy $15 includes postage; contact the Hawai‘i Journal of Medicine & Public Health for foreign subscriptions.

Helping Cancer Patients Across the Care Continuum: The Navigation Program at The Queen's Medical Center

Amanda L. Allison MA; Debra D. M. Ishihara-Wong RN, APRN, MN; Jermy B. Domingo MPH; Jocelyn Nishioka; Andrea Wilburn BA; JoAnn U.Tsark MPH; and Kathryn L. Braun DrPH

Abstract

Research suggests that cancer patient navigation improves care, but few reports describe the variety of patients managed by a hospital-based navigation program. Differences in navigated patients by the intensity (low, medium, or high) of navigation services they received were examined. The 835 clients seen by the navigators in a hospital-based cancer center were first stratified by quarter and by four ethnic groups. Randomized selection from each group assured there would be equal representation for analysis of Hawaiians, Filipinos, Japanese, and Whites and even numbers over all time intervals. Five professionals extracted data from these case records on demographics, type/stage of cancer, diagnosis and treatment dates, barriers, and navigator actions. Clients had breast (30.0%), lung (15.8%), esophageal (6.7%), colon (5.8%), ovarian (4.2%), prostate (3.3%), and other cancers (34.2%). The median number of actions taken on behalf of a client was 4 (range 1-83), and the median number of days a case was open was 14 (range 1-216). High intensity cases (those receiving more assistance over longer periods of time) were more likely than low-intensity cases to need help with education and reassurance, transportation, care coordination, and covering costs. Although there were no demographic differences across intensity groups, Neighbor Island patients from Hawai'i, Maui, Moloka'i, Lana'i and Kaua'i were more likely to need help with arranging travel, care coordination, and costs associated with getting treatment (all at P=.05), and patients on public insurance were more likely to have stage 4 cancer (P=.001) and to need help with costs (P=.006). Findings suggest that this hospital-based navigation program is filling a real need of patients across the cancer care continuum. A triage protocol and an integrated data capture system could help improve the targeting and documentation of cancer patient navigation services.

Introduction

Cancer patient navigation (CPN) programs are designed to help people complete recommended cancer screening and treatment in a timely manner.[1,2] Specifically, navigators link cancer patients to needed diagnostic tests, help them meet with the many cancer care providers who may be involved in their care, and overcome other barriers in our fragmented care system. They also may help individuals understand their diagnoses and overcome access barriers, such as lack of insurance, lack of transportation, or lack of providers (especially relevant for patients from rural and poor areas).[3] In the United States, CPN programs have been established as one way to help reduce cancer health disparities for populations that experience a disproportionate burden of cancer. In Hawai'i, cancer incidence and mortality rates vary widely by race/ethnicity.[4]

CPN programs have been instituted in a variety of settings (clinics, hospitals, and community organizations); they employ navigators from a diversity of backgrounds (eg, nurses, social workers, counselors, community health workers); and they require different amounts of CPN-specific training (from 12 to 400 hours).[5] Despite these differences, empirical research suggests that navigated patients are more likely than non-navigated patients to receive timely screening and follow-through with diagnostic tests.[6-13] For example, in Robinson-White and colleagues' review of 12 breast-cancer oriented CPN programs, findings from nine controlled trials suggest that navigation improved women's adherence to breast cancer screening, follow-up of diagnostic abnormalities, initiation of breast cancer treatment, and quality of life.[13] In another review of controlled trials, Wells and colleagues found that navigation improved adherence to screening by 11%-17% and adherence to diagnostic follow-up care by 21%-29%.[6]

The first two hospitals to offer CPN programs in Hawai'i were The Queen's Medical Center (Queen's) and Moloka'i General Hospital. This article focuses on Queen's CPN program, established in 2006. Queen's is the largest cancer care provider in the state, treating 40% of all cancer patients. Many of its navigators are health occupations-educated or college-prepared individuals with some health care experience, and complete a 48-hour CPN training provided by 'Imi Hale Native Hawaiian Cancer Network.[14] In the past three years (January 2009 - December 2011), Queen's navigators assisted 2,454 patients; approximately 75% were non-Caucasian patients, and almost 20% lived on islands other than O'ahu, home to about 70% of the state's population.[15]

While most CPN research looks at programs focusing on a single cancer site, the CPN program at Queen's serves patients with all types of cancer. This study was undertaken in order to quantitatively describe Queen's CPN program. Although the authors did not have an initial hypothesis, it was assumed that the more complicated the patient's situation, the greater the intensity of navigation. In this article, Queen's CPN clients and lay navigator actions taken to assist them are described, specifically examining differences in patients by the intensity (low, medium, or high) of navigation services received.

Methods

One hundred and twenty cases were randomly selected to review from the comprehensive list of the clients served by Queen's Cancer Patient Navigators between October 1, 2010 and September 30, 2011. To select cases, the client list was first stratified by quarter (Oct-Dec, Jan-Mar, Apr-June, July-Sept) and by ethnicity/race (Native Hawaiian, Filipino, Japanese, and White). This was done to assure representation of cases from across the 12 months and from each of Hawai'i's four predominant ethnic groups, including two groups, Native Hawaiians and Filipinos, that experience cancer health disparities.[16,4] From each quarter, 7-8 clients were randomly selected from each of

the four ethnic/racial groups, for a total of 30 clients per quarter. This study was approved by the Native Hawaiian Health Care System Institutional Review Board and by Queen's as a quality assurance initiative.

Data for this project were extracted from Queen's navigation progress notes and face sheets. The progress notes contain a navigator's record of activities carried out on behalf of the patient. Information is recorded in a narrative format, organized by date and time. The face sheet is a summary of a patient's demographic, medical history, and insurance information that is extracted from their full patient record. A Queen's employee downloaded the face sheet and progress notes of each randomly selected navigation patient to an electronic file and removed all identifying information from the record.

To quantify and analyze the cases, the progress note narratives were coded based on a coding system used for the Health Resources Services Administration's Patient Navigator Outreach and Chronic Disease Prevention Program (HRSA/PNDP).[17] This coding system closely fits the type of information collected by Queen's navigators. Two workers trained in the HRSA/PNDP system tailored the coding manual and data dictionary to the needs of the project. The coding schema was tested by working through three cases each, and the manual and dictionary were finalized. These two workers trained three other individuals and checked the first two cases of each, resolving any discrepancies. Once it was assured that all five coders were coding consistently, the remaining cases were coded independently, and randomly selected cases also were checked by another coder. In all, 10% of the 120 cases were reviewed by two different coders, and inter-rater congruence was 95%. Missing data were flagged and supplied by a Queen's Oncology Quality Improvement employee who had access to the full patient record.

Coders assumed that patients were English-speakers unless otherwise specified. When coding insurance status, private insurance was selected over public regardless of whether it was primary or secondary coverage. Public insurance was selected only if all health care coverage was provided by public sources (eg, companies providing Medicare and Medicaid services in Hawai'i: Evercare, AlohaCare, 'Ohana, etc). Coders also assumed that those over the age of 70 were unemployed/retired unless there was mention of an employer in the progress notes. Interactions that occurred outside of the study's time period were not coded. Finally, navigators are rarely notified of treatment completion, so in this study a case was considered closed when navigation activities ceased. Thus, a case was considered open for the period of time during which there were interactions. Extracted data elements were initially entered into Microsoft Excel®, and then imported into SPSS® version 20 for analysis. Outliers were rechecked by coders to ensure accuracy.

Intensity-based groups were created based on two variables — "number of actions the navigator undertook on behalf of the client" and the "number of days over which the navigator assisted the client." Patients for whom navigators took 1-2 actions over 1-2 days were grouped into the low-intensity group (n=40). Patients for whom navigators took 3-9 actions over 3 days to 7 weeks were grouped into the medium-intensity group (n=39). Patients for whom navigators took 10 or more actions over 2 or more months were grouped into in the high-intensity group (n=41). Frequencies were generated for the 120 clients together, and cross-tabulations and t-tests were used to test for differences among important subgroups of clients (eg, by ethnicity/race, cancer stage, island of residence, insurance, and intensity of navigation services). Three cases were chosen to illustrate each of the intensity groups. The "stories" of these clients were reconstructed from the information extracted from the progress notes. Any identifying details were generalized or changed when necessary to assure confidentiality. These changes were made after analysis in order to not affect quantitative outcomes.

In addition to data extracted from the progress notes, navigators mailed an anonymous patient satisfaction survey, which patients returned to 'Imi Hale for tabulation. In this short survey, patients were asked to indicate their level of agreement (from 1=strongly disagree to 5=strongly agree) with five statements: (1) the navigator helped me get answers to my cancer care questions; (2) the navigator helped make sure I missed very few appointments; (3) the navigator provided support and resources to help complete my treatment goals; (4) the navigator helped me and my family through the cancer journey; and (5) navigation services should be available to all cancer patients.

Results

Demographics

A staff of five navigators assisted 835 clients between October 1, 2010 and September 30, 2011. This translated into a caseload of about 15 patients per navigator per month. Our stratified random sample of 120 patients included 31 Whites, 29 Filipinos, 30 Japanese, and 30 Native Hawaiians (Table 1). Sixty percent of clients were women; 40.9% were age 40-59, and 55.8% were age 60-89 (remaining 3.3% were either younger or older than these two categories); and 62.5% were "partnered" (married or in a relationship). Fully 80% resided on O'ahu, while 20% resided on a neighbor island such as Hawai'i, Kaua'i, Lāna'i, Maui or Moloka'i. Only 1 was not insured, while 23.3% had public insurance only, and 75% had private insurance. Of the 120, just over one-third (35.8%) of referrals to CPN were generated by Queen's Cancer Center, another third were generated by Queen's Radiation Therapy Department (35.0%), 15.0% by a physician, 8.3% by client self-referral or a family member, and 5.8% by another person or agency.

Cancer

Of the 120 clients, 3 (2.5%) were found not to have cancer after diagnostic testing. All three had abnormal findings on screening and needed resection to obtain a definitive. All 3 clients were from neighbor islands and needed navigator assistance to travel to O'ahu for surgery. Of the 117 remaining clients, 105 (89.7%) had a newly diagnosed cancer and 10 (8.5%) had a recurring cancer; sufficient information was unavailable to classify 2 (1.7%) clients into the new or recurring categories. Altogether these 117 patients had cancers in 28 different sites;

however, the most common cancers were breast (30.0%), lung (15.8%), esophageal (6.7%), colon (5.8%), ovarian (4.2%), and prostate (3.3%). Among the 28 patients with public insurance exclusively (Medicare, Medicaid, MedQuest, etc.), 25 (89.3%) were diagnosed at Stage IV cancer. Type of initial treatment included surgery (45.0%), radiation (24.2%), chemotherapy (18.3%), or a combination of therapies (5.0%).

Barriers, Actions, and Case Days

The greatest barrier for the sample as a whole was difficulty obtaining on-island travel to treatment (48.9%). However, arranging and paying for inter-island travel was an even greater barrier for neighbor islands residents (18.3% of the entire sample, but 58.3% of neighbor islands residents). Difficulty scheduling tests, appointments, and treatment (11.2%) was the next greatest barrier.

Navigator actions were activities carried out for the patient, moving them to or through treatment. The number of actions taken per patient varied greatly. The mean number of actions taken was 9.5, and the median was 4. However, the actual number of actions taken per client ranged from 1 to 83, with 28 (23.3%) clients receiving only 1 action and 27 (22.5%) receiving 10 or more actions. Of the 1,139 actions, about 30% were with the patient (whether "in person" or by phone, email, or fax), and 29.4% were with the provider or health care staff on behalf of the patient. Another 21.8% were with social services organizations, and 17.6% were with the patient's social network (family and friends). Only 17% of all actions occurred in person, while 56.5% were handled by phone. As shown in Table 2, navigators helped schedule appointments (49.2%), arranged transportation (55.8%), coordinated social services (including linking clients to cancer organizations [71.7%]), discussed the patient's feelings and questions about their illness and care (26.7%), coordinated care (25.8%), and assisted clients with covering the costs of care (20.0%).

The number of days over which a case was open also varied greatly. For the entire sample, the mean number of days a case was open was 24.7, and the median was 14. However, the actual number of days a navigator helped a client ranged from 1 to 216. Forty clients (33%) only had their case open for less than a week; 39 (33%) had their case open for 1 to 7 weeks; and 41 (34%) had their case open for 2 or more months.

Intensity

In comparing characteristics of patients across the three intensity groups, we found that they were very similar to each other in age, gender distribution, island of residence, stage of cancer, ethnicity, and insurance. In other words, although we assumed that cancer patients living on neighbor islands, having metastatic cancer, or being on public insurance would be more likely to fall in the high-intensity group, this was not the case.

As shown in Table 2, several "needs" were associated with intensity of navigation services received. For example, significantly fewer patients in the low-intensity group needed help with education and reassurance, care coordination, travel, costs, and follow-up compared to patients in the mid-intensity and high-intensity groups. While this pattern also was seen for appointment scheduling and social services coordination

Table 1. Demographic Characteristics of 120 Navigated Cancer Patients, by "Intensity" of Services Received

	Total Cases (N=120)	Low-Intensity Cases (n=40)	Mid Intensity Cases (n=39)	High Intensity Cases (n=41)	*P*
Age (mean)	61.6	61.8	59.7	62.3	ns
Ethnicity					
Caucasian [n (%)]	31 (25.8)	14 (35.0)	6 (15.4)	11 (26.8)	ns
Japanese [n (%)]	30 (25.0)	11 (27.5)	9 (23.1)	10 (24.4)	
Hawaiian [n (%)]	30 (25.0)	9 (22.5)	9 (23.1)	12 (29.3)	
Filipino [n (%)]	29 (24.2)	6 (15.0)	15 (38.5)	8 (19.5)	
Female [n (%)]	72 (60.0)	24 (60.0)	27 (69.2)	21 (51.2)	ns
Spouse/Partner [n (%)]	75 (62.5)	23 (59.0)	25 (65.8)	27 (69.2)	ns
Neighbor Island [n (%)]	24 (20.0)	5 (12.5)	10 (25.6)	9 (22.0)	ns
Referral Source					
Queens Cancer Center [n (%)]	43 (35.0)	15 (37.5)	13 (33.3)	15 (36.6)	ns
Radiation Therapy [n (%)]	42 (35.0)	18 (45.0)	14 (35.9)	10 (24.4)	
Physician [n (%)]	18 (15.0)	3 (7.5)	6 (15.4)	9 (22.0)	
Self/Family/Other [n (%)]	17 (15.0)	4 (10.0)	6 (15.4)	7 (17.1)	
Public Insurance [n (%)]	28 (23.3)	7 (17.5)	13 (33.3)	8 (19.5)	ns
New Cancer [n (%)]	105 (89.7)	36 (97.3)	33 (84.6)	36 (87.8)	ns
Breast Cancer [n (%)]	36 (30.8)	13 (35.1)	13 (33.3)	10 (24.4)	ns
Stage 4 Cancer [n (%)]	34 (29.1)	12 (32.4)	14 (35.9)	8 (19.5)	ns

Table 2. Type of Assistance Received from Navigators for 120 Cancer Patients, by "Intensity" of Services Received					
	Total Cases (N=120)	**Low Intensity Cases (n=40)**	**Mid Intensity Cases (n=39)**	**High Intensity Cases (n=41)**	***P***
Interactions (mean)	9.49	1.5	6.0	20.6	<.001
Case Days	24.7	1.2	15.0	86.3	<.001
Education and Reassurance [n (%)]	32 (26.7)	4 (10.0)	9 (23.1)	19 (46.3)	.001
Scheduling of Appointments [n (%)]	59 (49.2)	15 (37.5)	22 (56.4)	22 (53.7)	ns
Coordination of Care [n (%)]	31 (25.8)	4 (10.0)	9 (23.1)	18 (43.9)	.002
Coordination of Social Service [n (%)]	86 (71.7)	24 (60.0)	32 (82.1)	30 (73.2)	ns
Travel Assistance [n (%)]	67 (55.8)	19 (47.5)	23 (59.0)	25 (61.0)	.01
Assistance with Costs [n (%)]	24 (20.0)	2 (5.0)	12 (30.8)	10 (24.4)	.01
Follow Up [n (%)]	29 (24.2)	3 (7.5)	11 (28.2)	15 (36.6)	.007

(with fewer patients in the low-intensity group needing help with this), the difference between the three groups was not significant. Bivariate analyses (data not shown) suggested that neighbor islands patients vs O'ahu-based patients were more likely to need help with travel, care coordination, and costs (all at $P<.050$), and patients on public vs private insurance were more likely to have stage 4 cancer ($P<.001$) and to need help with costs ($P=.006$).

The patient satisfaction survey collected during the study time frame showed that a majority (85%) of patients agreed or strongly agreed that the navigator helped them get answers to their cancer care questions. Over half (68%) of the patients agreed or strongly agreed that the navigator helped make sure they missed very few appointments. A preponderance (80%) agreed or strongly agreed that the navigator provided support and resources to help complete his/her treatment goals and 80% agreed or strongly agreed that the navigator helped him/her and his/her family through the cancer journey. Fully 90% agreed or strongly agreed that navigation services should be available to all cancer patients.

Case Studies

Three case studies were purposively selected from the 120 cases to illustrate the varying levels of intensity of navigation services.

Low-intensity

The cases of 40 patients in the low-intensity group were open only 1-2 days, during which time 1-2 actions were taken on their behalf. In one such case, the navigator provided a man with Stage II colorectal cancer with information about navigation and other Queen's services, but he had a strong support system and did not identify any needs for assistance.

Medium-intensity

The cases of 39 patients fell in the medium-intensity group, receiving 3-9 actions over 1-7 weeks. For example, an older patient with limited resources was referred to a gastroenterologist for a cancer workup, and the navigator was called in to help the patient obtain medical insurance. A MedQUEST application was filed, but the patient was denied coverage because of too many assets. Cancer was diagnosed, and the navigator then filed applications with a prescription assistance program to cover treatment costs. The navigator also interacted with the patient's family, including the spouse who was also caring for an elderly mother who lived out of state, and an adult child who lived in the continental US. At the patient's request, the navigator had the oncologist write a letter to support the adult child's relocation to Hawai'i, which was successful. The navigator also engaged the support of the oncology social worker to address the spouse's anxiety and depression. In all, the navigator provided 9 actions over 7 weeks, addressing financial, social, and emotional concerns.

High-intensity

The high-intensity group included 41 patients who had 10 or more actions over 2 or more months. One such patient was elderly with skin cancer and cognitive impairment, who was referred to a navigator by the Radiation Therapy department to assist with transportation. The navigator worked to get approval for insurance-assisted transportation services and, in the meantime, linked the patient with Queen's transportation service. Due to the patient's disorientation, it became apparent that an escort would be needed to help the patient safely get to and from appointments. The navigator worked to secure a physician certification for escort services but, due to lost paperwork and miscommunication, it took numerous actions to assure that a safe and effective transport routine was established. With cognitive impairment, the patient had difficulty understanding the diagnosis and treatment plan. The navigator and radiation oncologist worked with the patient's guardians to help the patient complete treatment. This case involved 83 actions over 5 months.

Discussion

The findings suggest that Queen's hospital-based CPN program is helping cancer patients across the continuum of care who have varying levels of need for support. The comprehensive review of patient navigation progress notes also provides insight as to what Queen's navigators are doing well. They transmit information about cancer and cancer services. They are successful in linking

patients to other care-team members within Queen's (physicians, social workers, financial counselors) and to community service providers (the American Cancer Society, transportation companies) to overcome barriers to care. They include and assist family members, as well as the patient, which enhances the family's ability to support the patient. They are excellent observers of patients' situations, so they seem to know when to ask what the patients need. CPN is being recognized as an essential cancer service, and the American College of Surgeons Commission on Cancer (CoC) is requiring CoC-accredited facilities to offer navigation to cancer patients by 2015.

Of interest is the current reach of navigation services. Although the program was successful in serving 835 patients in 12 months, physicians affiliated with Queen's Cancer Center treated 4,167 cancer patients in 2010. Of these patients, 2,439 (58%) were newly diagnosed with cancer, and 1,728 (42%) came to Queen's after they had been diagnosed and/or received their first course of treatment elsewhere. Thus, about 20% of all Queen's cancer cases received navigation services. Clearly, many of the individuals served were very needy, but about a third fell into the low-intensity group. Based on these findings, Queen's is instituting a system to identify and focus on patients that would most benefit from navigation services, including those with expressed or expected needs for help with inter-island travel, on-island transportation, costs, information, reassurance, linkages to social services, and care coordination. Future research should examine success with triaging the most needy clients to navigation.

In discussing potential reasons for the wide variance in number of actions and number of days over which navigation is provided, the research team felt that this reflected Queen's mission to serve all cancer patients at any point in the cancer care continuum. In this way, Queen's navigation program differs from many other cancer navigation programs that accrue clients at definitive time points and focus on specific types of cancer. For example, some programs focus on assisting community-dwelling individuals to obtain cancer screening. These include programs employing community-based navigators to increase breast cancer screening among Native American women, to increase breast and cervical cancer screening among Cambodian and Laotian women, and to increase colorectal cancer screening among Korean Americans.[7-9] Others accrue patients at the point of a suspicious finding, including clinic-based programs that help women with suspicious mammogram findings secure a definite diagnosis.[10-12] Other navigation programs employ navigators to help newly diagnosed patients.[18] Still others employ navigators only for a specific service, for example recruitment into clinical trials.[19] Many programs focus exclusively on breast cancer, by assisting women to screening and/or through breast cancer treatment.[13] Restricting navigation to patients at the same point in the cancer continuum (eg, need for screening, need for definitive diagnosis, or eligibility for clinical trials) allows for a meaningful exploration of the impact of navigation on outcomes.

Queen's, however, is a regional center for cancer services, receiving patients referred from other medical centers in Hawai'i and the greater Pacific basin, and navigation services can be provided to any cancer patient. Although the extracted data were not detailed enough to allow us to count exactly the number of patients referred in each phase of the cancer care continuum, it was apparent that some clients come to Queen's with suspected cancer, and the navigator helps them to secure a definitive diagnosis. Other clients meet the navigator at the point of definitive cancer diagnosis. This appears true for breast cancer and colon cancer instances, when the resection of a breast tumor or colon polyp for purposes of biopsy provides a definitive cancer diagnosis, and the client receives navigator assistance to help arrange radiation or chemotherapy appointments. Other clients may have a definitive cancer diagnosis, but treatment is delayed because the client is symptom free. Some men with prostate cancer, for example, undergo a period of "active surveillance" of the cancer before further cancer treatment is considered. Thus, treatment (and a visit with the navigator) may occur several years after diagnosis. Some clients may start their treatment at other facilities or at private physicians' offices, before coming to Queen's and seeing a navigator. For example, Tripler Army Medical Center and the Kaiser Permanente system perform cancer surgery and administer chemotherapy in-house. However, during the dates of our study (2010-2011), both facilities referred clients to Queen's for radiation therapy, where the navigator may assist in the scheduling of, or transportation to, appointments. Finally, clients from neighbor islands often experience expanded timelines for their diagnosis and treatment due to need for interisland travel.

These situations suggest that people with cancer have needs across the continuum and are tapping into Queen's CPN program at various points in their cancer journey. Fortunately, the 'Imi Hale navigation training program prepares navigators to provide care across the continuum and to help patients find answers to questions that navigators cannot directly answer. Unfortunately, this broad availability of navigation services restricts Queen's ability to test navigation's impact on outcomes, as ideal patient outcomes would vary greatly across patients depending on their stage of cancer and when they encounter the navigator (pre-diagnosis, suspicious finding, confirmed diagnosis, upon transfer from another diagnostic and/or treatment facility, survivorship, etc). Future evaluation of CPN should consider case controlled designs.

The collection of comprehensive patient data is essential to quality assurance and research. Queen's navigators have developed a data collection system that supports their service to patients. It includes a face sheet with basic information about the patient, followed by narrative progress notes. This narrative provides enough information to guide other navigators who may need to help the patient (eg, when the assigned navigator is on sick leave). However, a narrative format does not prompt the navigators to provide information in a standard way and, as noted in the methods section, requires subsequent coding before

analysis. Defining navigation case closure, ensuring that navigators are in the communication loop regarding patient treatment status, and finding effective ways to document navigation are extremely important to assure that patients in need of navigation do not fall through the cracks. Building a more effective data collection tool, preferably one that interfaces with both the in-patient and out-patient record, would facilitate future analysis and better understanding of cancer care barriers. It would allow, for example, the comparison of navigated and non-navigated cancer patients. It would also allow the linking of navigation actions to patient outcomes for specific clusters of navigated clients, such as timely diagnosis of those with suspicious findings and timely initiation of treatment for those with confirmed diagnoses.

Conclusion

Queen's Cancer Center is ahead of the curve in establishing a formal cancer patient navigation program. Navigated patients had a variety of needs related to cancer care, and navigators help patients address them. This essential service, soon to be required by the American College of Surgeons Commission on Cancer (CoC) for accredited facilities, helped patients understand their diagnosis and overcome barriers to accessing and following through with care. Triaging protocols and a better data collection system could improve the delivery and evaluation of this essential service.

Conflict of Interest

None of the authors identify any conflict of interest.

Disclosure Statement

This work is supported by grants from Human Resources and Services Administration (H4MHP20309) to The Queen's Medical Center and from the National Cancer Institute's Center to Reduce Cancer Health Disparities (3U01CA114630-05S1, U54CA153459-01) to 'Imi Hale Native Hawaiian Cancer Network, a program of Papa Ola Lōkahi.

Acknowledgements

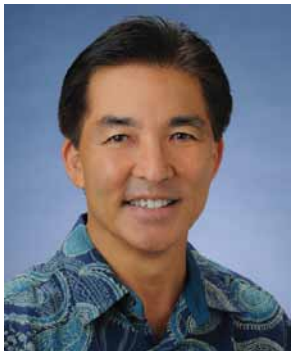
We acknowledge Elise Davis, May Rose Dela Cruz, Emily Scott, and Michael Smark for help with data collection and coding. We also would like to thank the cancer patient navigators at The Queen's Medical Center that contributed to the data reported here.

Authors' Affiliations:
- The Queen's Medical Center, Honolulu, HI (A.L.A., D.D.M.I., J.N., A.W.)
- 'Imi Hale Native Hawaiian Cancer Network, Papa Ola Lōkahi, Honolulu, HI (J.B.D., J.U.T., K.L.B.)
- Office of Public Health Studies, John A. Burns School of Medicine, University of Hawai'i, Honolulu, HI (K.L.B.)

Correspondence to:
Amanda Allison MA; The Queen's Medical Center, 1301 Punchbowl St., Honolulu, HI 96813; Ph: (808) 691-5383; Email: aallison@queens.org

References

1. Freeman H. Patient navigation: A community based strategy to reduce cancer disparities. *J Urban Health,* 2006 Mar;83(2):139-41.
2. Freund KM. Patient navigation: The promise to reduce health disparities. *J Gen Intern Med.* 2011 Feb;26(2):110-2.
3. Domingo J, Davis E. Allison A, Braun KL. Cancer patient navigation case studies: The complementary role of clinical and community navigators. *Hawaii Medical J.* 2011;70:257-261.
4. Hawai'i Cancer Facts & Figures 2012 p. 12
5. Braun KL, Kagawa Singer M, Holden AR, Burhansstipanov L, Tran JH, Seals B, Corbie-Smith G, Tsark JU, Harjo L, Foo MA, Ramirez A. Lay navigator tasks across the cancer care continuum. *J Health Care Poor Underserved.* 2012; 23 (2012): 398–413.
6. Wells KJ, Battaglia TA, Dudley DJ, et al. Patient navigation: State of the art or is it science? *Cancer* 2008 Oct 15;113(8):1999-2010.
7. Ma GX, Shive S, Tan Y, et al. Community-based colorectal cancer intervention in underserved Korean Americans. *Cancer Epi.* 2009 Nov;33(5):381–86.
8. Nguyen TN, Tanjasiri SP, Kagawa-Singer M, et al. Community health navigators for breast and cervical cancer screening among Cambodian and Laotian women: intervention strategies and relationship building processes. *Health Promot Pract.* 2008 Oct;9(4):356-7.
9. Burhansstipanov L, Dignan MB, Schumacher A, et al. Breast screening navigator programs within three settings that assist underserved women. *J Cancer Educ.* 2010 Jun;25(2):247-52.
10. Battaglia TA, Roloff K, Posner MA, et al. Improving follow-up to abnormal breast cancer screening in an urban population: a patient navigation intervention. *Cancer.* 2007 Jan 15;109(2 Suppl):359–67.
11. Ell K, Vourlekis B, Lee PJ, et al. Patient navigation and case management following an abnormal mammogram: a randomized clinical trial. *Prev Med.* 2007 Jan; 44(1):26–33.
12. Ferrante JM, Chen PH, Kim S. The effect of patient navigation on time to diagnosis, anxiety, and satisfaction in urban minority women with abnormal mammograms: a randomized controlled trial. *J Urban Health.* 2008 Jan;85(1):114–24.
13. Robinson-White S, Conroy B, Slavish KH, et al. Patient navigation in breast cancer: a systematic review. *Cancer Nurs.* 2010 Mar-Apr;33(2):127-40.
14. Braun KL, Allison A, Tsark JU. Using community-based research methods to design cancer patient navigation training. *Prog Community Health Partnersh.* 2008 Winter; 2(4):329-340.
15. http://hawaii.gov/dbedt/info/census/Census_2010/PL94-171/pltable1_County.pdf, table 1d
16. http://hawaii.gov/dbedt/info/economic/databook/db2010/section01.pdf table 1.35
17. Health Resources Services Administration, Patient Navigator Outreach and Chronic Disease Prevention Program http://bhpr.hrsa.gov/nursing/grants/patientnavigator.html.
18. Guadagnolo BA, Boylan A, Sargent M, et al. Patient navigation for American Indians undergoing cancer treatment: utilization and impact on care delivery in a regional health care center. *Cancer.* 2010. [Epub] doi: 10.1002/cncr.25823
19. Schapira L, Schutt R. Training community health workers about cancer clinical trials. *J Immigrant Minority Health,* 2010. [Epub] DOI 10.1007/s10903-010-9432-7.



Blenn Fujimoto
NMLS# 378910
Executive Vice President
Relationship Manager

SPECIALIZED MARKETS

A customized approach to working for you.

Specialized Markets offers a different kind of banking experience – a relationship built on understanding your industry's challenges and providing a single, simple solution – a Relationship Manager.

Proactive, flexible and responsive, your Relationship Manager is a single point of contact to a hand-selected team of financial experts that understand your industry. It's specialized service tailored to your needs from a team that's ready to work for you.

Call us for more information
808-544-3602

Chie Imamura
Assistant Vice President
Sr. Project Manager

Lisa Nillos
Vice President
Sr. Commercial Real Estate Officer

Jon Teraizumi
Vice President
Commercial Banking Officer

Keith Masuda
Vice President
Sr. Business Banking Team Manager

Scott Kurosawa
Vice President
Sr. Business Banking Team Manager

Reid Chung
NMLS# 798610
Vice President
Private Banking Officer

Joji Seta
Sr. Vice President
International Banking Manager
Japan Market

Gina Kim Nakamura
Vice President
International Banking Officer
Korea Market

Amery Lam
NMLS# 639230
Vice President &
East Honolulu Regional Manager

Herman Chang
NMLS# 639328
Vice President & Branch Manager

Diane S. J. Chong, CFP
Vice President
Trust Services Officer

Duncan Chun
Vice President
Investment Consultant

Gay McPhail, CMPS
NMLS# 377375
Vice President
Home Loan Manager

Erin Adaniya Palmer, CMPS
NMLS# 377720
Sr. Home Loan Consultant

CENTRAL PACIFIC BANK
Works. For You.

EQUAL HOUSING LENDER Member FDIC

centralpacificbank.com

The Effects of Extended Release Niacin on Lipoprotein Sub-Particle Concentrations in HIV-Infected Patients

Chunrong Lin MD; Andrew Grandinetti PhD; Cecilia Shikuma MD; Scott Souza PharmD; Nisha Parikh MD, MPH; Beau Nakamoto MD, PhD, MBA, MS; Kalpana J. Kallianpur PhD; and Dominic Chow MD, PhD, MPH

Abstract

With the advent of highly active antiretroviral therapy (HAART), Cardiovascular Disease (CVD) has emerged as the leading cause of death in Human Immunodeficiency Virus (HIV) infected patients. An atherogenic lipoprotein phenotype has been described in HIV- infected patients with a predominance of small, low density lipoprotein (SLDL) particles with accompanying elevated triglycerides and reduced high density lipoprotein cholesterol. This randomized controlled pilot study was conducted to evaluate the efficacy of Extended Release Niacin (ERN) in improving the lipid profile in HIV patients.

A total of 17 HIV positive subjects on HAART therapy with High Density Lipoprotein Cholesterol (HDL) levels below 40mg/dl and Low Density Lipoprotein Cholesterol (LDL) below 130mg/dl were enrolled. Nine were randomized to be treated with ERN titrated from a starting level of 500mg/night and titrated to a level of 1500mg/ night. Eight patients were assigned to the control arm. No placebo was used. Lipoprotein profiles of the subjects were analyzed at baseline and at the end of 12 weeks using Nuclear Magnetic Resonance (NMR) spectroscopy.

At the end of 12 weeks, NMR spectroscopic analysis revealed a significant increase in overall LDL size (1.2% in ERN treated subjects vs 2.0% decrease in control patients, P=.04) and a decrease in small LDL particle concentration (17.0% in ERN treated subjects vs 21.4% increase in control patients, P=.03) in subjects receiving ERN as compared to those in the control group. Only 1 subject receiving ERN developed serious flushing which was attributed to an accidental overdose of the drug. This pilot study demonstrates that ERN therapy in HIV-infected patients with low HDL is safe and effective in improving the lipoprotein profile in these patients.

Introduction

Highly active antiretroviral therapy (HAART) has resulted in the prolonged survival of most individuals infected with HIV. In tandem with the reduction in AIDS related deaths, cardiovascular disease (CVD) has emerged as the leading cause of death among HIV-infected patients.[1,2] A variety of metabolic abnormalities such as visceral fat deposition, insulin resistance, and dyslipidemia have become associated with HIV, and possibly as a side effect of HAART. In addition, cumulative exposure time to protease inhibitors (PI) has been found to be an independent risk factor for myocardial infarction.[3,4]

The CVD risk in the HIV-infected population has been in large part attributed to dyslipidemia - including low levels of high-density lipoprotein-cholesterol (HDL) and elevated levels of low-density lipoprotein-cholesterol (LDL).[4] LDL is instrumental in the transport of cholesterol into the artery wall where it becomes oxidized and ingested by macrophages that form foam cells. These foam cells, which are trapped in the walls of blood vessels, contribute to the formation of atherosclerotic plaque. Conversely, HDL particles prevent the oxidation of LDL particles and play a key role in reverse cholesterol transport.[5] HDL is also believed to maintain endothelial health through anti-inflammatory and antioxidant properties.[6] Therefore, LDL and HDL concentrations measurements have been the cornerstone of the clinical assessment and management of CVD.

Lipoprotein particle sub-fraction (size, density, and concentration) may better relate to risk for CVD than standard clinical lipoprotein measures. Direct assessment of the various lipoprotein particle concentrations was recently made possible by the development of Nuclear Magnetic Resonance (NMR) spectroscopic analysis. The different subclasses of Very Low Density Lipoproteins (VLDL), LDL and HDL emit distinctive NMR signals which can be accurately measured. The signal amplitude is also directly proportional to the numbers of subclass particles, allowing for accurate quantification of the lipoprotein particle numbers .[7] This is an advancement over the traditional assessment of the lipoprotein profile, as NMR allows for measurements of the actual number of particles within each lipoprotein sub-fraction, whereas traditional methods could only quantify the cholesterol concentrations of the various lipoproteins (eg, LDL and HDL). The cholesterol content and sizes of the lipoprotein particles vary among individuals and change over time as a result of medications or lifestyle modifications. As a result, direct measurements of the number of atherogenic and anti-atherogenic lipoprotein particles allow for a more accurate assessment of the patient's CVD risk.[8]

The use of HAART in HIV-1 infections has been associated with an unfavorable lipoprotein profile, based on a predominance of Small Low Density Lipoprotein (SLDL) particles with accompanying elevated triglycerides and reduced high density lipoprotein cholesterol.[4] Data on non HIV patients have demonstrated that high levels of SLDL particles and low levels of Large Low Density Lipoprotein (LLDL) particles are associated with an increased risk of CVD.[9-11] SLDL particles have a greater propensity for transport into the sub-endothelial space, are more susceptible to oxidative modification, and have a greater binding potential to arterial wall proteoglycans than LLDL particles.[12] Statins have been widely employed as the primary lipid lowering therapy in CVD risk management. Although effective in reducing circulating LDL, statins are less effective in reducing triglyceride (TG) rich lipoproteins, VLDL and Intermediate Density Lipoprotein (IDL), and ineffective in raising HDL.[13] A recent study of dyslipidemic patients receiving lipid lowering therapy (primarily statins) found that more than 40% had low levels of HDL concentrations.[14] Patients with 2 or 3 abnormal lipid levels (HDL, LDL, or TG) were found to be at a 22% to 45% greater risk of a CV event over a 2-year

period as compared to patients with all 3 lipids at normal levels.[15] Therefore statin therapy may only partially correct CVD risk associated with dyslipidemia.

Niacin (nicotinic acid or vitamin B3) is considered one of the most effective agents commercially available for elevating HDL plasma concentrations while reducing elevated TG and LDL concentrations.[16] It has also been shown to be equally efficacious in HIV infected patients.[17] Niacin has been shown to decrease LDL particle sub-fractions resulting in reductions of circulating SLDL levels while increasing circulating LLDL levels in non HIV patients.[18] The development of Extended Release (ER)-Niacin (ERN) has dramatically decreased flushing and virtually eliminated hepatotoxicity, making it safer and better tolerated by patients.[19]

Given the importance of low HDL on cardiometabolic risk in HIV and demonstrated effects of HDL subfractions on incident CVD, the purpose of our pilot study is to evaluate the effects of ERN on lipoprotein sub-fraction composition in HIV-infected patients with low HDL concentrations and normal LDL concentrations.

Methods

This secondary analysis was performed using data and lipid samples collected as part of a previous study on ERN and its effects on cardiovascular risk reduction in HIV positive patients on stable HAART (treated for at least 6 months) that has been previously described.[20] The parent study was a prospective, randomized 12-week clinical trial designed to assess the short term effects of ERN on endothelial function. All subjects signed informed consent, and the institutional review board (IRB) at the University of Hawai'i approved the study (CHS # 15727). The parent study included 17 men and 2 women over 18 years of age with low HDL (defined as HDL less than 40 mg/dl) and normal LDL (defined as LDL less than 130 mg/dl) lipoprotein levels. Exclusion criteria including individuals who were pregnant or had a history of cardiovascular disease, uncontrolled hypertension, diabetes mellitus, or were on concurrent treatment with statins, fibrates, nitrates, metformin, or thiazolidinedione. Subjects were randomized into either a treatment arm which received ERN (Niaspan®) or a control arm which received no intervention. A total of 10 subjects were assigned to the treatment group, and were started on ERN at a dose of 500 mg per night, which was titrated to a maximum dose of 1500 mg per night over 8 weeks. The maximum dose was maintained for another 4 weeks for a total of 12 weeks. Nine subjects were assigned to the control group, and were not given a placebo, but did receive the same follow up as the treatment group. Lipid parameters were obtained at baseline and at end of study.

Blood samples from 17 subjects (9 in the treatment arm and 8 in the control arm) were analyzed utilizing NMR spectroscopy, for 18 distinct lipid parameters (Table 1). Two patients were omitted from the parent study for this analysis (1 each from the treatment and control arm) as blood samples were not obtained from these patients. VLDL, LDL and HDL subclasses of different sizes in plasma samples simultaneously emit distinctive NMR signals which can be accurately and reproducibly measured. The subclass signal amplitudes are also directly proportional to the numbers of subclass particles emitting the signal, irrespective of variation in particle lipid composition.[7]

Table 1. Lipid Parameter Description by NMR Spectroscopy

Abbreviations	Parameter	Unit
VLDLC	VLDL & Chylomicron Particles (total)	nmol/L
LVLDLC	Large VLDL & Chylomicrons Particles	nmol/L
MVLDL	Medium VLDL Particles	nmol/L
SVLDL	Small VLDL Particles	nmol/L
VLDLS	VLDL Size	nm
TG	Triglyceride (Total)	mg/dL
VLDLTG	VLDL & Chylomicron Triglyceride (total)	mg/dL
LDL	LDL Particles (Total)	nmol/L
IDL	IDL Particles	nmol/L
LLDL	Large LDL Particles	nmol/L
SLDL	Small LDL Particles	nmol/L
LDLS	LDL Size	nm
HDL	HDL Particles (Total)	µmol/L
LHDL	Large HDL Particles	µmol/L
MHDL	Medium HDL Particles	µmol/L
SHDL	Small HDL Particles	µmol/L
HDLS	HDL Size	nm
HDL	HDL Cholesterol (total)	mg/dL

VLDL= Very Low Density Lipoprotein, LDL= Low Density Lipoprotein, IDL= Intermediate Density Lipoprotein, HDL=High Density Lipoprotein

Statistical Analysis

The primary aim was to assess any significant differences in lipid sub-particle measurements at week 12 between the treatment and control. Categorical variables were compared using the chi square test. Continuous variables are presented as medians along with their interquartile range (Q1, Q3) and analyzed by non-parametric Wilcoxon rank test. Differences between baseline and end of study NMR lipid sub-particle measures between groups were analyzed with Wilcoxan rank test. A two-sided probability of $P<.05$ was used to determine statistical significance. All statistical analyses were performed using the JMP statistical program (SAS Institute Inc, Cary, NC).

Results

Demographic and baseline clinical characteristics of the 17 participants are detailed in Table 2. The majority of participants were men (15/17) with a median age of 50.1 years (range 27 - 62). Participants had a median CD4 count of 479 cells/µl (range 280 - 1096). One participant had a detectable (≥48 copies) viral load of 1520 copies/ml. All participants were receiving HAART with 47% receiving an Efavirenz-based regimen and 42% receiving a protease inhibitor-based regimen. There were no significant differences in age, ethnicity, gender, heart rate, body mass index (BMI), blood pressure, CD4 count, propor-

Table 2. Baseline Clinical Characteristics of Subjects[a]			
Variable	**Control (n = 8)**	**ER Niacin (n = 9)**	***P*-value**
Age (years)	50.1 (38.3, 53.9)	50.2 (41.5, 55.6)	.78
Ethnicity (White/Other)	5/3	7/2	.62
Gender (male/female)	6/2	9/0	.21
Heart Rate (pulse/min)	55.0 (43.5, 60.0)	59.0 (51.2, 64.2)	.29
Body Mass Index (kg/m2)	25.6 (24.6, 28.4)	25.5 (22.2, 26.9)	.36
Systolic Blood Pressure (mmhg)	123.5 (116.8, 131.5)	127.0 (109.0, 129.0)	.77
Diastolic Blood Pressure (mmhg)	74.0 (70.5, 77.0)	79.0 (69.0, 82.0)	.53
CD4 cells (cells/µl)	479.0 (391.0, 620.2)	508.0 (362.0, 532.5)	.99
% with undetectable HIV RNA	100% (8/8)	89% (8/9)	.87
% on protease inhibitor based regimen	50% (4/8)	33% (3/9)	.49

[a]median (Quartile1,Quartile3) for all continuous variables

Table 3. Fasting Serum Lipid Profile at Baseline and End of Study[a]			
Lipoprotein	**Control**	**ER Niacin**	**p[β]**
Baseline			
Total Cholesterol (mg/dl)	173.0 (156.2, 220.0)	184.0 (138.5, 193.0)	0.66
HDL (mg/dl)	34.0 (24.5, 38.0)	38.0 (33.5, 41.0)	0.15
LDL (mg/dl)	115.5 (98.2, 149.5)	114.0 (70.0, 127.0)	0.33
Triglycerides (mg/dl)	128.5 (87.0, 191.0)	176.0 (119.0, 203.0)	0.26
End of study			
Total Cholesterol (mg/dl)	167.0 (135.0, 196.0)	174.0(154.0, 198.5)	0.64
HDL (mg/dl)	30.5 (24.0, 40.0)	44.0 (42.0, 44.0)	0.03
LDL (mg/dl)	104.5 (82.0, 129.0)	118.0 (81.0, 127.0)	0.90
Triglycerides (mg/dl)	116.0 (102.8, 181.2)	102.0 (86.5, 179.0)	0.93

[a]HDL = high-density lipoprotein-cholesterol; LDL = low-density lipoprotein-cholesterol. [β] Analyzed by non-parametric Wilcoxon rank test.

Table 4. Changes in NMR Spectroscopic Lipoprotein Profile from Baseline[a]			
NMR lipoprotein[a] (Units)	**Control (% change)**	**ERN (% change)**	**p[β]**
VLDLC (nmol/L)	-12.22	17.23	0.10
LVLDLC (nmol/L)	-44.56	-0.15	0.56
MVLDL (nmol/L)	-6.26	22.71	0.25
SVLDL (nmol/L)	-12.19	14.36	0.34
VLDLS nm	-1.81	3.37	0.60
TG mg/dL	-16.09	11.95	0.27
VLDLTG mg/dL	-24.43	14.84	0.21
LDL (nmol/L)	0.81	8.78	0.34
IDL (nmol/L)	37.51	-4.90	0.10
LLDL (nmol/L)	28.87	-22.31	0.12
SLDL (nmol/L)	21.42	-17.02	0.03
LDLS nm	-1.96	1.22	0.04
HDL µmol/L	-0.12	1.84	0.85
LHDL µmol/L	-6.93	30.68	0.21
MHDL µmol/L	-3.69	-3.08	0.85
SHDL µmol/L	3.23	11.47	0.47
HDLS nm	0.14	-2.37	0.12
HDL mg/dL	-2.92	-4.46	0.66

[a]See Table 1 for legend. [β] Analyzed by non-parametric Wilcoxon rank test.

tion of subjects with detectable viral load, and proportion of subjects on a protease-based antiretroviral regimen between treatment and control groups.

There were no significant differences in the fasting lipid profile at baseline between the treatment and control groups (Table 3). All treatment group participants achieved the titrated dose of 1500 mg/day of ERN. One participant experienced the niacin-induced side effect of flushing. This was likely due to accidently ingesting twice the prescribed dose, and resolved after the ERN dose was reduced. There were no other adverse reactions reported during the study period in either group. NMR spectroscopic analysis revealed a significant increase in overall LDL size (1.2% in ERN treated subjects vs 2.0% decrease in control patients, *P*=.04) and a decrease in small LDL particle concentration (17.0% in ERN treated subjects vs 21.4% increase in control patients, *P*=.03) in subjects receiving ERN as compared to those in the control group (Table 4).

Discussion

In this pilot study, we found that treatment with ERN is well-tolerated and associated with improvements in some LDL sub-particle levels. There were significant decreases in small LDL particle concentrations and increases in LDL particle size following treatment with ERN compared to the control group. These findings are consistent with other studies done on non HIV patients,[18] However, they differed from a study done in HIV patients where the decreases in total and small LDL particles were not statistically significant and the LDL particle sizes did not change.[21] Our findings are promising since SLDL particles and small LDL particle size are thought to be more atherogenic and associated with a greater risk of coronary heart disease. This suggests that niacin is well tolerated and effective in HIV patients on HAART, as it may reverse the unfavorable lipoprotein composition in these patients, akin to the atherogenic lipoprotein phenotype found in patients with obesity, diabetes and insulin resistance.

In contrast, utilizing NMR spectroscopy, we were unable to demonstrate a significant change in HDL levels in HIV-infected subjects with low HDL on stable HAART treated with ERN compared to those who were not. This was consistent with other studies done on HIV patients where no significant changes were detected in LDL and HDL levels[22].and may be due to a limitation of our study design, where the maximum dose of 1500mg was only taken for 4 weeks. In comparison, studies on the HIV-seronegative population have consistently demonstrated an increase in large HDL particle concentrations following treatment with ERN,[18,23] and continued increases in the HDL level were observed up to 36 weeks of full-dose niacin therapy.[23,24]

There are several limitations to this study associated with this being an unblinded pilot study with a small sample size. The results of this small study could be influenced by chance findings. The results of this pilot study will need to be verified within the HIV population on HAART with a randomized, placebo controlled study with a larger sample size. Such a study would reduce the inter-subject variation and provide a better estimate of the effects of niacin on the various lipoproteins. Also the effects of niacin on small LDL particle concentrations and LDL particle size in the HIV population must be confirmed. A recent study by the AIM-HIGH investigators failed to show any incremental benefit in CVD risk reduction from the addition of niacin to statin therapy.[25] The AIM HIGH study, however, was done on non HIV-infected patients and was conducted on patients already treated with intensive statin therapy. Our study also evaluated the short change in lipid sub-particle composition as a surrogate marker, as compared to the AIM HIGH study which was a clinical end point study.

In summary, this pilot study has demonstrated that short-term treatment with ERN therapy is safe and can improve lipid sub-particle composition in HIV-infected individuals on stable HAART who have low HDL.

Conflict of Interest

None of the authors indentify any conflict of interest.

Acknowledgements

This work was supported in part by the Department of Defense Telemedicine and Advanced Technology Research Center (proposal no. 06187003) and grants from the National Institutes of Health (NHLBI K23 HL088981, RCMI NCRR P20RR011091, NCRR 1 R25 RR019321, U54RR026136, U54MD007584 and NCRR 1 UL1 RR024150). We thank the study participants for generously donating their time and effort.

Authors' Affiliation:
- John A. Burns School of Medicine, University of Hawai'i, Honolulu, HI

Correspondence to:
Dominic Chow MD, PhD, MPH; Hawai'i Center for AIDS, Leahi Hospital, Young Building, 3675 Kilauea Avenue, 5th Fl., Honolulu, HI 96816; Ph: (808) 737-2751; Email: dominicc@hawaii.edu

References

1. Crum NF, Riffenburgh RH, Wegner S, et al. Comparisons of causes of death and mortality rates among HIV-infected persons: analysis of the pre-, early, and late HAART (highly active antiretroviral therapy) eras. *J Acquir Immune Defic Syndr.* 2006;41(2):194-200.
2. Krentz HB, Kliewer G, Gill MJ. Changing mortality rates and causes of death for HIV-infected individuals living in Southern Alberta, Canada from 1984 to 2003. *HIV Med.* 2005;6(2):99-106.
3. Friis-Moller N, Reiss P, Sabin CA, et al. Class of antiretroviral drugs and the risk of myocardial infarction. *N Engl J Med.* 2007;356(17):1723-35.
4. Carr A, Samaras K, Burton S, et al. A syndrome of peripheral lipodystrophy, hyperlipidaemia and insulin resistance in patients receiving HIV protease inhibitors. *AIDS.* 1998;12(7):F51-8.
5. Lewis GF, Rader DJ. New insights into the regulation of HDL metabolism and reverse cholesterol transport. *Circ Res.* 2005;96(12):1221-32.
6. Petraki MP, Mantani PT, Tselepis AD. Recent advances on the antiatherogenic effects of HDL-derived proteins and mimetic peptides. *Curr Pharm Des.* 2009;15(27):3146-66.
7. Jeyarajah EJ, Cromwell WC, Otvos JD. Lipoprotein particle analysis by nuclear magnetic resonance spectroscopy. *Clin Lab Med.* 2006;26(4):847-70.
8. Otvos JD, Jeyarajah EJ, Cromwell WC. Measurement issues related to lipoprotein heterogeneity. *Am J Cardiol.* 2002;90(8A):22i-29i.
9. Krauss RM. Dietary and genetic effects on low-density lipoprotein heterogeneity. *Annu Rev Nutr.* 2001;21:283-95.
10. Musunuru K, Orho-Melander M, Caulfield MP, et al. Ion mobility analysis of lipoprotein subfractions identifies three independent axes of cardiovascular risk. *Arterioscler Thromb Vasc Biol.* 2009;29(11):1975-80.
11. Mora S, Otvos JD, Rifai N, et al. Lipoprotein particle profiles by nuclear magnetic resonance compared with standard lipids and apolipoproteins in predicting incident cardiovascular disease in women. *Circulation.* 2009;119(7):931-9.
12. Krauss RM. Lipoprotein subfractions and cardiovascular disease risk. *Curr Opin Lipidol.* 2010;21(4):305-11.
13. Chapman MJ, Le Goff W, Guerin M, et al. Cholesteryl ester transfer protein: at the heart of the action of lipid-modulating therapy with statins, fibrates, niacin, and cholesteryl ester transfer protein inhibitors. *Eur Heart J.* 2010;31(2):149-64.

14. Bruckert E, Baccara-Dinet M, McCoy F, et al. High prevalence of low HDL-cholesterol in a pan-European survey of 8545 dyslipidaemic patients. *Curr Med Res Opin.* 2005;21(12):1927-34.
15. Stanek EJ, Sarawate C, Willey VJ, et al. Risk of cardiovascular events in patients at optimal values for combined lipid parameters. *Curr Med Res Opin.* 2007;23(3):553-63.
16. Backes JM, Gibson CA, Howard PA. Optimal lipid modification: the rationale for combination therapy. *Vasc Health Risk Manag.* 2005;1(4):317-31.
17. Balasubramanyam A, Coraza I, Smith EO, et al. Combination of niacin and fenofibrate with lifestyle changes improves dyslipidemia and hypoadiponectinemia in HIV patients on antiretroviral therapy: results of "heart positive," a randomized, controlled trial. *J Clin Endocrinol Metab.* 2011;96(7):2236-47.
18. Morgan JM, Capuzzi DM, Baksh RI, et al. Effects of extended-release niacin on lipoprotein subclass distribution. *Am J Cardiol.* 2003;91(12):1432-6.
19. McCormack PL, Keating GM. Prolonged-release nicotinic acid: a review of its use in the treatment of dyslipidaemia. *Drugs.* 2005;65(18):2719-40.
20. Chow DC, Stein JH, Seto TB, et al. Short-term effects of extended-release niacin on endothelial function in HIV-infected patients on stable antiretroviral therapy. *AIDS.* 2010;24(7):1019-23.
21. Dube MP, Wu JW, Aberg JA, et al. Safety and efficacy of extended-release niacin for the treatment of dyslipidaemia in patients with HIV infection: AIDS Clinical Trials Group Study A5148. *Antivir Ther.* 2006;11(8):1081-9.
22. Gerber MT, Mondy KE, Yarasheski KE, et al. Niacin in HIV-infected individuals with hyperlipidemia receiving potent antiretroviral therapy. *Clin Infect Dis.* 2004;39(3):419-25.
23. Bays HE, McGovern ME. Once-daily niacin extended release/lovastatin combination tablet has more favorable effects on lipoprotein particle size and subclass distribution than atorvastatin and simvastatin. *Prev Cardiol.* 2003;6(4):179-88.
24. Capuzzi DM, Guyton JR, Morgan JM, et al. Efficacy and safety of an extended-release niacin (Niaspan): a long-term study. *Am J Cardiol.* 1998;82(12A):74U-81U; discussion 85U-86U.
25. Boden WE, Probstfield JL, Anderson T, et al. Niacin in patients with low HDL cholesterol levels receiving intensive statin therapy. *N Engl J Med.* 2011;365(24):2255-67.

'Opae E (D. Varez)

Favorable Outcomes for Native Hawaiians and Other Pacific Islanders with Severe Traumatic Brain Injury

Kazuma Nakagawa MD; Reid R. Hoshide MPH; Susan M. Asai BSN; Katherine G. Johnson MS; Juliet G. Beniga BSN; Melanie C. Albano BSN; Johnna L. del Castillo BS, BA; Daniel J. Donovan MD; Cherylee W. Chang MD; and Matthew A. Koenig MD

Abstract

Traumatic brain injury (TBI) disproportionately impacts minority racial groups. However, limited information exists on TBI outcomes among Native Hawaiians and other Pacific Islanders (NHPI). All patients with severe TBI (Glasgow Coma Scale (GCS) <9) who were hospitalized at the state-designated trauma center in Hawai'i from March 2006 to February 2011 were studied. The primary outcome measure was discharge Glasgow Outcome Scale ([GOS]: 1, death; 2, vegetative state; 3, severe disability; 4, moderate disability; 5, good recovery), which was dichotomized to unfavorable (GOS 1-2) and favorable (GOS 3-5). Logistic regression analyses were performed to assess factors predictive of discharge functional outcome. A total of 181 patients with severe TBI (NHPI 27%, Asians 25%, Whites 30%, and others 17%) were studied. NHPI had a higher prevalence of assault-related TBI (25% vs 6.5%, P=.046), higher prevalence of chronic drug abuse (20% vs 4%, P=.02) and chronic alcohol abuse (22% vs 2%, P=.003), and longer intensive care unit length of stay (15±10 days vs 11±9 days, P<.05) compared to Asians. NHPI had lower prevalence of unfavorable functional outcomes compared to Asians (33% vs 61%, P=.006) and Whites (33% vs 56%, P=.02). Logistic regression analyses showed that Asian race (OR, 6.41; 95% CI, 1.68–24.50) and White race (OR, 4.32; 95% CI, 1.27–14.62) are independently associated with unfavorable outcome compared to NHPI. Contrary to the hypothesis, NHPI with severe TBI have better discharge functional outcomes compared to other major racial groups.

Introduction

In the United States, 1.7 million people experience a traumatic brain injury (TBI) each year, 52,000 of whom die in-hospital.[1] Direct medical costs and indirect costs such as lost productivity as a result of TBI are estimated to be $60 billion annually in the United States.[2] Furthermore, recent evidence suggests that the burden of TBI is not borne equally by all, with racial minority groups reported to have higher incidence and poorer outcomes than non-Hispanic Whites.[3-5] Prior studies have shown that African-Americans and Asians had higher in-hospital mortality than non-Hispanic Whites after TBI.[3] One longitudinal study of TBI patients showed that African Americans and Hispanics had worse functional outcome at discharge and 1-year post-injury compared to non-Hispanic Whites.[6] The long-term functional outcomes after severe TBI were also worse among the racial-ethnic minorities compared to non-Hispanic Whites.[4,5,7] Asian Americans with TBI have also shown similar disparities in the in-hospital mortality rate compared to non-Hispanic Whites.[8,9] Despite the racial disparities seen among many racial minorities with TBI, little is known about the outcomes of Native Hawaiians and other Pacific Islanders (NHPI) in Hawai'i who suffer severe TBI. According to the definition used in the 2010 Census, NHPI refers to persons with origins in any of the original peoples of Hawai'i, Guam, Samoa or other Pacific Islands.[10] Therefore, racial/ethnic differences in the discharge functional outcome after severe TBI were assessed among a unique patient population that primarily consists of NHPI, Asians, and non-Hispanic Whites. The hypothesis of the study was that NHPI race is an independent predictor of unfavorable outcomes among persons with severe TBI.

Methods

This was a single-center, retrospective study of all patients with severe TBI (Glasgow Coma Scale [GCS] score <9) from March 2006 to February 2011 who were hospitalized at The Queen's Medical Center (QMC). QMC is a 505-bed medical center located in Honolulu, and is the largest tertiary referral center for the Pacific Basin. As the only state-designated trauma center in Hawai'i, QMC receives all major trauma victims from the Hawaiian Islands. All patients with significant head injuries, including isolated head injuries as well as multitrauma victims admitted to QMC are treated in the neuroscience intensive care unit (NSICU) by a multidisciplinary team according to existing evidence-based guidelines for TBI.[11] Intracranial pressure (ICP) monitors and brain tissue oxygen ($PbtO_2$) monitors are placed when clinically indicated as part of standard neurocritical care practices. Decompressive craniectomy is performed for patients with clinical cerebral herniation syndromes due to mass effect or refractory intracranial hypertension. When indicated, removal of mass lesions is also performed at the time of surgery.

This study was approved by the QMC institutional research review committee. We reviewed the TBI-trac database™, a prospectively collected database of severe TBI patients who are treated at our institution. Additional clinical data were obtained from a retrospective chart review by 6 people. Abstracted data include patient demographics, mechanism of injury, whether the patient had undergone decompressive craniectomy, body mass index (BMI), admission GCS, Injury Severity Score (ISS), medical co-morbidities including history of diabetes mellitus, hypertension, coronary artery disease, prior stroke, and chronic obstructive pulmonary disease. Substance abuse history and urine toxicology results, if available, were also obtained. The race and ethnicity information were collected by the administrative personnel during the registration process, nurses during the intake process, or by the research staff personnel through chart review process. Since mixed racial background is relatively common in Hawai'i, race was defined as the racial background that the patient most closely associated with and was based on patient self-identification or family's identification if the patient

was incapacitated. The Native Hawaiian race and other Pacific Islander race were combined into one racial category (NHPI) for ease of comparison with national census-based data. Race was categorized as NHPI, Asian, White, and other. Clinical outcome measures such as total hospital length of stay (LOS), Intensive Care Unit (ICU) LOS, in-hospital mortality, and discharge Glasgow Outcome Scale (GOS) were also obtained. The GOS is commonly used to assess physical functioning after neurological injuries, and classifies subjects into broad categories: 1, death; 2, vegetative state; 3, severe disability; 4, moderate disability; 5, good recovery. The discharge GOS was estimated from the documentation provided by the physical therapists, occupational therapists, speech therapists, nurses, and physicians at the time of discharge. The primary outcome measure was discharge functional outcome, which was dichotomized to unfavorable outcome (GOS 1-2) and favorable outcome (GOS 3-5). All initial head computed tomography (CT) scans were retrospectively reviewed by a board-certified neurointensivist, blinded to race, ethnicity and clinical data, and scored according to the Marshall CT classification[12] and Rotterdam CT score.[13]

Data were analyzed using commercially available statistical software (SPSS 18.0, Chicago, IL). Patient characteristics were summarized using descriptive statistics appropriate to variable type. The Asian and White racial groups were compared to the NHPI group (reference group) using χ^2 test or Fisher's Exact test for categorical data and 2-tailed t-test for normally distributed, continuous variables. To determine racial disparities in functional outcome at discharge, multivariable analyses using a logistic regression model were performed to assess whether race, compared to NHPI race, is an independent predictor of functional outcome at discharge. Variables with $P \leq .10$ in the univariate testing were selected for entry in the model. Race was forced to enter in the model regardless of the statistical significance in the univariate testing. In the model, only the Rotterdam CT score, and not the Marshall CT classification, was included since the two CT scores are collinear. Levels of $P < .05$ were considered statistically significant.

Results

A total of 181 patients with severe TBI (NHPI 27%, Asians 25%, Whites 30%, and others 17%) were studied. Clinical characteristics are shown in Table 1. Among the severe TBI patients admitted to our institution, NHPI were younger (NHPI: 30 ± 15 years vs Asians: 45 ± 24 years, $P = .001$; vs Whites: 40 ± 18 years, $P = .005$) compared to Asians and Whites. Compared to Asians, NHPI had a higher prevalence of assault-related TBI (25% vs 6.5%, $P = .046$), higher prevalence of chronic drug abuse (20% vs 4%, $P = .02$), chronic alcohol abuse (22% vs 2%, $P = .003$), presence of alcohol on the urine toxicology study (39% vs 12%, $P = .009$), and longer ICU LOS (15 ± 10 days vs 11 ± 9 days, $P = .049$). There was no difference in the CT characteristics among the three racial groups. There was a trend toward lower in-hospital age-adjusted mortality in NHPI compared to Asians (27% vs 48%, $P = .06$). The proportions of patients with unfavorable discharge functional outcome (GOS 1-2) were lower among NHPI compared to Asians (33% vs 61% respectively, $P = .006$) and Whites (33% vs 56% respectively, $P = .02$; Figure 1).

Univariate analyses showed that the group with unfavorable discharge functional outcome (n = 90) had a different proportion of racial groups ($P = .03$), lower admission GCS score ($P = .01$), higher ISS score ($P = .045$), higher prevalence of fixed and dilated pupils ($P = .006$), higher prevalence of traumatic subarachnoid hemorrhage ($P = .009$) and compression of the basal cisterns ($P = .007$) seen on the head CT, and higher Rotterdam ($P < .001$) and Marshall ($P < .001$) CT scores compared to those with favorable discharge functional outcome (n = 91; Table 2). In the multivariable analyses (Table 3), after adjusting for age and variables with pre-specified significance, the independent predictors for unfavorable discharge outcome were Asian race (OR, 6.41; 95% CI, 1.68 – 24.50, $P = .007$) and White race (OR, 4.32; 95% CI, 1.27 – 14.62, $P = .02$) compared to NHPI race, and Rotterdam CT score (OR, 2.72; 95% CI, 1.25 – 5.90, $P = .01$).

Discussion

Contrary to the initial hypothesis, this study shows that NHPI are less likely to have an unfavorable outcome after severe TBI compared to Asians and Whites, after adjusting for age and other confounders. Furthermore, NHPI were younger compared to Asians and Whites, and had a higher proportion of assault-related injuries and history of chronic drug and alcohol abuse compared to Asians. To our knowledge, this is the first study to describe the clinical characteristics and disparities in outcome after severe TBI in a population that contains a large proportion of NHPI. Most prior studies assessing the racial disparities in the TBI population suggest worse outcome among the minority groups. In patients who visited an Emergency Department (ED) for mild TBI, Hispanics were more likely to receive nasogastric tube placement compared to non-Hispanics, possibly due to language barriers.[14] Similarly, ethnic minority groups with mild TBI were more likely to receive ED care by a resident than a staff physician and were also less likely to return to the referring physician for follow-up.[14] In a pediatric TBI population, African-American children with TBI were found to have worse functional outcomes at discharge compared to equivalently injured non-Hispanic White children with TBI.[15] Despite the disparities seen in other minority groups, there are no published data regarding TBI in the NHPI population. Overall, NHPI are underrepresented in TBI studies and are often grouped together with Asians into a single racial category, despite evidence that NHPI may substantially differ from Asian patients.

Reasons for racial differences in outcome seen in this study are likely complex. Since NHPI had a higher prevalence of assault-related injuries and lower prevalence of fall-related injuries compared to Asians and non-Hispanic Whites, it is possible that assault-related injuries would lead to a lower mechanical impact on the brain compared to fall-related injuries. However, since the mechanism of injury was not a significant factor in the univariate and multivariable analyses, it is unlikely that it contributed to the observed differences in outcome.

Table 1. Racial characteristics of severe TBI patients at The Queen's Medical Center (2006 – 2011)							
	NHPI	**Asians**	***P***	**Whites**	***P***	**Others**	***P***
n	49	46		55		31	
Age, years	30 ± 16	45 ± 24	**.001**	40 ± 18	**.005**	33 ± 16	**.46**
Female	8 (16)	12 (26)	.24	12 (22)	.48	6 (19)	.73
BMI, kg/m2	29 ± 9	26 ± 5	.08	26 ± 5	.14	27 ± 8	.54
Mechanism of injury			**.046**		.21		.06
Assault	12 (25)	3 (6.5)		6 (11)		2 (7)	
Fall	6 (12)	12 (26)		13 (24)		8 (26)	
MVA	26 (53)	21 (46)		26 (47)		13 (42)	
Sports injury	4 (4)	3 (6.5)		2 (4)		2 (7)	
Other	11 (12)	7 (15)		8 (15)		6 (19)	
Admission GCS	5.5 [3.0 – 7.0]	5.5 [3.0 – 7.0]	.95	5.0 [4.0 – 7.0]	.31	4.0 [3.0 – 6.5]	.25
ISS	34 [26 – 42]	29 [26 – 39]	.51	34 [26 – 41]	.39	34 [26 – 42]	.63
Fixed and dilated pupils	5 (12)	6 (15)	.71	7 (14)	.79	4 (13)	.90
History of chronic drug abuse	10 (20)	2 (4)	**.02**	9 (16)	.59	6 (19)	.91
History of chronic alcohol abuse	11 (22)	1 (2)	**.003**	12 (22)	.94	4 (13)	.29
Positive Methamphetamine	4 (11)	3 (9)	.75	6 (14)	.73	4 (18)	.45
Positive Alcohol	14 (39)	4 (12)	.009	18 (41)	.85	8 (36)	.85
Diabetes	3 (6)	8 (17)	**.09**	3 (6)	.88	0 (0)	.16
Hypertension	6 (12)	15 (32)	**.02**	5 (9)	.60	4 (13)	.93
Coronary artery disease	3 (6)	5 (11)	.41	4 (7)	.82	2 (7)	.95
Congestive heart failure	0 (0)	1 (2)	.30	0 (0)	-	0 (0)	-
COPD	1 (2)	1 (2)	.96	0 (0)	.29	0 (0)	.42
History of stroke	0 (0)	3 (7)	.07	0 (0)	-	0 (0)	-
Initial CT findings							
Intraventricular hemorrhage	7 (14)	8 (17)	.68	7 (13)	.82	4 (13)	.86
Subarachnoid hemorrhage	20 (41)	28 (61)	.05	27 (49)	.40	16 (52)	.34
Diffuse axonal injury	38 (78)	35 (76)	.87	42 (76)	.89	22 (71)	.51
Compression of basal cisterns	32 (65)	31 (67)	.83	44 (80)	.09	28 (90)	.01
Rotterdam CT score	3.0 [2.5 – 4.0]	4.0 [2.0 – 4.0]	.61	4.0 [3.0 – 4.0]	.50	4.0 [3.0 – 4.0]	.41
Marshal CT score	3.0 [2.0 – 3.5]	3.0 [2.0 – 4.0]	.13	3.0 [3.0 – 4.0]	.08	3.0 [3.0 – 4.0]	.02
ICP monitor	41 (84)	32 (70)	.10	47 (86)	.80	26 (84)	.98
PbtO2 monitor	28 (64)	18 (49)	.18	31 (60)	.69	19 (61)	.84
Decompressive craniectomy	11 (22)	11 (24)	.87	6 (11)	.11	8 (26)	.73
ICU LOS, days	15 ± 10	11 ± 9	**.049**	12 ± 9	.15	12 ± 10	.20
Total hospital LOS, days	53 ± 105	24 ± 33	.08	38 ± 82	.42	18 ± 16	.08
Unfavorable outcome (GOS 1-2)	16 (33)	28 (61)	**.006**	31 (56)	**.02**	15 (48)	**.16**
Age-adjusted Mortality	13 (27)	22 (48)	**.06**	24 (44)	.26	12 (39)	.31

Baseline patient characteristics. BMI, body mass index; MVA, motor vehicle accident; GCS, Glasgow Coma Scale; ISS, Injury Severity Score; COPD, chronic obstructive pulmonary disease; CT, computed tomography; ICP, intracranial pressure; $PbtO_2$, brain tissue oxygen; ICU, intensive care unit; LOS, length of stay. GOS, Glasgow Outcome Scale; NHPI is the reference category. Data are n (%), mean ± SD, or median [IQR].

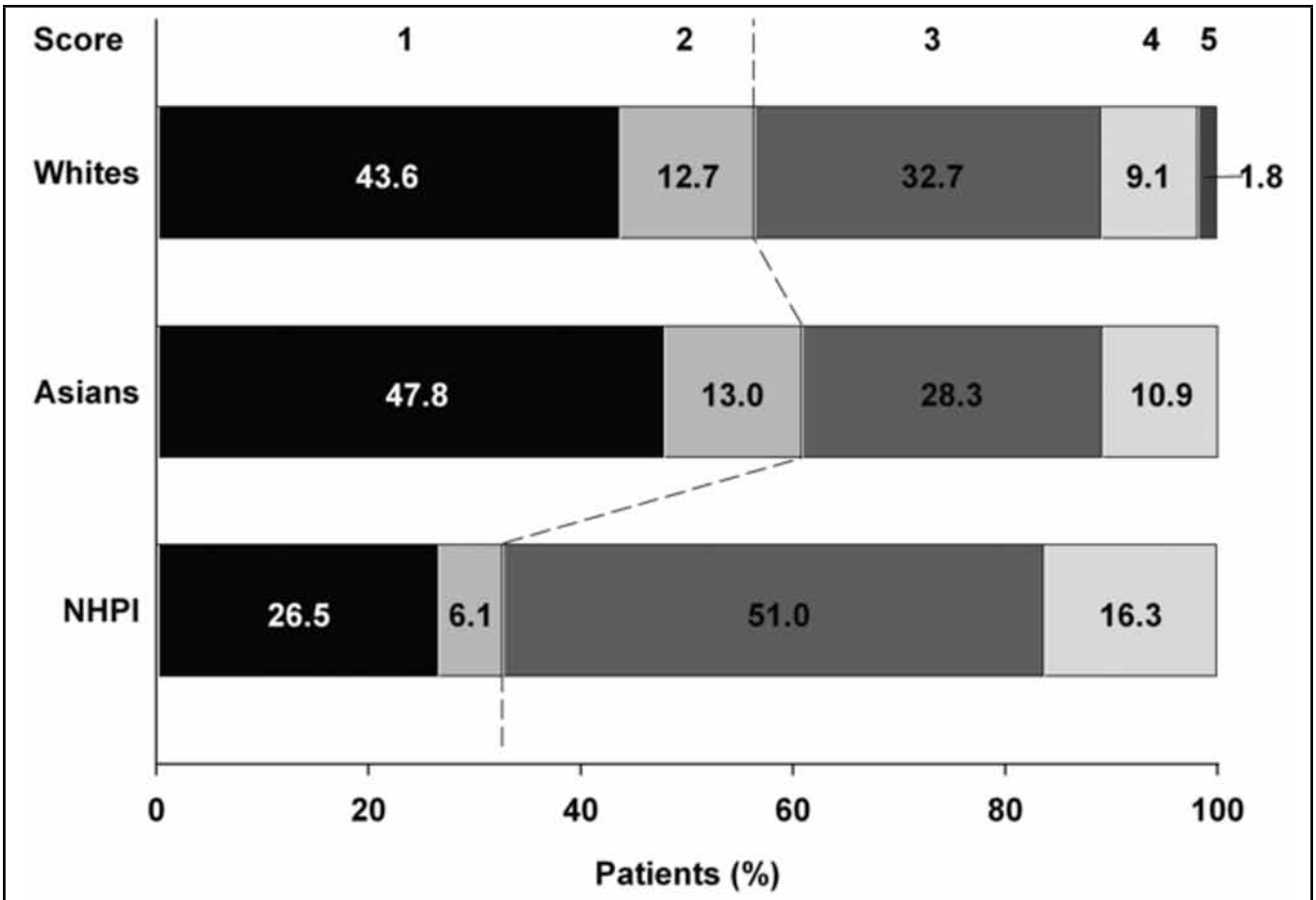


Figure 1. Distribution of the discharge Glasgow Outcome Scale (GOS) scores. The distribution of GOS scores is shown for Whites, Asians, and Native Hawaiians and other Pacific Islanders (NHPI). The dashed line separates unfavorable outcome (score of 1–2) from favorable outcome (score of 3–5).

Perhaps there may be biological differences in susceptibility to secondary brain injury after severe TBI among different racial and ethnic groups. The most extensively studied genotype associated with outcome after TBI is apolipoprotein E (APOE). Many studies have shown that APOE-ε4 allele is associated with poor outcome after TBI compared to those without the ε4 allele, possibly through various effects of APOE-ε4 allele on amyloid deposition, disruption of cytoskeletal stability, cholinergic dysfunction, oxidative stress, neuroprotection, and central nervous system plasticity in response to brain injury.[16-18] There are also other less well-studied genes that have been postulated to influence inflammatory, apoptotic, and blood flow regulatory pathways after TBI that may contribute to differences in outcome.[18] However, since most NHPI in Hawai'i are mixed race that include the genotype of NHPI, Asians, Hispanics and non-Hispanic Whites, it is unlikely that there were significant differences in genetic polymorphisms between races that led to our results.

Much of the differences in the discharge outcome could be explained by the racial differences in the aggressiveness of care that the patient's families seek in the neurocritical care setting, as supported by the longer ICU LOS seen among NHPI compared to Asians and Whites. The higher mortality and shorter ICU LOS among Asians and Whites compared to NHPI may reflect the fact the many of these patients' care were later changed to palliative care with expected natural death in the ICU. The changes in aggressiveness of care often occur after the providers and the patients' families discuss the long-term prognosis. Using the principle of autonomy as a guide to make decisions, patient families sometimes elect to stop the aggressive care if the expected long-term functional outcome and the quality of life are felt to be incongruent with the patient's known wishes. These decisions may be impacted by social, religious, or cultural factors that may differ by race. Since prior studies have shown that minority racial groups are more likely to seek aggressive care after brain injury and other critical conditions compared to non-Hispanic Whites, it is possible that NHPI may also have a similar attitude in the ICU setting.[19-23] Unfortunately, due to the retrospective nature of the study, all of the intricate end-of-life discussions that likely took place, including each patient's

Table 2. Factors Associated with Functional Outcome at Discharge			
	Unfavorable (GOS 1-2)	**Favorable (GOS 3-5)**	***P***
n	90	91	
Age, years	40 ± 21	35 ± 18	.10
Female, n (%)	19 (21)	19 (21)	.97
BMI	26 ± 7	28 ± 6	.17
Race			.03
White	31 (34)	24 (26)	
Asian	28 (31)	18 (20)	
NHPI	16 (18)	33 (36)	
Other	15 (17)	16 (18)	
Mechanism of injury			.22
Assault	15 (17)	8 (9)	
Fall	23 (26)	16 (18)	
MVA	36 (40)	50 (55)	
Sports injury	4 (4)	4 (4)	
Other	12 (13)	13 (14)	
Admission GCS	4.0 [3.0 – 6.0]	6.0 [4.0 – 7.0]	.01
ISS	34 [26 – 43]	33 [26 – 38]	.045
Fixed and dilated pupils, n (%)	17 (21)	5 (6)	.006
History of chronic drug abuse, n (%)	12 (13)	15 (17)	.55
History of chronic alcohol abuse, n (%)	12 (13)	16 (18)	.43
Positive Methamphetamine, n (%)	10 (15)	7 (10)	.33
Positive Alcohol, n (%)	20 (31)	24 (34)	.71
Diabetes, n (%)	6 (7)	8 (9)	.59
Hypertension, n (%)	19 (21)	11 (12)	.10
Coronary artery disease, n (%)	6 (7)	8 (9)	.59
Congestive heart failure, n (%)	1 (1)	0 (0)	.31
COPD, n (%)	1 (1)	1 (1)	.99
History of stroke	2 (2)	1 (1)	.55
Initial CT findings			
Intraventricular hemorrhage	14 (16)	12 (13)	.65
Subarachnoid hemorrhage	54 (60)	37 (41)	.009
Diffuse axonal injury	71 (79)	66 (73)	.32
Compression of basal cisterns	75 (83)	60 (66)	.007
Rotterdam CT score	4.0 [3.0 – 5.0]	3.0 [2.0 – 4.0]	<.001
Marshall CT score	3.0 [3.0 – 4.0]	3.0 [2.0 – 3.0]	<.001
ICP monitor, n (%)	69 (77)	77 (85)	.18
PbtO2 monitor, n (%)	40 (50)	56 (67)	.03
Decompressive craniectomy, n (%)	18 (20)	18 (20)	.97
ICU LOS, days	8 ± 7	17 ± 12	<.001
Total hospital LOS, days	13 ± 20	57 ± 98	<.001

Factors associated with functional outcome at discharge. BMI, body mass index; MVA, motor vehicle accident; GCS, Glasgow Coma Scale; ISS, Injury Severity Score; COPD, chronic obstructive pulmonary disease; CT, computed tomography; ICP, $PbtO_2$, brain tissue oxygen; intracranial pressure; ICU, intensive care unit; LOS, length of stay. Data are n (%), mean ± SD, or median [IQR].

Table 3. Multivariable Models for Unfavorable Discharge Outcome (GOS 1-2)			
	Model 1 Unadjusted OR (95% CI)	**Model 2 Adjusted for Age OR (95% CI)**	**Model 3 Fully Adjusted OR (95% CI)**
Race (NHPI – reference group)			
Asians	3.21 (1.38, 7.44)*	2.89 (1.21, 6.90)*	6.41 (1.68, 24.50)*
Whites	2.66 (1.20, 5.93)*	2.49 (1.10, 5.62)*	4.32 (1.27, 14.62)*
Others	1.93 (0.77, 4.87)	1.90 (0.75, 4.79)	2.86 (0.74, 11.00)
Age		1.01 (0.99, 1.02)	1.00 (0.97, 1.03)
Admission GCS			0.84 (0.65, 1.07)
ISS			1.04 (0.99, 1.10)
Fixed and dilated pupils			1.11 (0.28, 4.47)
Hypertension			2.04 (0.55, 7.63)
Subarachnoid hemorrhage			0.96 (0.32, 2.90)
Compression of basal cisterns			0.39 (0.10, 1.60)
Rotterdam CT score			2.71 (1.25, 5.90)*
PbtO2 monitor			0.55 (0.23, 1.32)

GOS, Glasgow Outcome Scale; OR, odds ratio; CI, confidence interval; NHPI, Native Hawaiians and other Pacific Islanders; GCS, Glasgow Coma Scale; ISS, Injury Severity Score; PbtO2, brain tissue oxygen; *statistically significant at $P < .05$.

previously stated wishes, known values, religion/spirituality, socioeconomic status, social support, etc, that ultimately led to the decisions to limit care in some of these patients could not be characterized. Also, the provider's attitude toward aggressiveness of care and the main factors that led to the decision to limit care in these patients could not be assessed.

Contrary to many prior TBI and stroke studies where long-term functional outcome is typically dichotomized to GOS of 1-3 (death, vegetative or severe disability) and 4-5 (moderate disability or good recovery), the dichotomized GOS cutpoint in this study was chosen between 2 and 3 for the following reasons: (1) Since the patient population was limited to severe TBI, excluding mild and moderate TBI, it was felt appropriate to include non-vegetative, severe disability as an acceptable outcome at the time of hospital discharge; (2) much of the disability in the acute setting may be confounded by other bodily injuries from multitrauma; (3) since the outcome measures were done at the time of hospital discharge, not at 6 or 12 months from admission as done by most prior studies, many of our survivors did not have sufficient recovery time to show the full potential of neurological improvement; and (4) GOS dichotomization using the more traditional cutpoint (1-3 vs 4-5) would have resulted in a disproportionately smaller number of patients with favorable outcome (n = 21), and the statistical power to show the impact of race on discharge outcome would have been lost.

This study has several limitations. Although the study population is representative of trauma patients in Hawai'i since QMC is the only state-designated trauma center, the results may not be generalizable to NHPI patients outside of Hawai'i. Also, specific information regarding the socioeconomic and insurance status of patients were not included in the study, which may have affected the clinical outcomes. The absence of data on pre-hospital hypotension and/or hypoxia, pre-hospital transport time and/or potential delay of care due to geographical factors may have also affected the prediction model. Due to the lack of long-term outcome data, any potential disparities that may exist in long-term outcome could not be assessed.

In summary, Native Hawaiians and other Pacific Islanders have different clinical characteristics and better discharge outcomes compared to the other major racial groups in Hawai'i. Further prospective studies are needed to determine other factors contributing to the differences in outcomes seen in this unique racial group.

The findings of this study do not necessarily represent the views of The Queen's Medical Center.

Disclosure and Conflict of Interest

The authors report no relevant disclosure or conflict of interest.

Authors' Affiliations:
- The Queen's Medical Center, Honolulu, HI (K.N., R.R.H., S.M.A., K.G.J. J.G.B., M.C.A., J.L.dC., D.J.D., C.W.C., M.A.K.)
- Department of Medicine, John A. Burns School of Medicine, University of Hawai'i, Honolulu, HI (K.N., R.R.H., C.W.C., M.A.K.)
- Department of Surgery, John A. Burns School of Medicine, University of Hawai'i, Honolulu, HI (D.J.D., C.W.C.)

Correspondence to:
Kazuma Nakagawa MD; Neuroscience Institute, The Queen's Medical Center, 1301 Punchbowl St., Honolulu, HI 96813; Ph: (808) 691-7152;
Email: kazuma.nakagawa@hawaii.edu

References

1. Faul M, Xu L, Wald M, Coronado V. Traumatic brain injury in the United States: emergency department visits, hospitalizations, and deaths. Centers for Disease Control and Prevention, National Center for Injury Prevention and Control. 2010.
2. Finkelstein E CP, Miller T and associates. The Incidence and Economic Burden of Injuries in the United States. New York: Oxford University; 2006.
3. Bowman SM, Martin DP, Sharar SR, Zimmerman FJ. Racial disparities in outcomes of persons with moderate to severe traumatic brain injury. *Med Care.* Jul 2007;45(7):686-690.
4. Mushkudiani NA, Engel DC, Steyerberg EW, et al. Prognostic value of demographic characteristics in traumatic brain injury: results from the IMPACT study. *J Neurotrauma.* Feb 2007;24(2):259-269.
5. Staudenmayer KL, Diaz-Arrastia R, de Oliveira A, Gentilello LM, Shafi S. Ethnic disparities in long-term functional outcomes after traumatic brain injury. *J Trauma.* Dec 2007;63(6):1364-1369.
6. Arango-Lasprilla JC, Rosenthal M, Deluca J, et al. Traumatic brain injury and functional outcomes: does minority status matter? *Brain Inj.* Jun 2007;21(7):701-708.
7. Shafi S, Marquez de la Plata C, Diaz-Arrastia R, et al. Racial disparities in long-term functional outcome after traumatic brain injury. *J Trauma.* Dec 2007;63(6):1263-1268; discussion 1268-1270.
8. Berry C, Ley EJ, Mirocha J, Salim A. Race affects mortality after moderate to severe traumatic brain injury. *J Surg Res.* Oct 2010;163(2):303-308.
9. Arthur M, Hedges JR, Newgard CD, Diggs BS, Mullins RJ. Racial disparities in mortality among adults hospitalized after injury. *Med Care.* Feb 2008;46(2):192-199.
10. Hixson L, Hepler B, Kim MO. The Native Hawaiian and Other Pacific Islander Population: 2010. 2012; http://www.census.gov/prod/cen2010/briefs/c2010br-12.pdf. Accessed December 6, 2012.
11. Guidelines for the management of severe traumatic brain injury. *J Neurotrauma.* 2007;24 Suppl 1:S1-106.
12. Marshall LF, Marshall SB, Klauber MR, et al. A new classification of head injury based on computed tomography. *J Neurosurgery.* 1991;75:S14-S20.
13. Maas AI, Hukkelhoven CW, Marshall LF, Steyerberg EW. Prediction of outcome in traumatic brain injury with computed tomographic characteristics: a comparison between the computed tomographic classification and combinations of computed tomographic predictors. *Neurosurgery.* Dec 2005;57(6):1173-1182; discussion 1173-1182.
14. Bazarian JJ, Pope C, McClung J, Cheng YT, Flesher W. Ethnic and racial disparities in emergency department care for mild traumatic brain injury. *Acad Emerg Med.* Nov 2003;10(11):1209-1217.
15. Haider AH, Efron DT, Haut ER, DiRusso SM, Sullivan T, Cornwell EE, 3rd. Black children experience worse clinical and functional outcomes after traumatic brain injury: an analysis of the National Pediatric Trauma Registry. *J Trauma.* May 2007;62(5):1259-1262; discussion 1262-1253.
16. Ariza M, Pueyo R, Matarin Mdel M, et al. Influence of APOE polymorphism on cognitive and behavioural outcome in moderate and severe traumatic brain injury. *J Neurol Neurosurg Psychiatry.* Oct 2006;77(10):1191-1193.
17. Friedman G, Froom P, Sazbon L, et al. Apolipoprotein E-epsilon4 genotype predicts a poor outcome in survivors of traumatic brain injury. *Neurology.* Jan 15 1999;52(2):244-248.
18. Jordan BD. Genetic influences on outcome following traumatic brain injury. *Neurochem Res.* Apr-May 2007;32(4-5):905-915.
19. Bardach N, Zhao S, Pantilat S, Johnston SC. Adjustment for do-not-resuscitate orders reverses the apparent in-hospital mortality advantage for minorities. *Am J Med.* Apr 2005;118(4):400-408.
20. Zahuranec DB, Brown DL, Lisabeth LD, et al. Ethnic differences in do-not-resuscitate orders after intracerebral hemorrhage. *Crit Care Med.* Oct 2009;37(10):2807-2811.
21. Wenger NS, Pearson ML, Desmond KA, et al. Epidemiology of do-not-resuscitate orders. Disparity by age, diagnosis, gender, race, and functional impairment. *Arch Intern Med.* Oct 23 1995;155(19):2056-2062.
22. Shepardson LB, Youngner SJ, Speroff T, O'Brien RG, Smyth KA, Rosenthal GE. Variation in the use of do-not-resuscitate orders in patients with stroke. *Arch Intern Med.* Sep 8 1997;157(16):1841-1847.
23. Shepardson LB, Gordon HS, Ibrahim SA, Harper DL, Rosenthal GE. Racial variation in the use of do-not-resuscitate orders. *J Gen Intern Med.* Jan 1999;14(1):15-20.

Creutzfeldt-Jakob Disease: A Case Report and Differential Diagnoses

Gotaro Kojima MD; Brent K. Tatsuno MD; Michiko Inaba MD; Stephanie Velligas BSc; Kamal Masaki MD; and Kore K. Liow MD

Abstract

Sporadic Creutzfeldt-Jakob disease is a rare neurodegenerative disorder of unknown etiology that causes rapidly progressive dementia. This disease is uniformly fatal and most patients die within 12 months. Clinical findings include myoclonus, visual disturbances, and cerebellar and pyramidal/extrapyramidal signs in addition to rapidly progressive cognitive and functional impairment. These findings are all non-specific and it is often difficult and challenging to diagnose premortem because of low awareness and clinical suspicion.

We present a 66-year-old woman with a 5-month history of rapidly progressive dementia. After a series of extensive diagnostic examinations and continuous follow-up, she was diagnosed with probable sporadic Creutzfeldt-Jakob disease based on Centers for Disease Control and Prevention (CDC) criteria, with key findings of rapidly progressive dementia, blurry vision, extrapyramidal signs (cogwheel rigidity), and abnormal hyperintensity signals on diffusion-weighted MRI. Her symptoms progressively worsened and she died 7 months after the onset. The postmortem brain autopsy demonstrated the presence of abnormal protease-resistant prion protein by Western Blot analysis.

A literature review was performed on differential diagnoses that present with rapidly progressive dementia and thereby mimic sporadic Creutzfeldt-Jakob disease. These include Alzheimer's disease, dementia with Lewy Bodies, frontotemporal dementia, meningoencephalitis, corticobasal degeneration, progressive supranuclear palsy, CADASIL, and paraneoplastic encephalomyelitis.

Keywords

sporadic Creutzfeldt-Jakob disease; prion disease; rapidly progressing dementia.

Introduction

Creutzfeldt-Jakob disease (CJD) is a progressive neurodegenerative disorder and one of the human prion diseases. It is uniformly fatal and the annual incidence rate is 1-2 per million worldwide. In addition to abnormal prion protein accumulation in the brain, CJD is characterized by spongiform change, neuronal loss, and gliosis.[1] It is often difficult and challenging to diagnose CJD premortem because of a low index of suspicion or a lack of knowledge of this rare disease.

The most common form of CJD is sporadic Creutzfeldt-Jakob disease (sCJD) (85%-90%), while the rest are familial, iatrogenic, and variant forms.[1] The mean onset age of sCJD is 65 years, and most of the cases are distributed within the age group between 60 and 80 years.[2] sCJD in patients aged less than 30 or over 80 years are rare. The etiology is still unknown and both genders are almost equally affected.

The clinical features mainly include a rapidly progressive dementia and multifocal neurological findings such as myoclonus, visual disturbances, cerebellar, and pyramidal/extrapyramidal signs. The disease course follows rapid progression of cognitive and functional impairment toward akinetic mutism in the late stage, and eventually death, most often within 12 months of the disease onset.[1]

Case Report

The patient was a 66-year-old woman who was referred to a memory clinic for further evaluation of a 5-month history of rapidly progressive dementia. The initial symptoms included memory loss, "feeling odd," anorexia, and unintentional weight loss. At her first visit to the memory clinic, her son and husband reported that her cognitive problems had acutely worsened in the previous two weeks. She now had problems with short-term memory and functional abilities, including getting dressed, using the toilet, and getting lost in her house. Her husband also stated that she had emotional lability and at times, did not trust her own family. Her vision was becoming blurry and she had increasing somnolence. Her family denied that she had any myoclonic jerks, tremor, gait unsteadiness, or visual, auditory, or sensory hallucinations.

Her past medical history was non-contributory. She had not had any previous surgeries, and her family history was significant for a myocardial infarction in her father and fatal leukemia in her mother, but there was no family history of dementia or prion disease. She had no known allergies and her medications consisted of naturopathic remedies that she started after the onset of her symptoms. She had travelled to Holland and Belgium 5 years previously, but was a strict vegetarian at that time. She had also travelled to the Caribbean, Mexico, and Belize, but did not have any exposure to raw livestock or brain matter. She had previously been a journalist in Washington DC, and did public relations for a real estate company in Hawai'i.

Her physical exam was significant for perseveration, anomic aphasia, alexia, agnosia, and apraxia. Her muscle tone was normal in all four extremities and her cranial nerves were grossly normal. She had normal sensation and normal coordination. Her reflexes were symmetric and there were no Babinski reflexes. Her gait was slow but non-ataxic. She was unable to complete the Mini-Mental State Examination (MMSE) or perform other complicated tasks due to perseveration. For example, when asked about the month, date, day, and year, she answered "December" for each, when in fact, it was already March. When she answered "December" for the state, the MMSE was stopped. Blood work was normal and included a basic metabolic profile, CBC, thyroid studies, liver studies, vitamin B1, vitamin B12 and folate levels, lactic acid, erythrocyte sedimentation rate (ESR), rapid plasma reagin (RPR), human immunodeficiency virus (HIV), angiotensin-converting enzyme (ACE) levels,

and ceruloplasmin. Pyruvate kinase, Purkinje cell antibody screen, Anti-Hu antibody, Anti-Jo antibody serum tests were also normal.

Cerebrospinal fluid (CSF) studies were also performed. Cell counts, glucose, and protein were within normal limits. Toxoplasma gondii, Bartonella DNA, venereal disease research laboratory (VDRL) test, and Lyme antibodies were negative. Her 14-3-3 protein level was also within normal limits at less than 1.0 ng/mL, with a normal reference range of less than 1.5 ng/mL.

A non-contrast Magnetic Resonance Imaging (MRI) of her brain was significant for global parenchymal loss. Diffusion-weighted images showed restricted cortical diffusion in the cingulate gyrus (Figure 1) and also in the bilateral parietal and posterior temporal lobes (Figure 2). Mildly restricted diffusion was seen in the thalami (Figure 3). There were no infarcts, masses, or extra axial fluid collections. An electroencephalogram (EEG) showed left temporal slowing with a diffusely slow and disorganized background, and there were no periodic discharges noted.

She returned one week later to discuss her test results, by which time she had developed cogwheel rigidity. We informed her that her condition was consistent with CJD. We spent considerable time speaking with her and her family about the course of CJD and regarding the prognosis. She and her family elected to travel to Mexico for experimental oxygen therapy. Her symptoms progressively worsened and she died 7 months after the onset. The postmortem brain autopsy demonstrated the presence of abnormal protease-resistant prion protein by Western Blot analysis.

Discussion

Although definite diagnosis of sCJD can only be made by confirming pathologic prion protein deposition in the brain, the diagnosis can be supported by periodic sharp wave complexes on EEG, determination of 14-3-3 protein in the CSF, and abnormal signal changes in caudate nuclei and/or putamen on diffusion-weighted or fluid attenuated inversion recovery (FLAIR) MRI.[1]

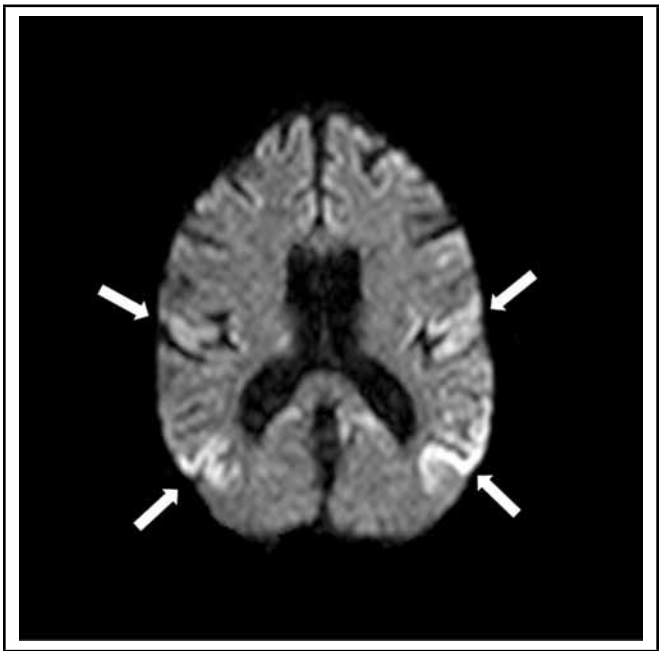


Figure 2. MRI diffusion-weighted images showing restricted cortical diffusion in the bilateral parietal and posterior temporal lobes.

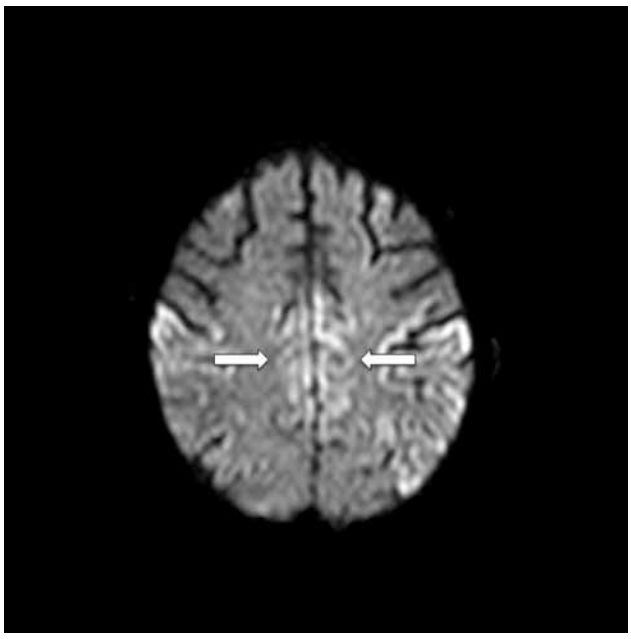


Figure 1. MRI diffusion-weighted images showing hyperintense signal in the cingulate gyrus.

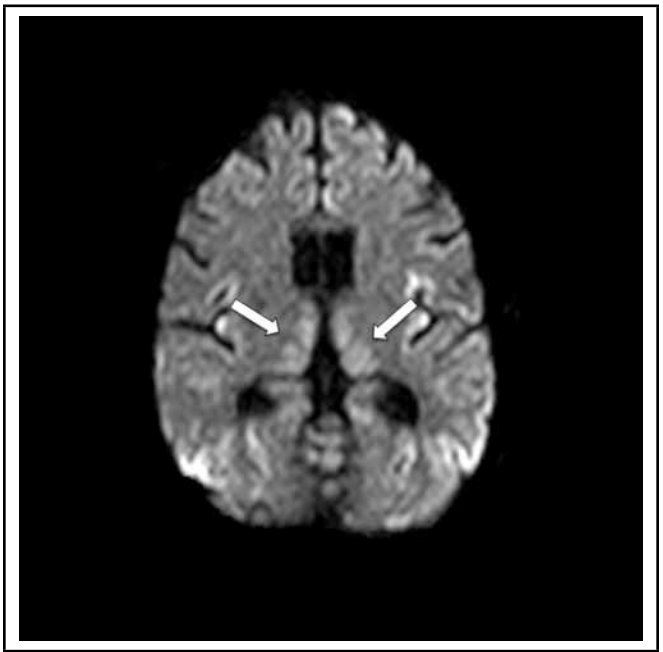


Figure 3. MRI Diffusion-weighted images showed mildly restricted diffusion in the thalami.

Table 1. 2010 CDC Criteria for Sporadic CJD	
Definite	Detection of protease-resistant Prion Protein or scrapie-associated fibrils by neuropathology, immunochemical technique, and/or Western blot.
Probable	No findings indicating alternative diagnoses AND progressive dementia with at least 2 of (i)-(iv) AND at least one of (a)-(c).
Possible	No findings indicating alternative diagnoses AND progressive dementia with duration of less than 2 years AND with at least 2 of (i)-(iv) AND at least one of (a)-(c).
(i) Myoclonus	
(ii) Visual or cerebellar problems	
(iii) Pyramidal or extrapyramidal features	
(iv) Akinetic mutism	
(a) Periodic sharp wave complexes on electroencephalography	
(b) Positive 14-3-3 protein in the cerebrospinal fluid with a disease duration of less than 2 years	
(c) High signal abnormalities in caudate nucleus and/or putamen on diffusion-weighted imaging (DWI) or fluid attenuated inversion recovery (FLAIR) MRI	

Common findings of sCJD on neurological examination include, but are not limited to, rapidly progressive dementia, myoclonus, visual disturbances, cerebellar ataxia, and pyramidal/extrapyramidal signs. These signs are non-specific and can be caused by a variety of diseases. Therefore, updated and broad knowledge base and diagnostic skills are necessary to differentiate sCJD from other mimicking disorders.

Based on the CDC criteria for sCJD (Table 1),[1] this case was diagnosed with probable sCJD while the patient was alive, with the key findings of rapidly progressive dementia, visual disturbances (blurry vision), extrapyramidal signs (cogwheel rigidity), and hyperintensity signals in bilateral parietal and temporal lobes and thalami on diffusion-weighted MRI (Figures 2 and 3). Myoclonus and akinetic mutism were not observed in this case and are often absent at the initial presentation.[3] Protein 14-3-3 was not found in the CSF, although this is not a specific finding. EEG demonstrated only diffusely slow and disorganized background without typical periodic sharp wave complexes, which may not be seen in the initial or later stages of sCJD. This patient underwent a post-mortem brain autopsy, which demonstrated the presence of abnormal protease-resistant prion protein by Western Blot analysis, thus confirming the diagnosis of definite sCJD by CDC criteria.

Differential Diagnoses of Rapidly Progressive Dementia

Alzheimer's Disease

Alzheimer's disease is the most common form of dementia. Typically, cognitive impairment starts and progresses gradually over years, often up to 10 years or more. The symptoms continue to progress and functional disabilities, behavioral problems, and personality changes are common along the disease course. Alzheimer's disease sometimes can progress rapidly and is one of the most common disorders which can be mistaken for sCJD.[4] Patients with Alzheimer's disease can have myoclonus, periodic waves on EEG, and positive 14-3-3 protein in CSF,[5] and may mimic sCJD. However, in Alzheimer's disease the CT or MRI typically shows diffuse cortical and cerebral atrophy, especially in temporal or hippocampal regions, while atrophy is often absent or minimal in sCJD. In addition, increased signal intensities in bilateral caudate nuclei and putamen are often seen on MRI of sCJD patients.[4] Although the incidence rate of Alzheimer's disease steadily increases with age, it is rare to have the onset of sCJD after 80 years of age.

Dementia with Lewy Bodies

Dementia with Lewy bodies (DLB) is also a progressive dementia with characteristic features of fluctuating cognitive function, visual hallucinations and Parkinsonism, and can present with myoclonus. However, the course tends to be less rapid than CJD and with more variable progression. Visual hallucinations tend to be a prominent feature early on. Some of these symptoms overlap with sCJD. Periodic sharp wave complexes on EEG, one of the suggestive findings of sCJD, were also reported in some cases.[6] There is no specific standard diagnostic test available for DLB and a definitive diagnosis can be made only by pathological examination of the brain, which makes it challenging for physicians to distinguish between these two dementias.[7] Imaging studies, especially MRI, might be helpful because patients with DLB typically do not show hyperintensities in the caudate nuclei or putamen on MRI.

Frontotemporal Dementia

This progressive dementia is characterized by personality and behavior changes in its early stage. Patients with frontotemporal dementia (FTD) may develop extrapyramidal signs, such as rigidity, tremor, or akinesia, and can mimic sCJD.[8] In most cases, frontal and/or temporal lobe atrophy is seen on MRI.

Meningoencephalitis

There are a broad variety of causes of meningoencephalitis, including viral (herpes simplex virus (HSV), Japanese encephalitis virus, HIV), bacterial (Streptococci, Lyme disease), fungal (Cryptococcus neoformans), parasitic (Toxoplasma gondii, malaria), and autoimmune diseases (Hashimoto's encephalitis, limbic encephalitis).[9] Most cases of meningoencephalitis have an acute onset associated with fever, headache, confusion, and sometimes seizure. Memory impairment usually progresses more rapidly than in sCJD and other dementias. Inflammatory findings such as elevated cell count or protein in CSF examination are

key features seen in most meningoencephalitis cases, which are absent in sCJD. Early HSV limbic encephalitis could present with memory loss, myoclonus, and seizures, and mimic CJD.[10]

Corticobasal Degeneration

Corticobasal degeneration is a neurodegenerative disorder with unknown etiology affecting the basal ganglia and the cerebral cortex, mainly the frontal and parietal lobes. This progressive disorder typically causes progressive dementia, myoclonus, hallucinations, "alien hand" phenomenon, and parkinsonism such as bradykinesia, rigidity, or gait disturbance, all of which can be seen in sCJD patients.[11] While the age of onset of corticobasal degeneration is similar to that of sCJD (60-80 years old), the disease course is less rapidly progressive and more protracted with much longer duration of 8-10 years.

Progressive Supranuclear Palsy

Progressive supranuclear palsy (PSP) is another neurodegenerative disorder characterized by cognitive impairment, vertical supranuclear ophthalmoplegia, visual disturbance, extrapyramidal signs, and a disturbance of gait resulting in falls.[12] Postural instability and limitation of vertical gaze are early findings.

Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL)

CADASIL, cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy, is characterized by progressive dementia, mood disorder, migraine headaches, and transient ischemic attacks (TIAs) or strokes.[13] The most frequent presentation is recurrent TIAs or strokes at the age of 40-50 years, which is earlier than the onset of sCJD. MRI shows characteristic multiple frontal lobe hyperintensities in periventricular white matter.[13] Family history provides helpful information, because CADASIL is a hereditary disorder caused by a mutation in the Notch 3 gene, and most CADASIL patients have a positive family history.[13]

Paraneoplastic Encephalomyelitis

Paraneoplastic encephalomyelitis (PEM) is often associated with malignancy, most frequently lung cancer (80%), and can involve multiple areas of the nervous system. Common clinical features are subacute cognitive impairment, in addition to various neurological findings including personality change, depression, anxiety, hallucinations, agitation, and seizures, depending on affected brain areas.[14] CSF examination is useful to differentiate sCJD from PEM. Although protein 14-3-3 in CSF can be detected in both PEM and sCJD,[15] inflammatory findings in the CSF are typically seen only in PEM but not in sCJD. Anti-Hu antibodies are frequently seen in PEM.

Conclusion

Although sCJD is incurable and there is no generally accepted treatment currently available, it is important to make an early and accurate diagnosis because some of the differential diagnoses such as viral or bacterial encephalitis are treatable. Early diagnosis will allow patients and their families to prepare for the expected disease course, consider goals of care, and possibly have palliative care consultation if desired. This patient and her family had the opportunity to discuss this disease thoroughly and had the freedom to choose an alternative, unproven treatment.

Disclosure Statement

None of the authors report conflicts of interest with commercial enterprises.

Funding

This work did not receive any specific grant from any funding agency in the public, commercial, or not-for-profit sector.

Authors' Affiliations:
- The John A. Hartford Foundation Center of Excellence in Geriatrics, Department of Geriatric Medicine, John A. Burns School of Medicine, University of Hawai'i, Honolulu, HI (G.K., M.I., K.M.)
- Department of Graduate Medical Education, Cedars Sinai Medical Center, Los Angeles, CA (B.K.T.)
- Hawai'i Center on Aging and Memory, Hawai'i Pacific Neuroscience Center, Harry and Jeanette Weinberg Medical Plaza and Wellness Center, Kailua, HI (M.I., S.V., K.K.L.)

Correspondence to:
Gotaro Kojima MD; Department of Geriatric Medicine, John A. Burns School of Medicine, University of Hawai'i, 347 N. Kuakini Street HPM-9, Honolulu, HI 96817; Ph: (808)523-8461; Email: gotarokojima@yahoo.co.jp

References

1. Department of Health and Human Services, Centers for Disease Control and Prevention, CJD (Creutzfeldt-Jakob Disease, Classic), 2010, http://www.cdc.gov/ncidod/dvrd/cjd/, accessed on June 1st 2012.
2. Ladogana A, Puopolo M, Croes EA, et al. Mortality from Creutzfeldt-Jakob disease and related disorders in Europe, Australia, and Canada. *Neurology.* May 10 2005;64(9):1586-1591.
3. Rabinovici GD, Wang PN, Levin J, et al. First symptom in sporadic Creutzfeldt-Jakob disease. *Neurology.* Jan 24 2006;66(2):286-287.
4. Poser S, Mollenhauer B, Kraubeta A, et al. How to improve the clinical diagnosis of Creutzfeldt-Jakob disease. *Brain : a journal of neurology.* Dec 1999;122(Pt 12):2345-2351.
5. Mahmoudi R, Manckoundia P, Morrone I, Lang PO, Drame M, Novella JL. Atypical case of Alzheimer's disease mimicking Creutzfeldt-Jakob disease: interest of cerebrospinal fluid biomarkers in the differential diagnosis. *Journal of the American Geriatrics Society.* Sep 2010;58(9):1821-1823.
6. Doran M, Larner AJ. EEG findings in dementia with Lewy bodies causing diagnostic confusion with sporadic Creutzfeldt-Jakob disease. *European journal of neurology : the official journal of the European Federation of Neurological Societies.* Dec 2004;11(12):838-841.
7. Marin LF, Felicio AC, Bichuetti DB, et al. Clinical findings in Creutzfeldt-Jakob disease mimicking dementia with Lewy bodies. *Arquivos de neuro-psiquiatria.* Sep 2008;66(3B):741-743.
8. Kertesz A. Frontotemporal dementia, Pick's disease. *Ideggyogyaszati szemle.* Jan 30 2010;63(1-2):4-12.
9. Long SS. Encephalitis diagnosis and management in the real world. *Advances in experimental medicine and biology.* 2011;697:153-173.
10. Chaudhuri A, Kennedy PG. Diagnosis and treatment of viral encephalitis. *Postgraduate medical journal.* Oct 2002;78(924):575-583.
11. Moreaud O, Monavon A, Brutti-Mairesse MP, Grand S, Lebas JF. Creutzfeldt-Jakob disease mimicking corticobasal degeneration clinical and MRI data of a case. *Journal of neurology.* Oct 2005;252(10):1283-1284.
12. Josephs KA, Tsuboi Y, Dickson DW. Creutzfeldt-Jakob disease presenting as progressive supranuclear palsy. *Eur. J. Neurol.* May 2004;11(5):343-346.
13. Herve D, Chabriat H. CADASIL. *Journal of geriatric psychiatry and neurology.* Dec 2010;23(4):269-276.
14. Rosenfeld MR, Dalmau JO. Paraneoplastic disorders of the CNS and autoimmune synaptic encephalitis. *Continuum (Minneapolis, Minn.).* Apr 2012;18(2):366-383.
15. Saiz A, Graus F, Dalmau J, Pifarre A, Marin C, Tolosa E. Detection of 14-3-3 brain protein in the cerebrospinal fluid of patients with paraneoplastic neurological disorders. *Annals of neurology.* Nov 1999;46(5):774-777.

Teen Health Camp Hawai'i: Inspiring Hawai'i's Youth to be Healthcare Leaders of Tomorrow

Brandyn S. Dunn MPH, MSI; Eduardo Duquez MSIV; Teresa Schiff MSIII, Nem Lau; Agnes R. Malate MEd; and Kelley Withy MD, PhD

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.

Introduction

The John A. Burns School of Medicine is committed to improving the health of the citizens of both the State and the Pacific Basin. An integral component of this goal is to recruit and retain local students in the healthcare professions. Disadvantaged ethnic groups typically do not have the educational or financial resources to prepare for college.[1] Furthermore, there is a lack of role models and mentors who can provide guidance, support and motivation, to encourage minority students to consider careers in the health professions.[2] This is especially true for rural areas in the state of Hawai'i.[3] Studies have suggested that increased patient satisfaction and better patient outcomes occur when the patient and physician are from the same ethnic group.[4,5] This discrepancy is highlighted in Hawai'i where 4% of the physicians are Native Hawaiians although Hawaiians and part-Hawaiians make up greater than 20% of the population.[6] This trend is similar for other Pacific Islanders (Micronesian and Polynesian).[4] Innovative and low cost programs are needed to attract students from ethnic minorities into the health professions.

To address this issue, a physician in San Antonio, Texas, initiated a program titled "Teen Health Camp" for inner-city Latino youths.[7,8] In 2010, a group of JABSOM students interested in social justice decided to adapt this approach and develop a similar program for Hawai'i. They named this program, Teen Health Camp Hawai'i (THCH). The goals of THCH are: (1) to motivate public high school students to consider a career in the health profession, (2) to expose these students to different healthcare professions, (3) to expose these students to local organizations involved in providing health services in their community, and (4) to recruit first year medical students to provide instruction, guidance, and mentorship for these students. In addition, THCH strives to help high school students prepare academically for college and post-graduate health professional programs by exposing them to community organizations and mentors that can guide them through this seemingly daunting and bewildering process.

Methods

Teen Health Camp Hawai'i Framework

A typical THCH experience involves one day of activities. Students rotate through 5 stations which includes: (1) "How to Put in Stitches," (2) "How to Put on and Remove Casts," (3) "Local Grindz," (4) "Public Health Outbreaks," and (5) "Your Future in Health Care." Each activity is approximately 30 minutes in length and is supervised by medical students, pre-health students, JABSOM faculty, and high school teachers. The first two rotations are hands on suturing and casting activities that allows participants to simulate a day in a clinic by suturing cuts on a synthetic arm and applying casts on their fellow campers. In the segment called "Local Grindz," participants learn nutritional facts about popular local food. Fat, sodium and carbohydrate content are emphasized along with learning to understand appropriate serving sizes and how to read food labels. In the public health segment, participants gain an understanding of the spread of infectious diseases, the importance of vaccination, and the current global health challenges to disease control. The last rotation helps to develop confidence in planning their future career choices. Careers in the various health professions are explained and advised on how to create a plan for reaching their goals.

During the lunch break students meet one-on-one with local community healthcare providers. THCH invites local physicians, nurses, pharmacists, physical therapists, emergency personnel, dental assistants, and alternative medicine providers.

After the camp, THCH provides opportunities for the participants to visit with various community organizations. Interacting with local healthcare providers will hopefully inspire the students to seek volunteer opportunities and become involved with health issues in their communities. In addition, participants learn about the services offered by the Health Careers Opportunity Program (HCOP), Native Hawaiian Student Pathway to Medicine (NHDPM), Na Pua No'eau, and other healthcare programs within the University of Hawai'i system. These programs provide support and encouragement as the participants move through college and into health professional schools.

Camp Evaluation

At each camp, participants are given a pre-camp and post-camp assessment to determine if the five rotations accomplished their objectives. Each assessment consists of 19 multiple-choice questions. The pre- and post-tests had different question stems but tested for similar overarching themes. Written feedback was also collected and used to improve subsequent camps.

Table 1. Summary of Activities by Teen Health Camp Hawai'i by Region								
	West O'ahu		Windward O'ahu			Hawai'i Island		
Camp Sites	Campbell	Waipahu	UH West O'ahu	Castle	Kahuku	Kealakehe	Hilo	Total
Participants	51	29	88	29	42	203	48	490

Results

Nine camps have been held on the islands of O'ahu and Hawai'i. Nearly 500 middle and high school students, primarily from public schools, have participated in THCH's program. Camps were held in the regions of West O'ahu, Windward O'ahu, and West and East Hawai'i Island. High schools in each region were invited to participate. Table 1 summarizes the camps.

The UH West O'ahu event was held in February 2013. Eighty-eight students participated. The mean pre-test score was 41.5% (range: 21%-68%) and the mean post-test score was 76.8% (range: 32%-95%). Greater than 95% of the participants improved their scores. The third Kealakehe High School camp was held on November 2012. Ninety percent of these students improved their post-test scores. Overall THCH is confident that the increase in scores from the pre-test to post-test indicates a positive gain in knowledge by the participants.

The written comments at the end of each camp revealed the experience was enjoyable and educational: The following are direct quotes from two of the participants:

> "It was a lot of fun and I am glad that I came. I learned a lot more about the careers that I was thinking about pursuing and got a lot more information than I ever imagined I would."*—10th grader from Kealakehe High School*

> "[The camp] was a very great opportunity for me to think about why I want to be a doctor and what kind of doctor I should become. As an exchange student, I was not sure if I could study to become a doctor in the USA, but after the different presentations, (especially about scholarships), I think if I try really hard I can succeed to become a doctor. All the workshops that I attended gave me great pleasure and the information changed my thinking. This camp helped me to decide to become more serious in my future profession. Thank you for this chance."*— 11th grade student at Honoka'a High School*

Discussion

THCH has developed a solid foundation in various communities across the State. For example, Ms. Nem Lau, West Hawai'i district resource teacher for the Department of Hawai'i's Career and Technical Education, has helped THCH to become an annual event on the Big Island. THCH hopes other teachers will follow her example.

THCH plans to keep in touch with the participants as they progress through high school and college. To do this a Teen Mentorship Academy (TMA) was formed. TMA will provide college preparation and career counseling to the camp participants through a year long program in accordance with a new first year medical elective.

THCH has become a community health option for the Class of 2017 at JABSOM. This option will fulfill the community health and service requirement for 3-4 first year medical students. Next year's first year medical students will plan and implement activities outlined in this article.

Reflections from THCH Leaders

Brandyn Dunn (1st year Medical Student)

I began working with Teen Health Camp-San Antonio during my sophomore year at Trinity University. At first, I followed in the path of other student volunteers, functioning more as a spectator. As time went on, I began taking on leadership roles and started learning the ins-and-outs of this unique program. Upon returning to Hawai'i, I quickly realized that our community was faced with similar problems to the ones I observed in San Antonio. An overwhelming number of local high school and middle school students had little knowledge and exposure to the field of healthcare despite a growing demand for healthcare workers throughout the community. Through numerous discussions with other students interested in social justice the concept of Teen Health Camp Hawai'i emerged.

Eduardo Duquez (4th year Medical Student)

I was exhilarated when Teresa and Brandyn introduced the idea of Teen Health Camp, as the mission and vision of the program aligned with my own views. As a proud graduate and former teacher's aide at Campbell High School, and having done public health research with youth in underserved areas of Hawai'i, I knew that Teen Health Camp would be a welcomed program in my community. I am excited for the future of Teen Health Camp as it continues to introduce and encourage local youths to explore this amazing field of health care!

Teresa Schiff (3rd year Medical Student)

My fondest memories of initiating THCH are around the dining table, where three friends gathered to discuss the immense problems surrounding physician shortages in our rural areas of Hawai'i and the potential THCH might have to amend this issue. Within a few months of planning we had created a new curriculum specific for our local communities and we had forged important relationships with AHEC and HCOP, two partner organizations whose friendship, expertise, and mentoring have proven invaluable. I am looking forward to the new directions THCH will take in the upcoming years, complete with new leaders and an expansion of our services offered. I am extremely excited to start the Teen Mentorship Academy as well as continuing to partner with other local organizations whose aim it is to improve opportunities for our islands' youth. I believe by working together we can make Hawai'i a healthier place for our future generations.

Nem Lau (West Hawai'i District Teacher)

I serve as the Career & Technical Education Resource Teacher for West Hawai'i District on the Kona Coast of the Big Island. My passion has always been, and continues to be, education whenever and wherever it is needed, ranging from pre-schoolers learning the basics to senior executives acquiring management insights and acumen to augment their technical knowledge and skills. Thus it was fortuitous that I got connected to the THCH co-founders and mentors/supporters, and was able to bring the Camp to the Big Island community.

The meeting of the forces and efforts was timely and most relevant. While most people are cognizant of the Hawai'i's healthcare worker shortages, the situation is even more dire for rural Neighbor Island communities. Our Camp gives students valuable exposure to healthcare career options and possibilities that they may not have considered or were aware of. The Camp opens doors for homegrown talents, as high school students who later become healthcare workers and professionals can serve and give back to their community literally in the comforts of their home. There will be no need for adjusting to new environments/cultures, nor will the tugs of family and friends be a major factor at play.

The recent Camp in Kona revealed a pleasant surprise: local healthcare professionals share the same desire to develop and nurture homegrown healthcare talents. Over 20 professionals answered cold calls to participate in the lunch hour activity in which they interacted with students and answered questions relating to their specific specialties. I believe this endeavor will become an integral part of future Big Island Camps.

Acknowledgments

THCH is thankful to the many individuals and organization that have sponsored their events. The local organizations that have contributed time and/or money to support THCH are: (1) at the University of Hawai'i: the John A Burns School of Medicine, the Health Career Opportunity Program, the Area Health Education Centers, and Na Pua No'eau, (2) from the State government: the Department of Education's Career & Technical Education, the Hawai'i Island Workforce and Economic Development 'Ohana, and the Hawai'i P-20/CACGP, (3) pre-health student volunteers from UH Manoa, (4) teachers from local high schools and (5) donations from Dr. Cedric Lorenzo and JABSOM's Department of Surgery, (6) Dr. Kenton Kramer, JABSOM's Office of Medical Education.

Authors' Affiliation:
- University of Hawai'i, John A. Burns School of Medicine, Honolulu, HI (B.S.D., E.D.,T.S.)
- Department of Education, West Hawai'i District Office, Kailua-Kona, HI (N.L.)
- University of Hawai'i at Manoa, Office of Student Equity, Excellence, and Diversity, Health Careers Opportunity Program, Honolulu, HI (A.M.)
- University of Hawai'i, John A. Burns School of Medicine, Area Health Education Center (K.W.)

References

1. Cooper RA. Impact of trends in primary, secondary, and postsecondary education on applications to medical school II: Considerations of race, ethnicity, and income. *Acad Med.* 2003;78:864-876.
2. Acosta D, Olsen P. Meeting the needs of regional minority groups: The University of Washington's programs to increase the American Indian and Alaskan Native physician workforce. *Acad Med.* 2006;81:863–870.
3. Withy K, Dall T, Sakamoto D. Hawai'i Physician Workforce Assessment 2010. *Hawaii J Med Pubic Health.* 2012;71:6-12.
4. Ambrose A, Arakawa R, Greidanus B, Macdonald P, Musa C, Shibuya K, Tavares T, Yamada S. Geographical Maldistribution of Native Hawaii an and Other Pacific Islander Physicians in Hawai'i. *Hawaii J Med Public Health.* 2012;71(4 Suppl 1):13-20.
5. Cooper, L, and Powe, N. 2004. Disparities in Patient Experiences, Healthcare Processes, and Outcomes: The Role of Patient-Provider Racial, Ethnic, and Language Concordance. The Commonwealth Fund, July Issue. Number 753.
6. US Census. NHOPI Population. Office of Minority Health and Health Disparities. 2011. Available at: http://www.cdc.gov/omhd/Populations/NHOPI/NHOPI.htm.
7. Oscós-Sanchez MA, Oscós-Flores LD, Burge S. The Teen Medical Academy: Using Academic Enhancement and Instructional Enrichment to Address Ethnic Disparities in the American Healthcare Workforce. *Journal of Adolescent Health.* 2008;42(3):284-293.
8. Oscós-Sánchez MA. Nosotros Teen Health Camp. Journal of Adolescent Health. 2003;32:150.

A New and Innovative Public Health Specialization Founded on Traditional Knowledge and Social Justice: Native Hawaiian and Indigenous Health

Maile Taualii PhD, MPH; Treena Delormier PhD, PDt; and Jay Maddock PhD

Insights in Public Health is a monthly solicited column from the public health community and is coordinated by HJMPH Associate Editors Jay Maddock PhD from the Office of Public Health Studies at John A Burns School of Medicine and Donald Hayes MD, MPH from the Hawai'i Department of Health in collaboration with HJMPH Manuscript Editors Tonya Lowery St. John MPH and Ranjani Rajan MPH from the Hawai'i Department of Health.

Background

There are approximately 370 million Indigenous Peoples worldwide, making up 6% of the world's population.[1] Indigenous People experience grave disparities, such as worse health outcomes, higher representation amongst the poor and disadvantaged, lower life expectancies, and limited success in improving disparities.[2-7] Many of the current inequalities are the result of historical, national, and local policies designed to eliminate and/or assimilate Indigenous People.[2-5]

Hawai'i's Indigenous People suffer some of the worst health disparities and socioeconomic status compared to other populations residing in the State. Native Hawaiians live 13 years less than those with greatest life expectancy[8] and have a high infant mortality rate, which is more than twice that of Caucasians (7.9 versus 3.5 per 1,000 live births).[9,10] Significant contributors to the infant mortality disparity are education, age and smoking; all of which could be improved with education and support services. Cardiovascular disease mortality is double and diabetes related mortality is three times higher than Caucasians.[11]

In an effort to address the disparities faced by Native Hawaiians and other Indigenous Peoples, the University of Hawai'i, Office of Public Health Studies has recently launched a specialization in Native Hawaiian and Indigenous Health (NHIH) within the Master of Public Health (MPH) degree. The need for such a program was identified by existing MPH students who felt the application of public health tools to serve the Native Hawaiian and Indigenous community did not meet its full potential. This specialization is designed to prepare students with public heath skills and training necessary to serve Indigenous People globally and assist in addressing their health and wellness needs by contextualizing health determinants within historical and political frameworks. In addition, the specialization will provide extensive training in culturally sensitive research ethics which is critical for safely and effectively implementing public health research and programs aimed to address and eliminate the inequities faced by Indigenous People.[12,13]

Public Health Competencies for Indigenous Health

The Core Competencies for Public Health Professionals were developed to help strengthen the public health workforce.[14,15] The core competencies represent a set of skills, knowledge, and attitudes necessary for the broad practice of public health in the United States. They transcend the boundaries of specific disciplines within public health and help to unify the profession.

Because the historical and political context for Indigenous People differs substantially from the mainstream population in which they are domestically dependent, public health professionals serving Indigenous Peoples may require an additional layer of skills and competencies. As an emerging field, there is no consensus on the knowledge, skills, and abilities of Indigenous public health professionals. Professional competencies have been identified by various disciplines serving Indigenous People, such as the First Nations, Inuit, Métis Health Core Competencies.[16] These competencies were developed to provide undergraduate medical education guidance on health knowledge, skills and attitudes to engage both patient and community-centered approaches to health care delivery for First Nations, Inuit, Métis (FN/I/M) Peoples. Like the FN/I/M health core competencies, the development of Indigenous public health competencies is critical to support all levels of public health professionals serving Indigenous People. Proficiency in these competencies will enable today's public health professionals to leverage the history of Indigenous People, combined with knowledge of the law, policy, health provision, culture and traditions as they relate to improving the health and wellness of Indigenous People.

In an effort to address this need for Indigenous public health competencies, international Indigenous health leaders convened a meeting in July 2011 to discuss competencies essential for the practice of Indigenous public health. Hosted by the University of Hawai'i, scholars from Canada, the United States, Australia and New Zealand gathered to discuss a collaborative project for

Table 1. Indigenous Public Health Competencies
1. Describe Indigenous People's health in a historical context and analyze the impact of colonial processes on health outcomes.
2. Analyze key comparative health indicators and social determinants of health for Indigenous Peoples.
3. Critically evaluate Indigenous public health policy and programs.
4. Apply the principles of economic evaluation to Indigenous programs with a particular focus on the allocation of resources relative to need.
5. Demonstrate a reflexive public health practice for Indigenous Peoples' health contexts.
6. Demonstrate a disease prevention strategy which values and incorporates Indigenous Peoples' traditional knowledge.

improving Indigenous health. They agreed by consensus that developing a core competency model for Indigenous public health would be their focus and named the project CIPHER, which stands for Competencies for Indigenous Public Health, Evaluation and Research. The core competency model is intended to promote cultural safety practices and influence Indigenous health policy, public health education, health service mandates, research methodology, and program evaluation.

The CIPHER group created a working list of competencies that would; (a) Define the discipline of Indigenous public health; (b) Provide a framework for Indigenous public health training and career development; and (c) Entwine traditional knowledge—including relationship-based and Indigenous value-driven ideologies and protocols—with current public health acumen, to include Indigenous viewpoints, community-level involvement, and systems-wide change management (Table 1).

These Indigenous Public Health Competencies are central to the development of the University of Hawai'i's MPH NHIH specialization. Students enrolled in the NHIH specialization are required to take advanced level training in Indigenous health policy, ethics and research design. In addition, students will participate in on-going research programs with Indigenous communities through a practicum assignment.

The NHIH specialization was officially launched in early March and will receive its first cohort in the fall semester of 2013. Applications are being accepted on an on-going basis. Students who would like to apply are expected to demonstrate their commitment to community service by providing a letter of support for their application by a community willing to continue the student's learning with them either through an internship or employment opportunity.

All specializations in the accredited MPH program are expected to complete core courses that count for 17 credits. Core MPH coursework, specialization requirements and personal electives total 42 credits required for graduation. For the NHIH specialization, there are 16 required specialization credits, which is comparable to other specializations. An integrative seminar is part of those credits and will serve a few specific purposes. For example, due to the close relationships students may have with the communities with whom they work, the dual expectations of being both a health professional and community member can present unique challenges and opportunities. This integrative seminar will create a space for students, professors and other faculty to navigate the unique context of NHIH health. Additionally the seminar is going to challenge students to merge their learning and practical experiences into new knowledge that can be disseminated locally, and appropriately with interested communities as well as internationally though publication and targeted conference settings, among others.

As other specializations, MPH students in the NHIH track complete a required practicum or internship. The practicum experiences ideally will provide an opportunity to work with their own or another Indigenous community. The program is working with partners in Australia, Canada, New Zealand and the United States to create international practicum opportunities.

The program aims to enroll individuals who are passionate and sincere in using and creating knowledge and skills to improve the conditions in which the lives and well-being of NHIH are influenced. We invite people who are ready to work hard and are dedicated to understanding the complex determinants of health. The goal of all this is to provide students with an exciting learning experience so that they can make a positive impact when they work with their own or other Indigenous communities.

Summary

The Native Hawaiian and Indigenous Health MPH is a new specialization in that it will be available to University of Hawai'i public health students in fall 2013. The curriculum integrates Indigenous Public Health Competencies with traditional competencies to help build a stronger, more effective public health workforce in Native Hawaiian and Indigenous communities. The NHIH specialization will prepare students for leadership roles in Indigenous health policy and culturally safe health services. Graduates will better meet the social and cultural needs of Indigenous People, thereby enhancing the quality and effectiveness of those health services and policies. The improved quality and effectiveness of Indigenous health services will contribute to the reduction of Indigenous health disparities and the improvement of Indigenous Peoples' health.

Authors' Affiliation:
Office of Public Health Studies, University of Hawai'i at Manoa, Honolulu, HI

References

1. World Health Organization (2007). Health of Indigenous People: Fact Sheet 326. Accessed January 10, 2013 from http://www.who.int/mediacentre/factsheets/fs326/en/index.html.
2. Bramley D, Hebert P, Tuzzio L, Chassin M. Disparities in indigenous health: a cross-country comparison between New Zealand and the United States. *American Journal of Public Health.* 2005;95(5):844-850.

3. Gracey M, King M. Indigenous health part 1: determinants and disease patterns. *Lancet.* 2009;374:65-75.
4. Ring IT, Brown N. The health status of indigenous peoples and others. *British Medical Journal.* 2003;327:404-405.
5. Durie M. The health of indigenous peoples: Depends on genetics, politics, and socioeconomic factors. *British Medical Journal.* 2003;326:510-511.
6. Thompson SC, Durey A. Reducing the health disparities of Indigenous Australians: time to change focus. *BMC Health Services Research.* 2012;12:151.
7. King M, Smith A, Gracey M. Indigenous health part 2: the underlying causes of the health gap. *Lancet.* 2009;374:76-85.
8. Park CB, Braun KL, Horiuchi BY, Tottori C, and Onaka AT. Longevity disparities in multiethnic Hawaii: an analysis of 2000 life tables. *Public Health Reports*. 2009; 124(4):579–584.
9. Schempf AH, Hayes DK, Taualii MM, Singh GP, Fuddy LJ. Excess Infant Mortality among Native Hawaiians: Identifying Determinants for Preventive Action. *American Journal of Public Health* (In Press).
10. Taualii MM, Quenga JA, Samoa RA, Samanani S, Dover D. Liberating Data: Accessing Native Hawaiian and Other Pacific Islander Data from National Data Sets. *AAPI NEXUS*. Fall 2011;9(1):1-7.
11. Mau MK, Sinclair K, Saito EP, Baumhofer KN, Kaholokula JK. Cardiometabolic Health Disparities in Native Hawaiians and Other Pacific Islanders. *Epidemiologic Reviews.* 2009;31:113–129.
12. Burnette CE, Sanders S, Butcher HK, Salois EM. Illuminating the Lived Experiences of Research with Indigenous Communities. *Journal of Ethnic & Cultural Diversity in Social Work.* 2011; 20(4):275-296.
13. Usher K. Indigenous higher degree research students making a difference to the Indigenous health agenda. *Contemporary Nurse: A Journal for the Australian Nursing Profession,* 2010;37(1):102-106.
14. Core Public Health Functions Steering Committee. 1994. http://www.cdc.gov/nphpsp/essentialservices.html. Accessed January 10, 2013.
15. Council on Linkages Between Academia and Public Health Practice. Core Competencies for Public Health Professionals, Revisions Adopted: May 2010. http://www.phf.org/programs/corecompetencies. Accessed January 10, 2013.
16. Indigenous Physicians Association of Canada and the Association of Faculties of Medicine of Canada. 2008. www.ipac-amic.org. Accessed January 10, 2013.

UPCOMING CME EVENTS

Interested in having your upcoming CME Conference listed? Please contact Brenda Wong at (808) 536-7702 x103 for information.

Date	Sponsor	Location	Meeting Topic	Contact
April 2013				
4/7-4/12	UC San Francisco School of Medicine	Wailea Beach Marriott, Maui	Primary Care Medicine & Update 2013	http://www.ucsfcme.com/2012/brochure/MDM13M06.pdf
4/26-4/27	Hawai'i Orthopaedic Association	Hawai'i Prince Hotel	28th Annual Hawai'i Orthopaedic Association Combined Spring Symposium	http://www.statesociety.org/hawaii/
June 2013				
6/29-7/5	Children's Hospital Los Angeles Medical Group	Hyatt Regency Maui, Lahaina	Pediatrics in the Islands…Clinical Pearls 2013	https://s08.123signup.com/servlet/SignUp?P=15329551911424919300&PG=1532955182300
6/30-7/5	UC San Francisco School of Medicine	Hapuna Beach Prince Hotel, Mauna Kea, Big Island	Essentials of Women's Health: An Integrated Approach to Primary Care & Office Gynecology	http://www.ucsfcme.com/2014/brochure/MDM14M01.02STDC.pdf
July 2013				
7/21-7/25	Orthopaedic Surgery Kaiser Permanente Hawai'i	Grand Wailea Resort & Spa, Maui	21st Annual Update in Orthopaedic Surgery Conference	http://cmxtravel.com/kpor/2013/default.htm

THE WEATHERVANE

RUSSELL T. STODD MD; CONTRIBUTING EDITOR

WATCH YOURSELF. THE PEDIATRIC POLICE ARE OUT THERE.

In Chicago a sixteen-year-old lad was admitted to Oak Lawn Advocate Hope Children's Hospital for tonsillitis. When the house physician was taking a history he asked the mother to step out of the room. She did so, thinking he would ask about alcohol, other drugs or tobacco. Later her son told her he was asked if there were guns in the house. He thought the question was strange and out of context, but he replied honestly that there were not. When the mother heard what was asked, she was enraged. "He was admitted for tonsillitis, not mental problems, or violence. The question was an invasion of our privacy." After she filed a complaint with the administration, she received a call from the chairman of the pediatric residency program. He said that the question is definitely part of the history protocol recommended by the American Academy of Pediatrics. It is an appropriate medical history question in cases of domestic violence, trauma, suicide fear, and related issues. However, as a general interrogation, it hearkens back to Germany of the 1930s. "Und wie know where you live."

GO TO THE HOSPITAL AND DIE!

Last year, a deadly infection untreatable by almost every antibiotic, stalked the National Institutes of Health medical center. Eventually a total of 17 desperately ill patients were infected and 11 died, one a 16 year-old boy. This deadly super-bacteria is labeled CRK (carbapenem resistant Klebsiella) and recommendations from the Centers for Disease Control and Prevention (CDC) could not contain it. The NIH staff built a wall to isolate patients, ripped out plumbing and sprayed rooms with vaporized disinfectant. Eventually every patient in the 234-bed hospital was tested with a rectal swab. The outbreak was finally contained with these rigid standards. With 99,000 deaths each year in the United States. attributed to hospital-borne infections and a superbug moving in, the hospital becomes an even more dangerous environment.

PREVIOUSLY A VULGAR INSULT, NOW IT'S LIFE-SAVING THERAPY.

Reporting at the American College of Gastroenterology annual meeting, researchers found that transplanting fecal material can be useful therapy. In the past the procedure was used in cases of ulcerative colitis and crohn's disease. The latest droppings transplant is for clostridium difficile. "C-diff" is a stubborn, debilitating, gastro-intestinal inflammation induced by prolonged use of antibiotics. It can cause severe diarrhea, nausea, vomiting, and can even be fatal. Fecal microbiota transplant (FMT) involves taking fecal material from a donor, usually a spouse or family member, after a light bowel prep. The material is mixed with normal saline to provide a specimen that can be handled in a 60 cc. syringe. The patient undergoes a routine colonoscopy and the material is inserted. Out with the old bowel flora, in with the new. In the study presented, 98% of C-diff patients had resolution of their disease with one or two treatments. Some had been suffering for many months, even treated in ICU units. The moral of the story it is okay to take s--- from somebody. Give thanks.

IT'S NICE FURNITURE IN THE LONG RUN.

Gardiners, a Baltimore furniture company, offered its customers free furniture purchased between January 31 and 3 PM on Super Bowl game day (February 3) if a kick-off was returned for a touchdown. Such an event had occurred in nine previous Super Bowls, but owners figured they were pretty safe. Still, they took out insurance coverage. This is the 3rd year Gardiners offered this promotion. So, when Baltimore's Jacoby Jones ran a kick-off back for 108 yards, over $600,000 worth of free furniture went to some happy customers. It turned out great for the Ravens, great for the customers and great for Gardiners. There might have been some unhappy faces at the insurance office.

SUGAR AND SPICE AND EVERYTHING NICE — NOT QUITE.

The consumption of sugar and high-fructose corn syrup in the United States has substantially increased in the past few decades. This has become a subject of intense debate and the stakes are high. An almost straight-line of fructose consumption parallels the increase in obesity in Americans of all ages. Sucrose and high-fructose corn syrup are added to sodas, energy drinks, and sports drinks. They are preferred by cooks over those containing only glucose due to intrinsically greater sweetness of fructose. It improves the appearance and texture of baked goods, and is added to snacks, processed meats, sauces, and many other foods consumed by adolescents and adults. A major new finding reported by Page, et al, (*JAMA* – 2013) is that a hypothalamic brain signal generated by fructose is different from glucose. Consumption of glucose is accompanied by an increased sensation of satiety and fullness, but not with fructose. Controversy centers around government policy on farm subsidies and health care costs, the marketplace involving food manufacturers, school revenues from beverage machines, and even mom-and-pop stores selling baked goods.

AND GOD SAID, "LET THERE BE LIGHT."

For decades medical scientists have been struggling to make a bionic eye. At last, a device known as Argus II, made by Second Sight Medical Products of Sylmar, California, is awaiting regulatory approval by the Food and Drug Administration (FDA). The device uses a video camera embedded in a pair of eyeglasses, and a retinal prosthesis implanted in the eye. The camera data triggers pixels on the prosthesis and the image is fired to the brain. Fine visual discrimination is limited by the number of electrodes implanted in the pseudo-retina. The Argus II has sixty where the normal human eye has millions. A group at MIT is developing a bionic eye with between 256 and 400 electrodes. They are planning to form a company to commercialize their technology. This is very good news for patients with retinitis pigmentosa and advanced macular degeneration.

YES, I WILL HAVE ONE MORE FOR THE ROAD, BOSS.

A 54-year-old woman in Ontario, Canada, got drunk at an office Christmas party. Although she was offered a cab ride or accommodations, she chose to drive herself home in the snow. She crashed her car and suffered serious injuries. She brought suit against her employer claiming she should not have been allowed to drive. She won the lawsuit and was awarded $300,000. The judge went on to declare, "it is the duty of employers to monitor employee alcohol consumption at company functions." Apparently it is not the duty of an individual to refrain from drunken driving.

ADDENDA

- Cost of 30 seconds of Super Bowl advertising time: $3.12 million.
- Venetian blinds aren't. They were invented by the Japanese.
- Your dog may be your best friend, but he won't pick you up at the airport.
- I got cut off in traffic by that huge new Ford SUV, the Exhibitionist.
- Like everyone else who makes the mistake of getting on in years, I begin the day with coffee and the obituaries.
- Casual sex is the best. You don't have to wear a tie, and you can leave your Cubs cap on.

ALOHA AND KEEP THE FAITH rts

(Editorial comment is strictly that of the writer.)

HMSA

Blue Cross Blue Shield of Hawai'i

An Independent Licensee of the Blue Cross and Blue Shield Association

BE A CHAMPION FOR HEALTH CARE

Be a leader in making Hawaii the best state in which to receive the safest, highest quality, and most cost-effective medical care. New data shows that primary care providers (PCPs) who are enrolled in HMSA's patient-centered medical home (PCMH) program outperform PCPs who have not. The PCMH providers showed higher performance and greater improvement in nearly all of the care standards measured by HMSA's 2012 Primary Care Pay-for-Quality Program which are based on 16 HEDIS quality measures for PPO and HMO patients.

Transform your practice today:

- Ensure your ability to thrive personally and professionally in the evolving health care system.
- Enhance patient safety and professional accountability.
- Connect to health care system innovations that result in high-quality, cost-effective patient care.
- Use data to both improve patient care and deliver cost-effective care.
- Position your practice to become an effective and financially sound entity to meet the needs of a diverse membership in a rapidly changing environment.
- Meet and collaborate with your peers to find solutions for improving your practice as well as helping your patients improve their quality of life.

To learn more, call 948-6820 on Oahu today.

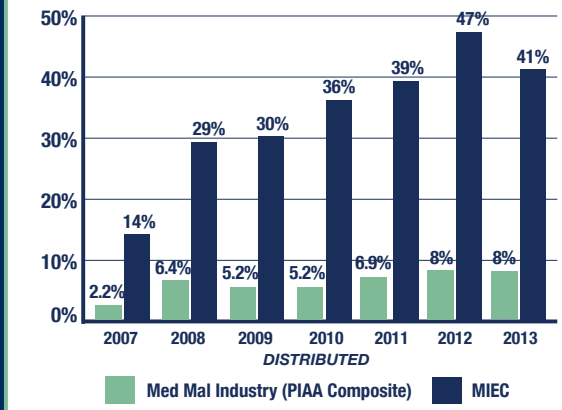
Join the Insurance Company that always puts policyholders first.

MIEC has never lost sight of its original mission, always putting policyholders (doctors like you) first. For over 30 years, MIEC has been steadfast in our protection of Hawaii physicians. With conscientious Underwriting, excellent Claims management and hands-on Loss Prevention services, we've partnered with policyholders to keep premiums low.

For more information or to apply:

- www.miec.com
- Call 800.227.4527
- Email questions to underwriting@miec.com

Policyholder Dividend Ratio*



* (On premiums at $1/3 million limits. Future dividends cannot be guaranteed.)

MIEC 6250 Claremont Avenue, Oakland, California 94618 • 800-227-4527 • www.miec.com

UCERA_ad_03.26.13

MIEC

Owned by the policyholders we protect.