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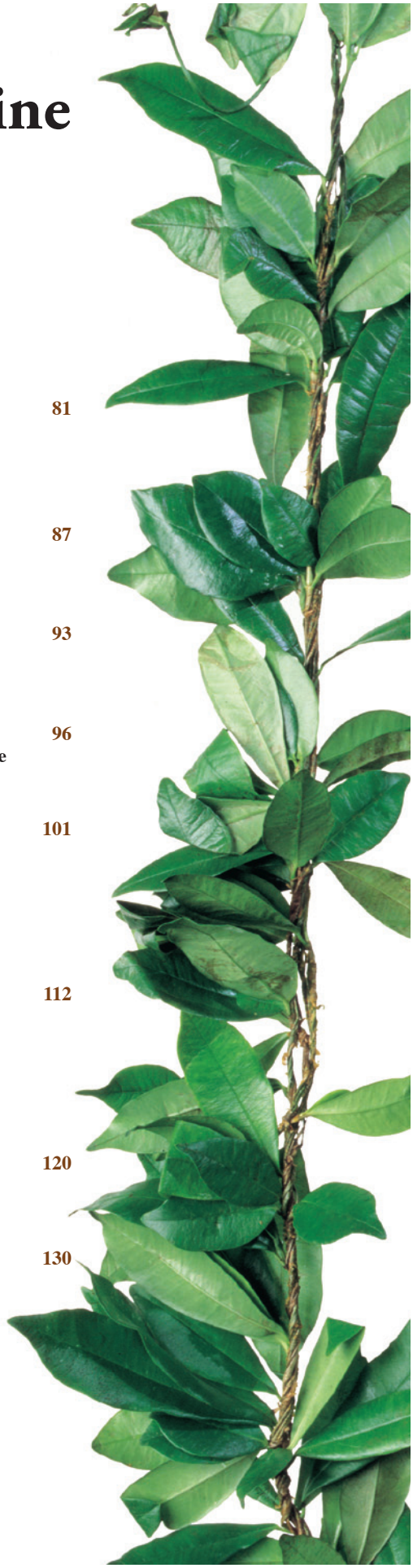

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The Hawai‘i Journal of Medicine & Public Health was formerly two separate journals: The Hawai‘i Medical Journal and the Hawai‘i Journal of Public Health. The Hawai‘i Medical Journal was founded in 1941 by the Hawai‘i Medical Association (HMA), which 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.

Fishing (D. Varez)

Adapting *SugarWatch* to Manage Metabolic Syndrome in a Partial Hospitalization Program: A Feasibility Study

Renee W. Latimer APRN-BC, Rx, MS, MPH and Rose Clute APRN-BC, Rx, MS, APRN

Abstract

A successful worksite diabetes prevention program, SugarWatch, was adapted for a seriously mentally ill patient population in a partial hospitalization program in Hawai'i. A feasibility study was implemented using an intervention with 3 components: SugarWatch curriculum, structured physical activity, and Create a Plate lunch.

Twenty participants completed the three month intervention. Only systolic blood pressure showed statistically significant improvement. However, trends in improvement were also seen with diastolic blood pressure and total cholesterol. Despite minimal improvement in physiological measures, the project changed practice in the setting to align with the 2004 American Diabetes Association and American Psychiatric Association Guidelines for the prevention of metabolic syndrome and better management of patients taking second generation antipsychotic medications.

Introduction

Chronic physical disease co-morbidities have a significant impact on persons with serious mental illness (SMI). Nationally, persons with SMI die approximately 25 years before the general population. In Hawai'i, recent data has indicated that the situation is worse; persons with Severe and Persistent Mental Illnesses (SPMI) in Hawai'i die on average 27.2 years before the general population.[1] Persons with SMI have a 1.5-2.0 times higher risk of diabetes and obesity than the general population, even after controlling for medications.[2,3] Being overweight or obese contributes to the constellation of risk factors known as Metabolic Syndrome, which is defined as the presence of 3 or more of the following.[4]

- Elevated waist circumference: at or greater than 40 inches in men, 35 inches in women;
- Elevated triglycerides: at or greater than 150 mg/dL (or on drug treatment for elevated triglycerides);
- Reduced HDL-Cholesterol: lower than 40 mg/dL in men, 50 mg/dL in women;
- Elevated blood pressure (BP): at or higher than 130 mm Hg systolic BP or 85 mm Hg diastolic BP;
- Elevated fasting glucose: 100 mg/dL or higher

In addition, persons with mental illness often lack health insurance, delay seeking care and are less likely to receive lifestyle behavior counseling and medication for conditions such as hyperlipidemia and cardiovascular disease. Calorie-dense, nutrient-poor diets and lack of exercise are other factors that drive weight gain in the seriously mentally ill population.[5,6]

Compounding the effects of these socio-behavioral influences, many of the medications prescribed for the treatment of serious mental illness, particularly atypical or second generation antipsychotics (SGAs), may cause metabolic and cardiovascular side effects.[2,7] The Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study showed that although not every antipsychotic drug induces serious metabolic disturbances, most have an effect on weight gain, glucose metabolism, dyslipidemia, and risk for metabolic syndrome.[8]

In 2004, consensus guidelines and strategies for addressing the metabolic side effects of medications compounded by the lifestyle risks often associated with serious mental illness were developed by the American Diabetes Association (ADA) and the American Psychiatric Association (APA).[2] These strategies included: (1) consideration of metabolic risks when starting medications, (2) patient, family, and caregiver education, (3) baseline screening, (4) regular monitoring, and (5) referral to specialized programs for weight management. Despite these consensus guidelines, 6 years after the ADA-APA consensus statement, glucose and lipid testing for SGA-treated adults was still infrequent leading to the pronouncement that "more effort is needed to improve diabetes and dyslipidemia screening in these at-risk patients."[9]

The burden of SMI on society is great. In the state of Hawai'i, the most recent available National Survey on Drug Use and Health (NSDUH)[10] reported the percentage of persons in Hawai'i with a SMI as 4.93 (3.84 - 6.31) similar to the US percentage of 4.99 (4.77 - 5.21).[10] In addition, according to the most recent Behavioral Risk Factor Surveillance System (BRFSS) data (2012), 29% of adults in Hawai'i report having at least one mentally unhealthy day in the past 30 days; 9% (95% Confidence Interval 7.6 - 9.6) reported experiencing greater than 14 days of mental distress during the past 30 days, an indicator of more frequent mental distress.[10] The burden of co-morbid mental and physical disease was highlighted in a special BRFSS report which noted the strong association between frequent mental distress and overweight/obesity, diabetes, and cardiovascular disease in the state of Hawai'i. Exact prevalence statistics were not available in this report and it has not been updated,[11] however, it is likely that the population affected by both serious mental illness and risk factors for metabolic syndrome is a large and frequently underserved population in our state.

Weight Management Interventions for Patients on Atypical Antipsychotic Medications

For patients meeting the criteria for Metabolic Syndrome the first line therapy is lifestyle modification including weight loss, increasing physical activity, eating a heart healthy diet, and quitting smoking.[12] These same strategies apply to those with a serious mental illness. Interventions addressing weight management and reduction of risk for Metabolic Syndrome for patients taking atypical antipsychotic medications have been

successful. A recent meta-analysis of 13 randomized clinical trials comparing a weight loss intervention to usual care found an overall reduction of 0.98 in body mass index (BMI), a corresponding loss of 3.12% of initial weight supporting the statement that "when compared with treatment as usual in psychotic patients, preventive and individual lifestyle interventions that include diet and physical activity generally prove to be effective in reducing weight."[13] The average weight loss found in this meta-analysis was below the 5% to 10% weight loss generally accepted as sufficient to improve cardio-metabolic complications and can be explained by study limitations most notably the heterogeneity of the studies included in the analysis.[13] An earlier meta-analysis by Alvarez-Jimenez, et al, found a statistically significant reduction in mean body weight for those in the weight loss intervention groups compared with those on treatment as usual (mean weight loss = -2.56 kg [95% CI: 3.20 to 1.92 kg, $P < .001$]).[14]

Educational Interventions for Management of Diabetes in Hawai'i

In Hawai'i, several educational interventions for the prevention and management of diabetes have been shown to be effective. The Diabetes Prevention Program (DPP), a landmark national study, found that weight loss of 7% coupled with increasing physical activity to150 minutes per week could prevent or delay diabetes onset in a high risk population.[15] The Hawai'i site of the DPP followed the study protocol by offering 16 individualized education sessions to the Lifestyle group, promoting exercise and setting weight loss goals.

In addition, a diabetes worksite research project, the Diabetes Worksite Pilot Program (DWPP) used an abbreviated curriculum, *SugarWatch,* to focus on the core areas of diet, exercise, and the clinical aspects of disease prevention and self-management. The intervention was delivered at worksites across Hawai'i to a population that was predominantly "local" with a Pacific Islander or Asian ethnicity participation of 83%. The curriculum included diet and exercise guidance adapted for Hawai'i's multi-ethnic population. Clinical improvements were seen in the program group compared to the control group for: HbA1c, Fasting Blood Glucose, BMI, systolic blood pressure (SBP), total cholesterol, and percentage with hypertension and/or hyperlipidemia.[16,17]

The success of the DPP and the DWPP laid the groundwork for an additional Hawai'i-based study *Managing metabolic syndrome in a partial hospitalization program: A feasibility study,* described in this paper. The purpose of this study was to test the feasibility of implementing an intervention similar to the DWPP, with a group at high-risk for developing diabetes and heart disease, seriously mentally ill patients participating in a partial hospitalization or day treatment program.

This was a feasibility study using a quasi-experimental single group with a pre-/post-test design.

Setting: Life Enhancement (LE) – A Day Treatment Program

The Life Enhancement Program (LE) is a partial hospitalization day program designed for adults with SMI. The LE Program runs Monday-Friday and enrolls approximately 100 patients a year with a daily census of 20-25 patients and an average length of stay of 16 weeks.

The LE Program offers a multi-disciplinary approach to teach coping skills for managing chronic mental illness, predominantly schizophrenia and/or severe mood disorders. As many of the patients also have multiple medical co-morbidities, Advanced Practice Nurses (APRNs) assist patients with both psychiatric and medical self- management. Nurse-delivered group education historically focused on psychiatric medication management and management of side effects with little to no focus on the prevention and management of diabetes, obesity, and metabolic syndrome. The newly developed curriculum specifically addressed the risk factors associated with metabolic syndrome by incorporating modules that focused on health diet, physical activity, partnering with your physician, and understanding long term effects of uncontrolled blood sugar, blood pressure, and cholesterol. At the start of this program there were no residential or day treatment programs for the SMI in Hawai'i offering a structured, multi-dimensional program targeting risk factors for metabolic syndrome.

Methods

The project and consent form were approved by the Research and Institutional Review Committee at the Queen's Medical Center in June 2010 and the project was completed in April 2012.The recruitment goal was a convenience sample of 20 patients who continued in the LE Program for 12 weeks. To compensate for individuals who dropped out, over-recruitment by 50% was done. Eligibility was not limited to specific mental illness diagnoses as all patients in the LE Program were taking a variety of psychiatric medications, including antipsychotics, mood stabilizers, and/or antidepressants.

Because admission to the LE Program was ongoing, it was not feasible to assemble a cohort of 20 participants to complete the intervention simultaneously. Instead, sessions 1-6 of *SugarWatch* were offered repeatedly over the 6 months of intervention delivery. Because of the structure and staffing of the LE Program, it was not possible to exclude patients from the Health and Wellness sessions if they did not consent to participate in the study. The *SugarWatch* curriculum replaced the weekly Health and Wellness sessions for the duration of the study so session presentations included patients in the study and one patient who chose not to participate. No data was collected from the participant who declined to participate.

Components of the Intervention

This research project incorporated ADA and APA strategies into an intervention targeting a high risk population in a partial hospitalization program (ie, the LE Program). The 3 important components of the proposed intervention were: *SugarWatch* curriculum; Structured physical activity; and Promotion of *Create a Plate lunch* through modules focused on a healthy diet.

SugarWatch curriculum

The *SugarWatch* curriculum was described above, and session objectives for *SugarWatch* can be found in Table 1.The adapted *SugarWatch* curriculum written at a 5th graded reading level was introduced into the established "Health and Wellness" sessions already offered during the LE Program. Sessions 1-3 focused on diet and exercise, and needed little adaptation for the patient population at the LE Program. Sessions 4- 5 were adapted to incorporate information about psychiatric medications and the impact of these medications on cardio-metabolic systems. In addition, information on the management of hypertension and hyperlipidemia were woven throughout the curriculum, since *SugarWatch*'soriginal curriculum focused on diabetes rather than the constellation of risk factors described as metabolic syndrome (Table 1).

Structured Physical Activity

Daily physical activity was added into the LE Program. The goal for participants was to increase walking to 150 minutes per week (five, 30-minute sessions) so the schedule of classes was shifted to accommodate walking sessions as part of the daily schedule. Program staff assisted with the walking sessions. Participants were encouraged to walk on their own on non-program days. In addition, the curriculum provided opportunities for individual goal setting for physical activity.

Create a Plate lunch

The program offered a daily lunch to patients with a goal of serving many people for few dollars. Standard lunches provided mostly protein and carbohydrate food sources and portion size was not controlled. With the initiation of the feasibility study, the daily lunch offering included unlimited servings of one vegetable offering and a fruit. Due to the cost of individual servings of dairy such as milk or yogurt, participants were encouraged to include these foods at other times of the day. Participants were also encouraged to follow the Create a Plate method (Figure 1) for determining serving size, however there was no monitoring of portion sizes either during the daily lunch or outside of the program day.[18] Discussion of local foods as part of a healthy diet was already a part of the curriculum.

Data Collection

Demographic data (eg, age, sex, and ethnicity) were collected from each participant. Ethnicity was collected by asking participants: What is your ethnicity (the ethnicity that makes up the largest proportion of your ethnic background)? Participants were given a list of ethnicities from which to select but not restricted to one choice. Participants who selected more than one ethnicity were categorized as "reports more than one ethnicity." Physiological measures, medical history, and questionnaires were collected at baseline and end of study. For data points, the ADA and APA recommendations for baseline assessment and monitoring of patients receiving atypical antipsychotic medications were used (Table2).

Table 1. Session Objectives for *SugarWatch*

Session 1: Create-a-Plate
1. Use the "Create-a-Plate" method to choose appropriate portion sizes and a balanced diet.
2. Learn about benefits of exercise.
3. Demonstrate how to use a pedometer.
Session 2: Stepping Out
1. Identify at least two activities that can be incorporated into their daily lives long term.
2. Learn how to measure the level of intensity of any exercise activity.
3. Learn how to prepare and choose lower fat choices when cooking and eating away from home.
Session 3: Be a Buddy
1. Learn how to use food labels.
2. Learn how to choose lower fat snacks.
3. Demonstrate ability to set and maintain exercise goals
Session 4: Check your Health
1. List the types of medicines used to treat chronic physical illnesses.
2. Describe target range for physiological measures in persons with risk factors for metabolic syndrome.
3. Define important lab tests and how often they should be checked.
Session 5: Talk to Your Doc
1. Learn how to talk with their doctor to take better care of your health.
2. Make a plan to prevent long term complications of chronic disease by partnering with the doctor.
Session 6: Planning for the Road Ahead
1. Review information from previous sessions and tie it all together.
2. Recognize areas of personal success in making positive lifestyle behavior changes.
3. Develop a plan for improving areas of difficulty that impact lifestyle behavior.

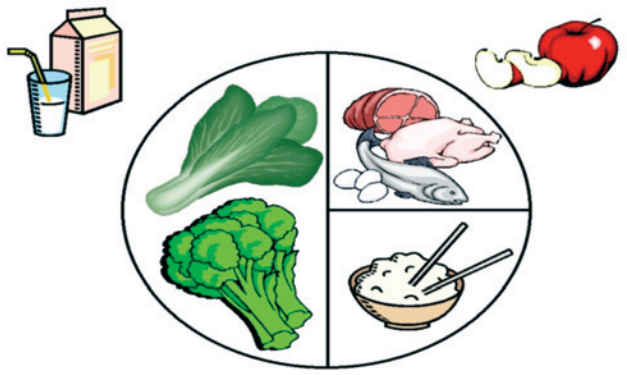

Figure 1. Create a Plate

Table 2. Data Collection Plan				
Measurement	**Instrument**	**Frequency of data collected**		
		Base-line	**Weekly**	**12 week**
Personal/family History	Medical records	X		
Weight/BMI	Scale	X	X	X
Waist circumference	Tape measure	X		X
Blood pressure	Sphygmomanometer	X		X
Fasting plasma glucose	Laboratory test	X		X
Fasting lipid profile	Laboratory test	X		X
HbA1c	Laboratory test	X		X
Diabetes/lifestyle knowledge	Pre- and post-test	X		X
Feasibility Measures				
Attendance	Attendance records		X	
Satisfaction	Session evaluations		X	X
Compliance	Completion of data collection, dropout			X

Feasibility Indicators

To determine the feasibility of implementing this intervention into an existing partial hospitalization program, data was collected on attendance, recruitment, participant compliance (eg, completion of questionnaires, dropout rate) knowledge, and satisfaction. In addition, participants were asked to complete session evaluations on a weekly basis.

Data Analysis

Due to the small sample size, data analysis was limited to descriptive statistics including means, medians, and frequencies. Paired Sample t-tests were used to compare physiological measures pre and post intervention.

Results

Thirty-seven (37) participants consented to take part in the feasibility study and 20 completed the entire 12 weeks of the study. Demographic data described in this article reflect only the 20 participants who completed the study. Twelve (60%) study participants were male. Sixteen (80%) of the participants were less than 50 years old with a mean age of 43 and 13.2 mean years of education (range 11-20). Thirteen (65%) participants reported that they were Asian American or Pacific Islander and five (25%) reported greater than 1 ethnicity; 3 of those were Native Hawaiian combined with other ethnicities. One participant was African-American and one participant chose "other" with no specification.

The majority of participants reported a family history of chronic disease [diabetes at 45% and hypertension at 60%]. Thirty five percent (35%) were smokers a percentage greater than both the Hawai'i population at 17% [19] and the U.S. population at large (19.0% of all adults aged 18 years or older)[20] but similar to the US smoking rates of 36.1% for persons with SMI (Tables 3 and 4).[21]

Only 13 participants' physiological measures were collected at the end of study; therefore, the analysis of change in physiological parameters pre- and post-intervention was limited to these participants. Post intervention, no improvements were found for the following physiological measures: Weight, BMI, Waist circumference, fasting blood glucose, Hemoglobin A1c (HbA1c), Low Density Lipoprotein (LDL), High Density Lipoprotein (HDL), and Triglycerides. Slight, but not statistically significant improvements were seen in systolic and diastolic blood pressure and Total Cholesterol (TC). Knowledge about metabolic syndrome, as measured by pre and post test increased slightly, but not significantly. (Table 4).

Table 3: Characteristics of the Sample		
Characteristics of the Sample	**n**	**Value (n=20)**
Male gender	12	60%
Mean age	20	43 years (range?)
Mean years of education	20	13.2 (range 11-20)
% Asian American or	9	45%
Part Native Hawaiian or other Pacific Islander	4	20%
% reporting more than 1 ethnicity	5	25%
Family history of diabetes	9	45%
Family history of hypertension	12	60%
% current smokers	7	35%

Table 4. Results: Comparing Mean Physiological Measures at Baseline and 12 Weeks (End of Study)*			
Variable	**Baseline Mean; (S.D.) (n=13)**	**12 Weeks Mean; (S.D.) (n=13)**	***P*-value (*P* < .05)**
Weight	181.4 lbs (35)	182.1 (34.8)	.679
BMI (kg/m^2)	30.1 (5.7)	29.9 (5.4)	.578
SBP (mm Hg)	129.3 (29.6)	121.2 (24.7)	.128
DBP (mm Hg)	75.6 (16.1)	75.1 (19.3)	.867
Waist circumference (inches)	39.7 (4.5)	39.8 (4.0)	.853
Fasting Blood Glucose (mg/dL)	105.6 (31.2)	124.5 (45.2)	.054
HbA1c (%)	6.6 (1.63)	6.8 (1.75)	.724
Total Cholesterol (mg/dL)	194.9 (43.2)	183.5 (63.8)	.503
Low Density Lipoprotein Cholesterol (mg/dL)	114 (32.5)	123.9 (34.3)	.38
High Density Lipoprotein Cholesterol (mg/dL)	46 (9.7)	41.5 (11.8)	.052
Triglycerides (mg/dL)	173 (110.5)	251.7 (265.4)	.25
Knowledge about Metabolic Syndrome (# correct out of 10 questions)	5.3 (1.5)	5.8 (1.58)	.74

*A paired samplest-test was used to compare means pre and post intervention

Discussion

This feasibility study demonstrated that it is possible to implement recommendations from the APA-ADA guidelines into an existing partial hospitalization program for persons with SMI. Baseline screening of new patients in the day program was also implemented, consistent with the APA-ADA guidelines. The three component intervention adapted from two previous research studies completed in Hawai'i included the *SugarWatch* curriculum, daily exercise offering, and Create a Plate lunch activity. These interventions were introduced as new practices into an existing program and continue to this day. The new practices introduced into the program were acceptable to patients who took part in the full set of activities and reported liking the program.

A statistical difference in physiological measures was not discernable over the course of this study. However, some improvements were seen in SBP, DBP and TC. Potentially, fidelity to the exercise component of the study may have impacted blood pressure although a small sample size and large standard deviations for many of the physiological measures make the results less compelling.

Limitations

Numerous limitations affect the internal validity of the study. First, a small sample of twenty and a quasi-experimental one group, pre-post-test design limit the conclusions we can make. The convenience sampling was likely biased toward those who would participate in a day treatment program and agree to take part in research. This sample would likely not be generalizable to the many patients with SMI who are not receiving treatment and/or do not have health insurance. Seventeen of the 37 participants who consented to be in the study dropped out. This high dropout rate is common in the LE program and was due to patients not being successful in the LE milieu rather than participants dropping out of the study. Dropout from the program was uncontrollable as LE is an optional day treatment program, allowing clients to discontinue at anytime at will unless court ordered to attend. Common reasons for dropout are relapse, rehospitalization, relocation, and inability to adapt to the daily schedule reflecting potential sources of non-representativeness of the patient pool that remained enrolled in the study.

In this study, there was no control for extraneous variables, in particular, changes in second generation anti-psychotic medications (SGAs). Certain SGAs are likely to affect cardiometabolic risk factors differently than others. Adjustments of medication during the course of the study may have impacted any or all of the physiological measures.

Another limitation was that healthy food and portion sizes were not provided as part of the study due to financial constraints. Rather, participants discussed a healthy diet following the Create-a-Plate recommendations, and were advised to follow this guidance on their own. Given the financial challenges that many patients with SMI have, and knowing that many patients live in group settings with little control over their diets, it is unlikely that significant dietary change took place during the study.

Finally, only 13 participants' physiological measures were collected at the end of study. Participants were given lab slips and asked to go to the lab on their own. This reduced compliance led to a lower number of laboratory data points at end of study and a decreased ability to make statistically sound comparisons to baseline data.

Conclusion

Persons with serious mental illness are disproportionately affected by chronic conditions such as Type 2 diabetes, hyperlipidemia and cardiovascular disease but are less likely to access the same resources for prevention as the general population.[5,6]

Patients with SMI have an increased risk of both greater morbidity and earlier mortality than the US population as a whole. Healthcare providers at all levels must provide guidance and support to assist this population in the prevention of chronic physical disease while also providing care for the symptoms of mental illness. A partial hospitalization day treatment program may provide an appropriate setting for offering health education, physical activity, and a healthy diet since patients attend the program for 5 days a week for most of the day. This study demonstrates that a change of practice to achieve ADA-APA guidelines is feasible using the LE program in SMI. However the design and limitations in data collection precluded evaluation of the efficacy of the program in this study. Nevertheless, baseline lab screening has been instituted at intake for lipids, FBG, HbA1c for all patients. The curriculum has been introduced into the health and wellness component of the weekly schedule. Most importantly, daily walking or other physical activity has been incorporated into the LE program and awareness of the importance of healthier diet has increased.

Conflict of Interest

None of the authors identify a conflict of interest.

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Hawaiian — English
'Onipa'a — Stand firm

A Discrete System Simulation Study in Scheduling and Resource Allocation for the John A. Burns School of Medicine Clinical Skills Center

Henry W. Glaspie MS and Celeste M. Oshiro Wong MPH

Abstract

The Center for Clinical Skills (CCS) at the University of Hawai'i's John A. Burns School of Medicine (JABSOM) trains medical students in a variety of medical practice education experiences aimed at improving patient care skills of history taking, physical examination, communication, and counseling. Increasing class sizes accentuate the need for efficient scheduling of faculty and students for clinical skills examinations. This research reports an application of a discrete simulation methodology, using a computerized commercial business simulation optimization software package Arena® by Rockwell Automation Inc, to model the flow of students through an objective structure clinical exam (OSCE) using the basic physical examination sequence (BPSE). The goal was to identify the most efficient scheduling of limited volunteer faculty resources to enable all student teams to complete the OSCE within the allocated 4 hours. The simulation models 11 two-person student teams, using resources of 10 examination rooms where physical examination skills are demonstrated on fellow student subjects and assessed by volunteer faculty. Multiple faculty availability models with constrained time parameters and other resources were evaluated. The results of the discrete event simulation suggest that there is no statistical difference in the baseline model and the alternative models with respect to faculty utilization, but statistically significant changes in student wait times. Two models significantly reduced student wait times without compromising faculty utilization.

Introduction

The Center for Clinical Skills (CCS), at the University of Hawai'i's John A. Burns School of Medicine (JABSOM), supports the school's medical education program by supplementing the traditional education modes with simulated clinical encounters.

As simulated clinical encounters were introduced into traditional medical education they were historically focused on the advanced training given to residents during Graduate Medical Education. As simulation was introduced to the Undergraduate Medical Education, the primary focus was on using Standardized Patients (SPs), or actors, to simulate patients with a variety of ailments.[1] In the 1990s the National Board of Medical Examiners started an initiative to test clinical skills of medical school students as part of their licensure exam. In turn, the SPs' ability to present different medical scenarios and give feedback became critical to preparing the students for the board exam.[2,3]
Using SPs to train students has become a vital part of the medical school's curriculum.[4] One study showed that the use of SPs along with traditional assessment improves student's long-term retention and application of knowledge.[5]

The SPs are trained to assess and provide feedback regarding a student's clinical skills. These innovative education experiences are aimed at teaching and evaluating the patient care skills of history taking, physical examination, interpersonal communication, and counseling.[6]

Study Background

The CCS trains medical school students in a variety of medical practice scenarios and performs assessments through objective structured clinical exams (OSCE). OSCEs are graded examinations of medical students in which SPs are used to simulate real patient encounters.[7] Student performance in these encounters is graded by trainers/facilitators and SPs. The JABSOM Clinical Skills Center conducts OSCEs with a fixed number of skills stations or examination rooms, instructors, staff, and SPs. One key assessment grades the medical students' ability to conduct a comprehensive basic physical examination.

The Basic Physical Examination Sequence (BPES) is a comprehensive head-to-toe examination to be performed on a patient during their visit with a physician.[8] The BPES Exercise requires students to demonstrate competence in performing the steps of the basic physical examination in the correct order, using the correct technique. All JABSOM students are required to successfully complete this exercise.

Decreased funding for faculty with no attrition in enrollment (the first year class size of 66 has remained essentially unchanged) has generated increased staff workload and increased difficulty in securing and scheduling volunteer faculty to facilitate and perform the student assessments. The purpose of this study is to examine the BPES exercise to optimize utilization and minimize wait times. The study uses Arena® Simulation Software, Version 14, by Rockwell Automation, Inc., Wexford, PA, to create a flowchart-style modeling methodology of the BPES exercise. This software helps to measure the performance of the system being modeled.[9] The exercise was modeled to analyze current and alternative scheduling designs to identify the most efficient utilization and scheduling of faculty members, while decreasing student wait times.

Description of the BPES Exercise

First year medical student class size varies, so logistics and planning projections approximated 60-66 student participants in the exercise. OSCE sessions are scheduled for three groups of 20-22 students each and held over three days. Each group is segregated into 10-11 teams with two student participants per team. Each team completes the OSCE session, with a BPES exam conducted by each student. The entire OSCE session is conducted during a 4 hour block of time. Following a checklist, teammates sequentially complete a full physical exam on each other, in one examination room. One volunteer faculty member is assigned (on a first-come, first-served basis) to enter the examination room to facilitate, assess, and give constructive

feedback to each student immediately following the patient examination exercise. When the exercise and feedback are completed, the faculty member leaves the room and the student team takes approximately 5 minutes to switch roles as the patient becomes the practitioner and vice versa. A new faculty member then enters the room and another exam sequence is started. On completion of the second exercise, both team members leave the exam. The faculty members used for this exercise are practicing physicians who volunteer to participate and have been trained by the CCS staff for the OSCE.

For this exercise the CCS provides 10 examination rooms outfitted to simulate medical examination rooms (Figure 1). Each room is equipped with cameras and microphones that can record digital video of student-patient encounters.

The general format of the exercise requires the two-member student team to arrive in one of the open rooms. Each student has 30 minutes to complete the BPES and receive feedback from the faculty member. The faculty member then exits the room and students have 5 minutes to changes roles, clean up and reset the room while waiting for the next available faculty member to arrive. CCS OSCE design seeks to avoid use of any given faculty member to assess the same student team twice. This strategy, based on the preference of the CCS staff, allows a wider range of expertise and feedback to be provided to students during the exercise. Once both students on the team have finished the BPES, they exit the CCS.

Problem Description

The CCS staff routinely encounters problems recruiting the necessary number of volunteer faculty for the 4 hour time blocks required for medical student assessment. It is imperative that the CCS staff schedule enough faculty members to allow adequate time to move the students through the exercise within the given time. At the same time, it is equally important not to recruit too many faculty members. Under-recruitment results in long wait times between encounters for students, and undue hardship for faculty who are forced to grade the student team twice. Over-recruitment means that the volunteer faculty members are underutilized and idle time leaves an impression that they are not really needed, making it more difficult to recruit volunteer faculty for future exercises.

Study Objectives

There are two primary objectives for this study. First, we seek to use the Arena Simulation Software to model and analyze the current CCS scheduling methodology to establish baseline parameters for faculty utilization and student wait times. Second, we seek to vary and model the scheduling parameters, including the number of faculty members and their scheduling, to identify an optimally efficient model that maximizes faculty utilization while minimizing wait times. We analyze the changes in the model inputs on three primary outcome measurements: faculty utilization (percentage of the scheduled time that the faculty member is engaged with the students); the number of students seen by each faculty member; and, student wait times.

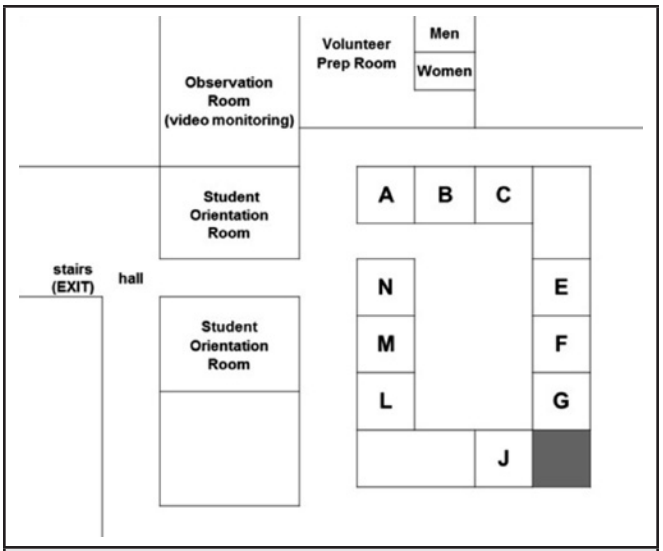

Figure 1. CCS Facility and Exam Room (A-J) Configuration

Research Questions:

- Will increasing or decreasing the number of volunteer faculty and/or their hours decrease student wait times?
- Will increasing or decreasing the number of volunteer faculty and/or their hours improve the volunteer faculty utilization?
- What is the average number of assessments performed by each faculty member?

Methodology

Logistics and operations performance outcome measures evaluated by the project included three primary simulation model output parameters: (1) faculty utilization (percent of time that faculty member engages with students); (2) the number of students seen by a faculty member; and (3) student wait times in minutes. Observation of these measures will help determine efficiencies in scheduling.

The baseline Arena® faculty scheduling model was transposed from a paper-based method currently in use by the staff at the CCS. Table 1 shows the typical schedule.

CCS staff used a wall clock to manually record the times the student teams entered and exited exam rooms, and the duration of the exam including time used for providing feedback. The method of timing does not afford a high level of precision but gives an approximation suitable for this research.

The design of the baseline model (the control) was compared to the alternative designs (the experimental groups) for evaluation and recommendations to optimize faculty utilization and decrease student wait times. The null hypothesis is that there is no difference in faculty utilization and student wait times between the base and alternative models. The study examines the effect of changes to the number and distribution of volunteer faculty hours and how it affects the system.

For the analysis, the means of the faculty utilization and the student wait times was compared using a One-way Analysis

of Variance (ANOVA). The ANOVA was used to evaluate measurements between the baseline model and the alternative models observations to see if the means showed a difference. A .05 level of significance was used.

Constraints and Assumptions

CCS staff survey and BPES observations generated the following constraints and assumptions to guide development of the Arena® simulation models. These standard parameters were applied across all simulations:

- Once the student teams pick an exam room, they will stay there until both students complete the exam.
- Faculty members must evaluate the student in the room they are assigned to by the CCS staff.
- Students are given 5 minutes to change roles and reset the room between the sequential examinations.
- Students are given a maximum of 60 minutes per student to complete the physical exam and receive faculty feedback. This is controlled by a timer. This amount is constrained by the CCS due to the fact that the individual BPES examination should take no more than 45 minutes.
- Due to the capacity of the CCS (10 exam rooms), the staff restricts the number of student teams to 11. This allows for 10 teams to occupy the exam rooms and for one team to be waiting "on deck" in the student orientation room.
- Faculty should assess no more than 3 individual students (if possible) regardless of the length of time the faculty member is scheduled.
- Faculty should not assess the same student team more than once.
- BPES exercise should finish within 4 hours.
- Historically, it has been difficult for the CCS staff to recruit more than 8 total volunteer faculty

Data Collection

The data for the baseline model was collected from the BPES OSCE on January 29, 30, and 31 of 2013. During the 2013 OSCE, there were 66 students broken into 11 groups per day and evaluated over that 3 day period. With the help of CCS staff, student, and faculty member examination counts and specific time data was recorded.

Analysis of Data for Simulation

Arena Input Analyzer® was used to analyze the data observed for student arrival times and exam length times. While the examination was scheduled to start at a specific time, students were free to enter the rooms when ready. The student arrival times are the time intervals between each student team's arrival in the examination room. The exam length times were the observed length of time each faculty member was in the examination room. Observed samples of student arrival times (in minutes) showed a beta distribution with the following expression: 4.5 + 33 * BETA (0.228, 1.54). The observed sample of exam lengths (in minutes) showed a triangular distribution with a minimum time of 40 minutes, a maximum time of 60 minutes and a most observed value of 50 minutes.

Modeling, Design, and Analysis

In this discrete event simulation model, we are trying to optimize resource utilization and time along with the time that objects move through the process/exercise. Therefore, in our model, the faculty is the resource that we are trying to optimize and the students are the objects that are moving through the simulation and waiting in the queue for the resource to become available. The baseline simulation model of BPES scheduling was constructed using 8 volunteer faculty members, based on historical recruitment of volunteers and successful completion of the exercise. In this model 4 faculty members each participated in the full (FT) 4 hour session and 4 faculty members participated part time (PT) for 2 hours. The 2 hour part time sessions are balanced with 2 faculty members for the first half of the OSCE and 2 faculty members for the second half of the exercise. The simulation design begins as each student arrives at the CCS and moves to the first available room (this is the same point at which the timer was started to record the input data for the simulation when the exercised was observed in real time). If no faculty resources are available, the student team has to wait. In the Arena software, resources are idle (not assigned to a student team) or busy (assessing a student). Additionally, the software treats resources as stationary (faculty) and entities (students) seeking resources must move to find an open an idle resource, the faculty. Although different from the stationary student teams and moving faculty which happens in real life, the software treats resources as stationary objects. The time it takes for an entity to find an available resource is measured and is equivalent to the real life situation of students waiting in a room for a faculty member to arrive. In the simulation, student team is assigned a counter and the faculty member that evaluates each student is recorded. The counter makes sure the student completes the BPES only once, and recording the faculty member assures that the student group does not use the same faculty resource more than once. The simulation ends when all student teams have completed the process.

This base model was validated by discussions with the CCS staff and historical observation. The model is a terminating simulation run for a total of 1000 replications to reduce variance and provide the best results. The CCS staff also validated that the input parameters were consistent with the times measured during the BPES. This information was valuable in the calibration and debugging of the model.

After the baseline simulation was completed and the results were recorded, alternative simulation models were constructed. The first model (Model 1) decreased the faculty number to 4 members scheduled for the full 4 hour OSCE. The next model (Model 2) slightly increased the total number of faculty members used to 5, though far fewer that the 8 faculty members used in the baseline. Model 3 used 8 faculty members for the full OSCE session and Models 4 and 5 used 8 faculty members with 4 members used for the full OSCE session and 4 members

used in the first or last halves of the OSCE session respectively. The final 2 models (Models 6 and 7) used 6 faculty members with 4 members used for the full OSCE session and 2 members used in the first or last halves of the OSCE session respectively Table 1 shows the models analyzed.

Results and Output Analysis

Models 1 and 2, with 4 full time faculty members and 5 full time faculty members respectively, could not be completed within the 4 hour exercise limit. Model 3, shows a 13.55 minute reduction in student wait time from the baseline, but a drop in faculty utilization of 6.10%. In Model 4, with 4 full time resources and 4 part time resources in the first half of the BPES, the faculty utilization increases 5.14% but the students wait time increases by 9.13 minutes. Model 5, with 4 full time resources and 4 part time resources in the last half of the exercise, has a similar student wait reduction as Model 4 and the faculty utilization is almost the same as the base model. Although Model 6 shows a utilization increase of 10.87% over the base model, the average wait time increases by 7.47 minutes. With 4 full time resources and 2 part time resources in the first half of the BPES, Model 7 shows a 5.36 minute decrease in wait times but only showed a 1.17% increase in faculty utilization. Moreover, in Models 6 and 7, the average number of assessments is higher than the CCS staff desired in the model constraints (3.66 and 3.14 respectively). All other models were similar to the base model is this area.

Discussion of Results

In this study discrete event simulation and the Arena® Simulation Software was applied in the modeling of medical education scheduling. Discrete event simulation is useful to build the business process model and make changes "virtually" without impacting the real life model. This is effective in evaluating changes without the cost of putting changes in practice.[9] The simulation method and software has had many medical applications and more specifically has been used in modeling of clinical patient scheduling and clinical organization resource scheduling. In one study, a hospital used discrete event simulation and the Arena Simulation Software® to increase emergency department efficiency and decrease patient length of stay.[10] Discrete event simulation was used in a similar way by the Department of Anesthesia at the University of Iowa, to maximize the operating room utilization and patient scheduling.[11] Therefore, by extension, this type of simulation and related software may be used to model medical education training scenarios, where student time, instructor utilization, or equipment use needs to be optimized.

The ANOVA results in Tables 2 and 3 show that we should reject the null hypothesis and conclude that there is a significant difference difference between the models. Because there is a statistically significant between the models we tested further for significance in faculty utilization and student wait times between the baseline and each of the alternative models individually. A multiple comparisons test was completed between the base model and each alternative model. The results in Table 4 show no significant difference between the faculty utilizations and the results in Table 5 show significant differences between the student wait times. Given that improved faculty utilization was the primary goal of the exercise, the study revealed that varying the scheduling and/or decreasing the number scheduled faculty members failed to produce any better results in the simulation. Given that the only statistically significant differences between models occurred in student wait times, a practical look at the models for feasibility is warranted. The models with less than 6 faculty members were not evaluated against the base model because the system could not complete an average throughput of 11 student teams. The Model with 8 full session faculty members displays the lowest student wait times but it is not desirable because it shows the lowest faculty utilization. The CCS staff has also determined that it is not a desirable model due to the difficulty of recruiting 8 volunteer faculty members for the full 4 hour exercise. Models 4 and 6 showed non-significantly higher faculty utilization over the baseline model, but significantly higher student wait times. The model with 4 full session faculty members and 4 faculty members in the second half session (Model 5) along with the model with 4 full session faculty members and 2 in the first half session (Model 7) showed significant decreases in student wait times without sacrificing faculty utilization.

Table 1. Details of the Baseline and Alternative Models

Model	Number of Faculty for the full session (4 hours)	Number of Faculty for the first 2 hours of the session	Number of Faculty for the second 2 hours of the session	Total Number of Faculty Required	Faculty Full Time Equivalent (FTE)	Avg. Faculty Utilization	Avg. # of Assessments per Faculty	Avg. Student Wait Time (Min)
Baseline	4	2	2	8	6	57.00%	2.75	23.78
Model 1	4	0	0	4	4	Could not finish within the 4 hour time		
Model 2	5	0	0	5	5	Could not finish within the 4 hour time		
Model 3	8	0	0	8	8	50.90%	2.75	10.23
Model 4	4	4	0	8	6	62.14%	2.75	32.91
Model 5	4	0	4	8	6	57.25%	2.75	10.23
Model 6	4	0	2	6	5	67.87%	3.66	31.25
Model 7	4	2	0	6	5	58.17%	3.14	18.42

Table 2. ANOVA for Faculty Utilization					
Faculty Utilization	**Sum of Squares**	**df**	**Mean Square**	**F**	**Signifi-cance**
Between Groups	0.113	5	0.023	2.895	0.026
Within Groups	0.303	39	0.008		
Total	0.416	44			

Table 3. ANOVA for Student Wait Time					
Student wait time	**Sum of Squares**	**df**	**Mean Square**	**F**	**Signifi-cance**
Between Groups	986.338	5	197.268	6492.247	0.000
Within Groups	0.182	6	0.03		
Total	986.521	11			

Table 4. Multiple Comparisons Test for Student Wait Time			
Baseline vs	**μ1-μ2**	**Significant (*P*<.05)**	**t**
Model 3	13.55	Yes	78.231
Model 4	-9.13	Yes	52.712
Model 5	13.55	Yes	78.231
Model 6	-7.47	Yes	43.128
Model 7	5.36	Yes	30.946

Limitations

The study was conducted based on the observation of one BPES exercise over a 3 day period in January 2013. Data collected from OSCEs in previous years were disposed of before the need for this study was recognized. More research and observations are needed to fully analyze the most efficient faculty schedule. Lack of CCS staff also made the accurate collection of travel time between exams rooms and arrival time of faculty difficult. Use of video recording in the CCS main walkways would have helped in this process. Additionally, use of time keeping on the evaluation forms would have provided additional accuracy in exercise completion times.

Because the CCS staff limits the number of student teams per four hour period, increases in student numbers and decreases in available faculty resources have caused the CCS staff to extend the BPES over additional days.

Conclusion

Based on statistical analysis, we would suggest that the CCS continue to use the baseline model. As a possible alternative, the model with 4 full session faculty and 4 faculty scheduled in the first half session (Model 5) could be suggested only to increase the faculty member utilization. The negative to not using this alternative scheduling configuration is the rise in student wait times. The original aim of the study was to increase faculty utilization and decrease student wait times. But, because of constantly decreasing faculty resources, utilization is given preference. It is extremely difficult to get the practicing/volunteer physicians to commit to participating in the BPES exam. In the last exam, the CCS staff was forced to use faculty who hadn't practiced medicine in 10 years. Because of this, CCS leadership and staff felt that efficient utilization of the faculty was a higher priority than the wait times of the students.

An important limitation of any simulation study is the fact that the modeling cannot account for the scheduling limitations imposed by the lack of staffing and faculty participation, which severely restrict the operation of this exercise. The BPES is an essential foundation for medical education and clinical practice.[4] Knowing this, the school does its best to staff the exercise with volunteer physicians from the community, where the biggest incentive is free parking. The volunteer faculty who do participate are dedicated to cultivating future doctors for this region but more resources are needed to make this exercise, the CCS and JABSOM a successful school. JABSOM is isolated to the pacific region with one state-run university and one medical school. The school produces 80% of the "Best Doctors" who practice in the state and will continue to need support from the physician community to maintain and continue to improve the quality of medical education.[12] For more information on the John A. Burns School of Medicine or becoming a volunteer faculty member, please visit http://jabsom.hawaii.edu/faculty/volunteeraffiliated-faculty/.

Conflict of Interest

None of the authors identify a conflict of interest.

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Comparing the Utility of the Non-Mydriatic Fundus Camera to the Direct Ophthalmoscope for Medical Education

Ming Chen MD; Christian Swinney BA; Mindy Chen BS; Minder Bal BS; and Austin Nakatsuka BS

Abstract

Visualization of the fundus is an important component of any ophthalmologic exam. Students are taught to visualize the fundus using a direct handheld ophthalmoscope. However, this device has many limitations, which may be a detriment to medical education and patient care. The invention of the non-mydriatic automatic fundus camera could significantly improve medical education. Our study examined the ability of a group of 5 medical students to visualize pathology and form a diagnosis with a traditional handheld ophthalmoscope and an automatic fundus camera. With the direct ophthalmoscope, none of the students were able to visualize the macula, a crucial aspect of the ophthalmologic exam. With the automatic fundus camera, all students were able to visualize the fundus. The latter modality also increased the proportion of students that was able to correctly diagnose the patients with diabetic retinopathy, 100% vs 40%. On average, students were also more confident in their ability to visualize basic retinal anatomy with the automatic fundus camera, 9.6/10 vs 6.4/10. Thus, incorporating the non-mydriatic automatic fundus camera into medical education, alongside the handheld ophthalmoscope, has the potential to improve both learning outcomes and patient care.

Keywords

Ophthalmoscope, Medical Education, Fundus, Physical Exam

Introduction

Since the invention of the ophthalmoscope by Helmholtz in 1851, it has become a standard item in the repertoire of nearly every medical student.[1] Although the device has undergone many changes over the past 150 years, the basic principles have remained the same. Using a source of illumination and a series of reflecting surfaces, the ophthalmoscope allows the clinician to observe the fundus. This can be an enormous benefit to the clinician, as it provides significant insight into a variety of conditions. Two notable examples include cardiovascular disease and diabetes, the number one and number seven cause of death in the United States, respectively.[2] While both are potentially lethal, early detection can significantly reduce complications.[3] Thus, it is vital that the aspiring clinician be able to accurately and clearly view the fundus, as a matter of patient safety.

The handheld direct ophthalmoscope has many useful features. It is a lightweight, portable, and relatively inexpensive means of carrying out the fundoscopic examination. Over the past century it has become an important diagnostic tool for teaching medical students and residents the fundoscopic exam. However, due to the inherent difficulty in viewing the elderly non-dilated eye, its usage and utility for medical education is limited.[4] Currently, many general practitioners do not even attempt to perform a fundus exam on patients with diabetic retinopathy and instead refer directly to an ophthalmologist.[4]

There are other more effective methods to view the fundus. Recent technological advances have resulted in the creation of the non-mydriatic automatic fundus camera (Table 1). This tool allows the clinician to clearly observe the fundus on an electronic screen. This enables one to zoom in on the retina, measure the vessels and lesions, share the images with patients, and document the images in the patient's file for follow up. It also reduces the many risks associated with dilation, including closed angle glaucoma, allergic reactions, and transient visual impairment. All of these benefits could translate into a more effective educational experience for medical students, as well as more effective patient care. Furthermore, a recent study from Emory suggests that students prefer the automatic fundus camera to the direct ophthalmoscope for examining the fundus.[4]

This study seeks to compare the diagnostic capability of a handheld direct ophthalmoscope to an automatic fundus camera in diagnosing retinopathy for a group of medical students. We hypothesize that the latter will be more effective. Our study expands on a similar study by having students examine patients with macular pathology, [4] instead of examining normal eyes. This will provide insight and foster discussion on the possible benefits and drawbacks of incorporating a non-mydriatic automatic fundus camera into medical education clinics, alongside a traditional handheld ophthalmoscope.

Table 1. Comparing the non-mydriatic camera and direct ophthalmoscope

Equipment	Cost	Portability	Clarity and Magnification	Training and Education	Digitally capable for electronic medical record	Comfort/ Ease of Use/ Patient Safety
AFC-230 Non-Mydriatic camera	$15000 / unlimited use	Poor	Excellent	Excellent	Yes	Excellent
Direct ophthalmoscope	$150/ person	Excellent	Poor	Poor	No	Poor

Methods

Institutional Review Board approval was obtained from the University of Hawai'i. None of the authors had any conflict of interest. A group of five medical students from the University of Hawai'i John A. Burns School of Medicine participated in the study. All students had previously received basic ophthalmoscope training during the first month of medical school. Immediately prior to the event, each student was given a short lecture handout on relevant retinal pathology, including common manifestations of diabetes mellitus type 2 and cardiovascular disease. Prior to examining the patients, the students were given a 15-minute introduction to direct ophthalmoscopy by a clinical associate professor in a private practice setting. This introduction demonstrated proper examination technique and reviewed the relevant anatomical structures of the eye. Each student then conducted a supervised fundoscopic examination on a fellow student without dilation in a dark room, to ensure that the exam was being correctly performed (Figure 1).

Each student then conducted a fundoscopic exam using a standard direct handheld ophthalmoscope (Welch Allyn Inc., Skaneateles Falls, USA) on two undilated patients with known diabetic retinopathy. These patients had clearly observable pathology and a pupil size of 3 mm, which exceeded the minimum pupil size for the automatic fundus camera. Students were given no information on the patients' conditions beforehand. Each student examined the patients with a direct handheld ophthalmoscope, recorded his or her observations, and made a hypothesis. Students then examined the same patients using the AFC-230 Non-Mydriatic Auto Fundus Camera (Nidek Inc., Fremont, USA) (Figure 2). Again, each student recorded his or her observations and made a hypothesis.

Figure 1. Student practicing ophthalmoscope technique

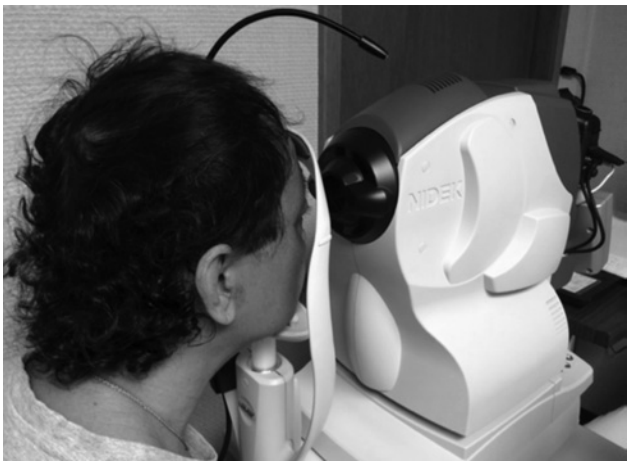

Figure 2. Patient receiving exam with non-mydriatic automatic fundus camera

Results

The ability of the students to visualize relevant anatomical structures with each of the two imaging modalities is listed in Table 2. Each of the 5 students examined 2 patients for a total of 10 responses. None of the students were able to visualize the macula with the direct ophthalmoscope in either patient. Students were able to view the remaining anatomical structures in 9 of 10 cases. All students were able to visualize all relevant anatomical structures with the automatic fundus camera.

While using the direct handheld ophthalmoscope, 40% of the students accurately diagnosed the patients with diabetic retinopathy. While using the automatic fundus camera, 100% of the students accurately diagnosed the patient with diabetic retinopathy. Students were also asked to rate their confidence in visualizing basic retinal anatomy and pathology using the two modalities after conducting the exams. On a scale of 1 to 10, with 10 being the most confident, the average student response was 6.4 (range 6-7) for the direct handheld ophthalmoscope (Figure 3). The average response for the automatic fundus camera was 9.6 (range 9-10).

Table 2. Comparison of visualization capabilities

Structure	Direct Handheld Ophthalmoscope (# of students able to visualize)	Nonmydriatic Automatic Fundus Camera (# of students able to visualize)
Macula	0/10	10/10
Vasculature	9/10	10/10
Optic Disk	9/10	10/10

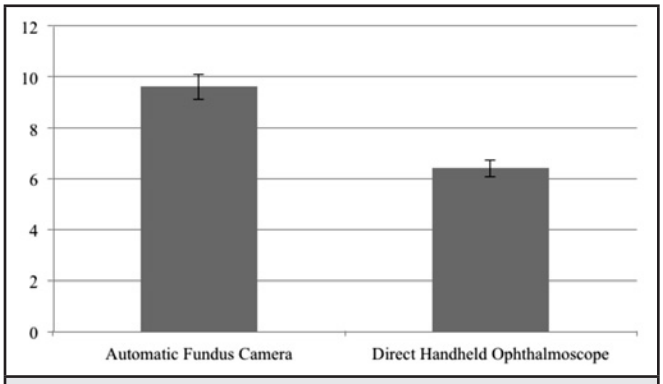

Figure 3. Mean student confidence in visualizing basic anatomical structures and pathology (0-10 scale)

Medical Student Survey

Pre-experiment Survey:
How confident are you in your ability to detect basic retinal structure with a handheld Ophthalmoscope. Please use a 1-10 scale, with 10 being the most confident and 1 being the least. 1 2 3 4 5 6 7 8 9 10

Have you ever conducted a fundoscopic examination using a non-mydriatic fundus camera? Yes No

Questions to be asked after ophthalmoscope examination AND after fundus camera examination:

Can you see the following with ophthalmoscope		with image from camera?	
Macula	Yes No	Macula	Yes No
Blood Vessels	Yes No	Blood Vessels	Yes No
Optic Disk	Yes No	Optic Disk	Yes No
Any lesions	Yes No	Any lesion	Yes No
Diagnosis:		Diagnosis:	

Post-Experiment Survey:
How confident are you in your ability to detect basic retinal structure in patients with Automatic Fundus Camera. Please use a 1-10 scale, with 10 being the most confident and 1 being the least. 1 2 3 4 5 6 7 8 9 10

Discussion

The most notable discrepancy between the two imaging modalities was observed when trying to view the macula. Not a single student was able to confidently visualize the macula with the direct handheld ophthalmoscope, while all of the students were able to do so with the automatic fundus camera. This discrepancy is notable, given the numerous pathological lesions that can occur in this region of the eye. Macular pathology can be related to diabetes mellitus, as well as a variety of other conditions, such as senile macular degeneration and trauma.

Students were able to visualize the vasculature and optic disk with the handheld ophthalmoscope. However, there were multiple instances in which the crucial pathological cues, such as microaneurysms, flame shaped hemorrhages, and macular edema were missed (data not shown). Nearly all of these findings were observed by students when using the automatic fundus camera. The reason for this is evident, as the automatic fundus camera provides a stable image that can be magnified for greater clarity. Students were also significantly more confident about their diagnostic abilities when examining the patient with the automatic fundus camera. This confidence has the potential to translate into more effective patient care.

The automatic fundus camera also has many benefits from a teaching standpoint. It allows the educator to point out or confirm specific findings that may be relevant to the student's educational experience. It also allows the student and clinician to review the findings for longer periods of time or at a later time if needed. Having this new device more readily available could also reduce costs associated with diabetes mellitus type II. At this time, most diabetic patients, regardless of the extent of their disease, must be referred to an ophthalmologist at the expense of both time and money. Having automatic fundus cameras more readily available in clinics outside the ophthalmologist's office could reduce this burden.

All of these benefits suggest that the automatic fundus camera can be a useful accessory tool to help teach a proper fundoscopic examination. An ideal situation would be to use the automatic camera to take an initial picture and then let the students try to find the pathology with the handheld ophthalmoscope. This would be more effective than the current method of teaching, in which students have very little initial direction. Despite its evident utility, the automatic fundus camera is not utilized in most medical education settings. Only 40% of students in this study had ever used the device before. None of them had done so on a regular basis. One of the likely reasons for this is the cost of the device. While the device is indeed expensive, only a single device is needed at a given location. We believe that installing a single device at community health centers, outpatient clinics, and emergency rooms could provide the numerous aforementioned benefits.

Conclusion

The direct handheld ophthalmoscope is an essential part of the physical exam and an important skill for all medical students to learn. However, providing access to an automatic fundus camera, in addition to a direct ophthalmoscope, would benefit medical education and overall medical care.

Conflict of Interest

None of the authors identify a conflict of interest.

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The Evolution of the Japanese Medical Education System: A Historical Perspective

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Abstract

The Japanese Medical Education system has been influenced by political events throughout the country's history. From long periods of isolation from the western world to the effect of world wars, Japan's training system for physicians has had to adapt in many ways and will continue to change. The Japanese medical education system was recently compared to the "Galapagos Islands" for its unusual and singular evolution, in a speech by visiting professor Dr. Gordon L. Noel at the University of Tokyo International Research center.[1] Japanese medical schools are currently working to increase their students' clinical hours or else these students may not be able to train in the United States for residencies. Knowing the history of the Japanese Medical education system is paramount to understanding the current system in place today. Studying the historical foundation of this system will also provide insight on how the system must change in order to produce better clinicians. This article provides a glimpse into the medical system of another nation that may encourage needed reflection on the state of current healthcare training in the United States.

Introduction of Western Medicine to Japan

During the Edo period (1603-1867) and starting from 1633, Japan was isolated from the rest of the world.[2] Travelling abroad was forbidden and trade with the outside world was restricted by limited ties to China and the Netherlands.[2] During this time period, Japan learned about western medicine primarily from physicians at the Dutch merchants' office or from Dutch medical books. Japanese medicine otherwise consisted of eastern Chinese medical teachings that utilized crude drug preparations and herbal medications. All foreign books were banned during this time. This mandate lasted nearly a century until the year 1720. When this ban was lifted, the primary influence on literature from Europe was Dutch, as trading patterns were well established with this country even during the period of isolation. Japan realized the importance of the scientific method through exposure to both Dutch and German medicine following the Edo period. In the latter part of this period, interactions with Dutch traders and physicians occurred initially through the port of Nagasaki. The influence of Western medicine was quickly felt all throughout Japan.

During the start of the Meiji restoration of 1868, a new era (1868-1912) began in Japan's history. Trade and interactions with the western world were now encouraged and the government imported German medicine as a national policy. In 1871 they started to invite physicians from Germany to lecture at the precursor of the University of Tokyo. This event demonstrated a significant change from the isolationist policies of the previous regime. The extent of German influence on Japanese medical education can still be seen today. The six-year training system used in Japan today is actually derived from German medical education systems (Figure 1). Many words used in Japanese medical literature are Germanic in origin. For example, German medical terms like adrenalin and allergy have Japanese words similar to them like "adorenarin" and "arerugii."[3] It is interesting to see that some of these words with Germanic origin are also used in American medicine. Following the lifting of the ban on Western books, scientific books were some of the first imported into Japan. As an example of the influence of the Netherlands on Japan and area of study relating to the Dutch language was called "Rangaku," or Dutch Learning.[4] One of the earliest scientific works translated was a book titled "Ontleedkundige Tafelen," a complete work on the subject of anatomy and was translated in 1771-1774 and renamed the "Kaitai Shinsho."[4] The influences on the Japanese training system for physicians by both the Germans and Dutch remain today. During the following years of Japanese medical history western medicine was rapidly introduced into Japan. Using the scientific method Japanese medical doctors worked on treatment for tetanus and syphilis, studied the plague and dysentery bacilli, as well as the neurosyphilis spirochete.[5]

History of National Medical Examinations in Japan

In 1875, during the Meiji era, the government began to administer national examinations to license medical practitioners.[6] This requirement furthered the shift away from Eastern medicine in favor of a more Western style. With this shift, there began an attempt to standardize medical care in Japan. Surprisingly, this initial exam was available to anyone who wanted to become a doctor whether or not they had undergone any formal training. In 1906, the government mandated that applicants for the national examination must be physicians who had graduated from a medical school-mirroring the Western process of formal medical education before licensing. This licensing exam became

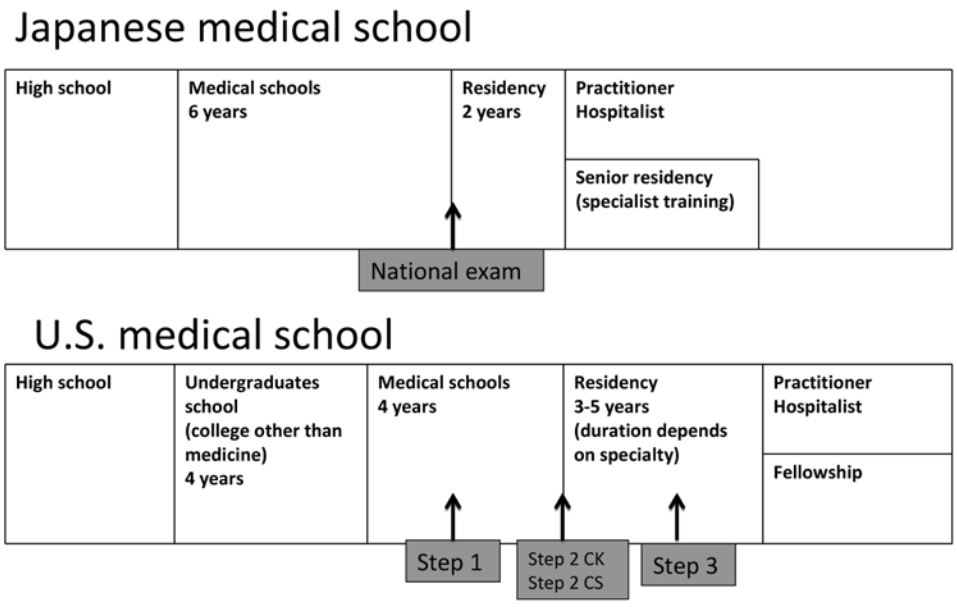

Figure 1. The Framework of Medical Schools and National Exam
Japanese medical school is 6 years, when compared to US medical school at 4 years after completion of the undergraduate work. The Japanese national exam is only one step, which is much less then the United States Medical License Exam (USMLE) which is a three step examination. In 2004 the training schedule changed and following this examination, Japanese medical graduates will do a two-year rotating residency where they get much of their hands-on training in the primary care areas, which is much later then US graduates who get this type of training during their 3rd and 4th years of medical school. Once this is completed the Japanese graduates will either go into practice or into further Specialty training. Prior to 2004 medical graduates could go right into Specialty training without any training in primary care areas like Internal Medicine, Pediatrics, OB/GYN, Surgery or Psychiatry.

the predecessor of the current national exam. During this period, the number of Japanese traditional herbal doctors dwindled as the population of modernized doctors grew.

During World War II, the necessity of advanced medical and surgical knowledge became apparent to those on the battlefield. Following this war, with the reparations of Japan directed by the United States, the dominant Western influence on an area of Japanese society was US type Medical care and training of physicians. In 1946, a medical internship system and the current national medical license examinations were introduced. As we will see below, American based resident training programs are increasing in popularity in Japan.

Early Internship Program

Despite developing this internship system to train physicians there were some significant hardships on the Japanese Interns of this era.[7] These first year residents worked long and arduous hours and were not compensated for their efforts. They were required to work volunteer for a year in order to take the national medical license examination. This system caused many young physicians substantial financial hardship. This system was highly unpopular among young trainees. During the 1960's when many student movements actively denounced the Vietnam War in the United States, a similar type of student protest moved to Japan in 1968. Medical students went on strike demanding to be fairly compensated for their work during their training programs. The students viewed the internship training as detrimental to good clinical practice. They recognized that the system in place put patient safety at risk due to an increased likelihood of mistakes by exhausted and overwhelmed interns. This patient safety issue remains an active source of debate in the training of physicians for both Japan and the United States, and has led to the mandatory 80 hour work week in American residency training programs.

Protests that began at the University of Tokyo quickly spread to other medical universities.[8] The protests led eventually to a nation-wide boycott of the national medical license examination. This movement also triggered the development of a radical group named "Zenkyoto" (All-Campus Joint Struggle Committee) that also protested the US safety treaty and the Vietnam War. The event ended when Zenkyoto forcibly occupied Yasuda Auditorium which was the symbolic center of the University of Tokyo. Eight thousand riot police were dispatched to secure the Auditorium. A violent battle transpired. Some students lost their lives, and many more were severely injured during this event. Shock and grief over these violent protests radiated across Japan. Following this event, significant changes were made to the internship program. Students could finally take the medical license examination after graduation from their medical university. The year of uncompensated internship was removed from being a part of the training requirements, and was replaced by the current system of residency training in Japan.

Current National Medical Examination: Japan and the United States

The current national medical license examination in Japan is held once annually during mid-February for three days (Figure 1). It is comprised of 500 questions covering basic medicine, clinical medicine, and social medicine. During the most recent examination (2014) the pass ratio was 90.6%.[9] This examination is held in twelve prefectures: Hokkaido, Miyagi, Tokyo, Niigata, Aichi, Ishikawa, Osaka, Hiroshima, Kagawa, Fukuoka, Kumamoto and Okinawa. The pass ratio in each university is critical to medical schools.[10] The level of government subsidies the universities receive is related to the pass ratio. National financial subsidies to the universities are cut if the pass ratio does not meet 70%. Some private medical universities require students to repeat a year if they are expected to fail the national medical license examination. These universities may benefit financially from the extra tuition fees from these students, however, this may add additional stress to the struggling student as they are forced to finance an additional year of schooling. This pressure to pass the examination provides further incentive for the students to study more diligently through their medical school years. Once the medical students pass this examination they can obtain a medical license to practice.

This exam and the students training do not include clinical skills evaluation like Objective Structured Clinical Examinations (OSCE), which is a part of medical training in the United States. For much of Japanese student's medical school training they are simply observing rather then conducting hands on training as medical students in the United States. This point is of concern to the Educational Commission for Foreign Medical Graduates (ECFMG) in the United States. Changes are being implemented in the requirements for Japanese medical students to apply to US residencies such as having more clinical exposure and testing in Japan.

The History of the *Ikyoku* System

Once the internship system was abolished, the government recommended but did not require a two-year clinical training program. These apprentice style programs do not have a standardized curriculum nationally as the content of medical education is based on the individual university or department. Most of the Japanese medical graduates went into a training program named *Ikyoku* after graduation from their own or other universities.[11,12] *Ikyoku* translates to: "medicine – office/department." American medical universities develop contracts with teaching hospitals and send medical students and residents to both learn and service the patients in those hospitals. In comparison, every Japanese medical university has its own university hospital and has the *Ikyoku* physician group serving its patients. *Ikyoku* is symbolic of the Japanese university hospital. Grasping the idea of *Ikyoku* is extremely important in understanding the Japanese medical post-graduate training system. Three primary goals of the Iyoku groups are: education, research, and patient care. The *Ikyoku* system originated in Germany.[13] It was introduced in Japan following the Meiji restoration. Many *Ikyoku* based medical departments viewed this period as the start of the modern medical system, and will thus have self-proclaimed names like the "first department of internal medicine," or the "second department of surgery." However, this can lead to more than one department with the same proclamation making this a bit of an artificial and sometimes redundant description of their department if compared to other hospitals across the country.

In the *Ikyoku* system, the professor is at the top of the hierarchal totem pole, and the professor will not only make the tough clinical decisions for patients but will also make many personal decisions for the trainees. Professors decide where the trainees can practice and live. In contrast, the American medical system allows its residents to make these types of career decisions in an autonomous fashion. The assistant professors, lecturers, and young trainees follow the professor down the hierarchical totem pole. The professor has enormous influence, and decides where to place personnel in the medical community which is sometimes based on political contracts with other hospitals and clinics, and not a choice of the individual trainee. Medical students and residents in the United States are accustomed to choosing where they want to live and practice within the country. In the *Ikyoku* system, the medical resident's autonomy is limited. The professor will make the decision for the trainee that will affect job placement not only in the university system, but also in any affiliated hospital. These decisions may affect the entirety of the trainees' career. The professor decides where the trainees will find a job, where they will work, and what populations they will treat. The Japanese best-selling book *White Big Tower* is based on an *Ikyoku* group in Osaka University.[14] It is about a fictional surgeon Dr. Goro Zaizen who becomes a professor of surgery by ruthlessly gaining power within an Osaka *Ikyoku* group. Meanwhile, a classmate of Dr. Zaizen's, who was more interested in caring for his patients, does not reach a similar level of prominence. *White Big Tower* was written more than forty years ago. The contents still remains relevant to understanding the Japanese medical system today. Both a novel and later a television series based on *White Big Tower* became acclaimed critically in both Japan and South Korea.

In Japan, the *Ikyoku* group at times will send doctors to affiliated hospitals based on political reasons rather than their individual skills. Under universal health insurance coverage, patients pay a specified amount for their care. This fee is not based on the doctor's skill or experience level. Even being board-certified does not increase the compensation for a physician's care. Physicians are instead often paid based on how many years of clinical experience they had following their graduation from medical universities. Unlike the American system, pay scales between specialties are not appreciably different. Some hospitals prefer to hire young staff rather than experienced doctors in an attempt to cut costs. The *Ikyoku* group determines the placement of young doctors based on hospital demands. These decisions are based on political and financial issues rather then on the training level of the clinicians. Young inexperienced doctors ordered by the *Ikyoku* system, may be sent to rural or small local clinics or hospitals where they may not get the exposure or training

they need. Physicians that would benefit from learning at large urban institutions are denied this opportunity and are instead placed in smaller clinics. This is often called "exile," within trainee circles, and this may happen to a resident especially if they do not get along with certain professors. This differs from the American concept of some well-trained doctors choosing to go to a remote area to service a rural community once they acquire knowledge and experience after completing residency in a larger urban center. Increasing numbers of medical students are choosing to bypass the *Ikyoku* system of training and train in medical systems that are similar to those in the United States (Figure 2).

The Rise of Non-University Hospital Training (Non-*Ikyoku*)

Besides the *Ikyoku* residency training system, there are a number of non-university hospitals that are offering medical students in Japan a training program similar to that offered in the United States. These non-university hospitals include Okinawa Chubu Hospital, Tokusyukai Hospital group, St. Luke Hospital, and Kameda Medical Center, which have long histories of offering US type residency programs. The John A. Burns school of Medicine in Hawai'i has a long relationship with Okinawa Chubu Hospital.[15] Visiting Professors and students from select medical schools have traveled reciprocally each way to enhance the training programs in both countries. This option of training in a residency program similar to a US residency initially attracted a minority of the medical school graduates. Subsequently, this type of residency is growing in popularity and is providing an opportunity for Japanese medical school graduates seeking to train in the American system.

The *Ikyoku* system presence has diminished since 2004 when the new residency system was established. Recently, the number of doctors who choose non-University/non-*Ikyoku* training programs has been increasing see Figure 2. Over half of medical school graduates chose non-university hospitals in part to become exposed to increased clinical exposure, evidence based medicine, and education.

The Need for Medical Education in Japan to Require More Clinical Experience

A major change in the amount of clinical exposure is going to be required in Japanese medical schools by the year 2023. With close to 25% of all practicing physicians in the United States being comprised of international medical graduates (IMG), the Educational Commission for Foreign Medical Graduates (ECFMG) announced that IMGs applying for ECFMG certification will be required to have graduated from a medical school that has been accredited through a formal process similar to those used by the Liaison Committee on Medical Education (LCME).[16] Other accepted criteria like The World Federation for Medical Education (WFME) standards will also be recognized. This announcement has a huge impact on Japanese medical education, as currently they will need to increase significantly the number of clinical rotation hours. New guidelines stipulate that students must train at a minimum of 72 weeks of clinical rotations. The average number of clinical rotation hours in Japanese medical universities is now at only 50 weeks.[17] Japanese graduates will not be allowed to participate in US training programs in the future if this lack of clinical hours continues. The first graduates who are expected to graduate in 2023 will enter medical universities in 2017, which is very close at hand. Many of these

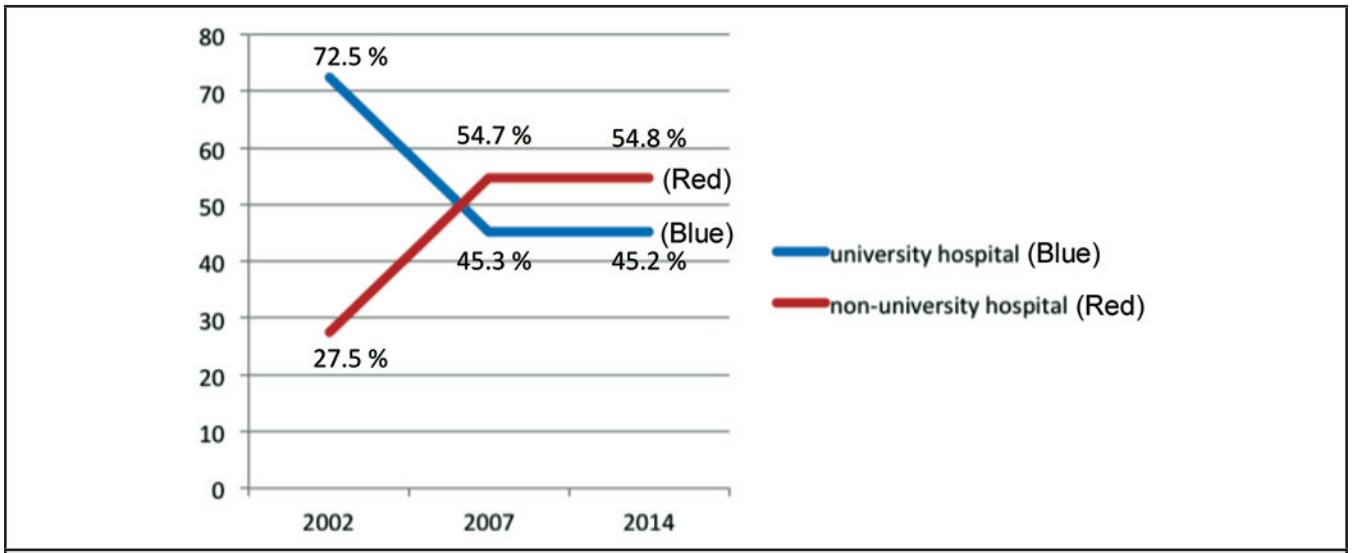

Figure 2. The Impact of Japan's 2004 Postgraduate Training for University Hospital Training (*Ikyoku*)
The blue line is the percentage of the graduates choosing the traditional university hospital (*Ikyoku*) training system compared to the red line which are those choosing the non-university hospital training (non-*Ikyoku*) system. There have been an increasing percentage of Japanese medical students choosing non-University/non-*Ikyoku* post graduate programs which are patterned after US residencies since 2004.

schools are scrambling to meet the ECFMG criteria. If these requirements are not met, Japanese Medical school graduates will lose their opportunities to train in US residency training programs following 2023.

Conclusion

Historical context is crucial in understanding the development of any health care training system. The Japanese medical system is a product of both historical and societal changes that have occurred over the last two centuries. From the isolationist governmental philosophy of the Edo period with crude herbal preparations to the present day modern hospitals with foundations in science and technology demonstrate the enormous changes in the practice of medicine in Japan. The national license examination has gone through an evolutionary process and now provides some standardization of medical training and knowledge. However, an emphasis on primary care and on introducing clinical medicine teaching earlier to trainees will be required in the next few years if Japan's physicians are to remain competitive in the global market. The Japanese Medical Education system must fundamentally change some of its educational curriculum and standardize aspects of its post-graduate training in order to better serve its population in an effective and efficient manner.

Conflict of Interest

None of the authors identify a conflict of interest.

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Healthy Mothers Healthy Babies: Awareness and Perceptions of Existing Breastfeeding and Postpartum Depression Support among Parents and Perinatal Health Care Providers in Hawai'i

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Abstract

Healthy Mothers, Healthy Babies Coalition of Hawai'i (HMHB) is a local non-profit organization dedicated to eliminating health disparities and improving Hawai'i's maternal, child, and family health though collaborative efforts in public education, advocacy, and partner development. A review of HMHB services revealed overwhelming requests for both breastfeeding and postpartum depression (PPD) support. The purpose of this article is to present the findings of two surveys that highlight the awareness of existing breastfeeding and PPD resources based on both parents and health care providers; perceptions of where and how care is accessed; and whether mothers throughout Hawai'i have equitable access to support. Results helped assess gaps in resources and determine barriers to care, as well as provide suggestions for new services or resources.

Web-based surveys were sent to 450 providers and 2,955 parents with response rates of 8.9% and 4.0%, respectively. Less than half of parent participants reported that their health provider discussed PPD with them. Participants identified a number of barriers to increasing access and utilization of PPD support resources, including: not feeling like symptoms were server enough, feeling embarrassed to seek help, not knowing where to find support/information, and not able to afford or insurance wouldn't cover PPD support. Only 40% of providers reported screening for PPD and 33% felt they had not received adequate training. Barriers identified by providers were a lack of trained providers, lack of PPD specific support groups, cultural stigma, and lack of PPD awareness among providers.

Of the women who did not exclusively breastfeed for the full six-month recommendation, the most common breastfeeding concerns included: perceptions of low milk supply; lack of lactation support; medical reasons; and pain. Providers described an environment of uneven distribution of resources, general lack of awareness of available resources, along with a widespread lack of support for breastfeeding efforts.

Recommendations for future efforts include comprehensive breastfeeding and PPD training for health care providers enhanced support groups, and improving awareness and access to information and support resources.

Background

Founded in 1992, Healthy Mothers Healthy Babies Coalition of Hawai'i (HMHB; http://www.hmhb-hawaii.org) is a local non-profit organization dedicated to eliminating health disparities and improving Hawai'i's maternal, child, and family health. HMHB offers services statewide, with a focus on increasing access to resources and information among low-income communities.

HMHB operates a free and confidential *MothersCare* phone line in addition to a detailed website to help clients access preconception, prenatal and postpartum resources, referrals, and information. HMHB staff manages client resources, including comprehensive directories of health information, in addition to providing sensitive, caring, and personal support. The information helps link pregnant women and families to resources including health care providers, health insurance, family planning services, prenatal educational classes, substance use/abuse intervention services, domestic violence support services, mental health providers, breastfeeding supports, and oral health providers.

HMHB also operates a mobile health messaging service, *Text-4baby*. This service provides timely, evidence-based information to subscribers every week on topics related to pregnancy and the baby's first year, and refers recipients to local resources, such as health insurance, WIC, breastfeeding support, and immunization information. This service has been demonstrated to increase consumer health knowledge, facilitate interaction with health providers, improve adherence to appointments and immunizations, and strengthen access to health services.[1,2]

Hawai'i Cribs for Kids is a comprehensive family-oriented safe sleep education program offered by HMHB to high-risk, low-income families. Education is culturally tailored, utilizing American Academy of Pediatrics (AAP) safe sleep guidelines, in addition to providing a crib for parents to take home. The program is currently available on O'ahu, with immediate plans to implement on Maui and future plans to expand throughout neighboring islands.

Further, HMHB accomplishes the following: coordination and planning of trainings for perinatal support service providers and collaborative meetings with community partners and stakeholders; development and dissemination of educational and informational material to target audiences; and advocacy efforts at the state and federal level. To appropriately reach the target population, HMHB also utilizes various social media outlets to provide information, outreach, news and updates.

The continuous monitoring and review of social media, calls to the *MothersCare* phone line and HMHB website visits revealed overwhelming requests for postpartum support information and resources with breastfeeding and postpartum depression as important recent topics. Periodically, HMHB conducts surveys to gather more information in order to improve planning efforts. This article summarizes some information from a recent set of surveys to highlight an example of some of the work that HMHB does with both individuals in the community and providers.

Postpartum Health

Postpartum depression (PPD) and breastfeeding support are each critical to influencing health outcomes. PPD is a serious mental health condition affecting an estimated 10–20% of women within six months of giving birth.[3] PPD can interfere with a woman's ability to function. Women with PPD are less likely to interact with their infants or to breastfeed. Untreated PPD can impact the long-term developmental health and well-being of a child.[4] According to data from the Hawai'i Pregnancy Risk Assessment Monitoring System (PRAMS), about 1 in 7 women (14.5%) with a recent live birth reported Self-Reported Postpartum Depressive Symptoms (SRPDS), and an additional third had possible SRPDS.[3] All Asian and Pacific Islander groups have a higher odds of experiencing SRPDS than white women. For Asian and Pacific Islander groups, the adjusted odds ratios ranged from 1.7 to 3.3.[3]

Breast milk is the most complete form of nutrition for infants and one of the most effective preventive health measures.[5] Also cost-effective, breastfeeding reduces the risk for developing various chronic conditions compared to formula. According to the Centers for Disease Control and Prevention's (CDC) 2014 Breastfeeding Report Card, of the infants born in 2011 in the United States, 79.2% were ever breastfed, 49.4% were still breastfeeding at six months (18.8% receiving exclusively breast milk), and 26.7% were still breastfeeding at 12 months.[6]

In Hawai'i, 89.5% of mothers initiated breastfeeding, 61.5% were still breastfeeding at six months, and 36.5% were still breastfeeding at 12 months among infants born in 2011.[6] According to a recent study, "In Hawai'i, breastfeeding rates are higher than national averages except in Native Hawaiian and other Pacific Islander populations."[7] Further, Hawai'i PRAMS data indicates that, "women who initiated breastfeeding but did so for less than eight weeks were more likely to be Black, Hawaiian, Samoan, Filipino, …[have] a high school or lower education, … [and be] Medicaid/QUEST insured."[8] It is important to highlight the discrepant low rates among Asian, Black, and Native Hawaiian or Other Pacific Islander subgroups with each 20-40% less likely to breastfeed exclusively compared to white mothers.[9]

Efforts to improve access to information, resources, and services are critical to improving statewide maternal and child health outcomes. Two surveys were used to determine the awareness and utilization of existing local resources and support among both parents and perinatal health care providers in Hawai'i. The study asked participants to identify and assess existing resources and trainings, and suggest strategies for addressing services gaps. Results are currently being used to assist in improving postpartum support programs, with the potential to improve the quality of support for Hawai'i residents, particularly among populations considered most at-risk.

Methods

In 2014, data was collected via two anonymous web-based surveys for two distinct audiences throughout the Hawaiian Islands: (1) parents who may have used or needed breastfeeding or PPD support resources and (2) perinatal health care providers, health educators, and home visitors. Provider contacts consisted of perinatal providers at health centers, government agencies, and nonprofit organizations with long-established relationships with HMHB.

Participants were drawn from HMHB's social media accounts, and contact databases of parents and providers for a total 3,405 potential participants (2,955 parents and 450 providers). Potential participants were sent an email with a link to the survey and a reminder email was also sent. Parent contacts had an existing relationship with HMHB, having received services, connected at parent support events, and/or volunteered with the organization. Both surveys included a combination of qualitative and quantitative questions. Basic demographics were collected in both the parent and provider survey. For the parental survey questions about postpartum depression and breastfeeding included experience, awareness of resources, perceived challenges, and recommendations to improve access to resources. Similar categories were also included in the provider survey, but also included questions about clients served and experience of working with women on postpartum depression and breastfeeding.

Analysis of quantitative responses was conducted utilizing SurveyMonkey® (Palo Alto, CA, www.surveymonkey.com) analysis feature and qualitative responses were coded and quantified by HMHB researchers.

Results

Demographics

A total of 112 parent participants completed the survey (4.0% response rate), with the majority at 84% living on O'ahu (Table 1). All parents reported speaking English at home with 26% also speaking other languages in the home (Hawaiian, Spanish, Japanese, Chinese, Ilocano, Korean, Portuguese, Tagalog, Vietnamese, Chamorro, Thai, and Tokelauan). The majority of participants were White (61%), followed by Chinese (24%), Japanese (18%), Hawaiian (17%), Filipino (15%), Hispanic (9%), or Other Asian (6%), with participants able to select multiple races. All participants had a high school diploma or higher, with just under half the respondents (47%) having a college degree and 29% having a postgraduate degree. Income levels varied widely, but 58% were of middle-upper SES (incomes above $50,000), 36% were of low SES (incomes <$50,000), and 7% declined to report their income. The age of participants also varied, with 10% between 18-25 years of age, more than half (54%) between 26-35 years of age, and 37% over the age of 35.

Table 1. Characteristics of Parental Respondents		
	Frequency of Responses	**% of Respondents (N=112)**
County of Residence		
Hawai'i	9	8%
Honolulu	94	84%
Kaua'i	3	3%
Maui	6	5%
Language Spoken at Home*		
English	112	100%
Hawaiian	6	5%
Spanish	5	4%
Other (Japanese, Chinese, Ilocano, Korean, Portuguese, Tagalog, Vietnamese, Chamorro, Thai, Tokelauan)	18	16%
Race/Ethnicity*		
White	68	61%
Chinese	27	24%
Japanese	20	18%
Hawaiian	19	17%
Filipino	17	15%
Hispanic	10	9%
Other Asian	7	6%
Black	6	5%
Korean	6	5%
Other Pacific Islander	8	7%
Other	6	5%
Education		
I didn't finish high school	0	0
High school diploma or GED	5	4%
Some college	21	19%
College degree	53	47%
Postgraduate degree	32	29%
Preferred not to answer	1	1%
Income		
Low SES	40	36%
Middle-Upper SES	64	58%
Preferred not to answer	8	7%
Ages		
18–25 years	11	10%
26–35 years	60	54%
Over 35	41	37%

*Participants were able to choose more than one option.

Table 2. Characteristics of Provider Respondents		
	Frequency of Responses	**% of Respondents (N=40)**
Provider Types		
Registered nurse	11	28%
Nonprofit/community advocacy	6	15%
Health educator	5	13%
Home visitor	5	13%
Physician	5	13%
Other (lactation consultant, mid-wife, mental health professional, support group facilitator)	8	20%
Care Venue*		
Community health center/local medical center	19	48%
In-home	11	28%
Hospital	9	23%
Community or nonprofit organization	9	23%
Other (private practice clinic, and birth center)	4	10%
SES		
Low SES	32	80%
Middle-Upper SES	8	20%
Languages Spoken by Patients*		
English	40	100%
Chuukese	16	40%
Marshallese	15	38%
Ilocano	9	23%
Tagalog	9	23%
Samoan	8	20%
Spanish	5	13%
Other (Chinese, Japanese, Korean, Vietnamese, and Hawaiian)	8	20%
County Where Services are Provided*		
O'ahu	19	48%
Hawai'i	15	38%
Maui	8	20%
Kaua'i	5	13%

*Participants were able to choose more than one option.

A total of 409 health care providers participated in the second survey (8.9% response rate). Eleven of the respondents were registered nurse; the remaining 29 included nonprofit/community advocates, health educators, home visitors, lactation consultants, and OB/GYNs (Table 2). Provider participants provided services in a variety of settings but primarily at community health centers or an in-home setting. Providers reported working primarily with low-SES patients/clients who spoke a variety of languages other than English, including Chuukese, Marshallese, Ilocano, Tagalog, Samoan, Spanish, and others). By geography, 48% provided services on O'ahu, 38% on Hawai'i, 13% on Maui, and 13% on Kaua'i.

Postpartum Depression Support Assessment

Parent Participant Results (N=112)

Only 49% (n=54) of parents reported that their health care providers discussed PPD with them (Table 3). Of those 44% reported that they did so while still pregnant, 26% indicated that it was brought up immediately after birth while they were still in the hospital or birthing center, 15% indicated at a well-baby check up, 9% at a post-partum checkup, and 6% reported an other setting.Nearly half (45%; n=50) reported receiving PPD patient education materials, 24% reported no materials, and 29% reported not knowing or didn't answer the question. More than half (53%; n=59) reported not being aware of providers who provide PPD support on the island where they live, 16% reporting not knowing, 15% reporting yes, and 16% not answering the question.

Participants were able to select multiple reasons why women don't access PPD support resources with the four leading reasons focusing on not feeling like symptoms were severe enough (61%), feeling embarrassed/ashamed to seek help (58%), not knowing where to find support/information (46%), and couldn't afford or insurance wouldn't cover PPD support (23%). When asked about recommendations for what parents would like to see more widely available, the four leading reported postpartum screening for PPD (57%), private counseling (53%), health care provider support (52%), and support groups (48%).

Provider Participant Results (N=40)

Only 40% (n=16) of providers reported screening for PPD, 33% reported not screening, and 28% didn't answer the question (Table 4). Of those that did screen, six reported providing support and the other 10 referred out for PPD support. Approximately 33% (n=13) of providers did not feel that they received adequate training around PPD support and treatment; 38% (n=15) of providers perceived that they received adequate training, and 31% did not know or didn't answer the question. Of the 15 that perceived they had adequate training, 10 said they could use additional training. When asked about categories of PPD support resources available, over half (56%) reported not knowing or didn't answer the question. Among providers who could identify resources, the four leading categories were: private counseling (23%); community health center/local medical centers (23%); hotlines or support lines (20%); and pamphlets/factsheets (15%).

When asked about barriers to accessing PPD support resources, over one-third (38%) didn't answer the question. Of those that answered, the

Table 3. Parent Participants' Experience with Health Care Providers on PPD Discussion and Support Resources

	Frequency of Responses	% of Respondents (N=112)
Provider discussed PPD		
Yes, they discussed it	54	48%
Time frame of provider discussion (N=54)		
While I was pregnant	24	44%
Right after I gave birth	14	26%
At a well-baby check-up	8	15%
Post-partum check up	5	9%
Other	3	6%
No, they did not discuss it	34	30%
I don't know/I'm not sure	7	6%
Non-response	16	14%
Received PPD patient education materials		
Yes	50	45%
Source of PPD education materials* (N=50)		
Health care provider/OB/GYN	24	48%
Hospital	20	40%
WIC or other community health care provider	9	18%
Other	6	12%
Pediatrician	2	4%
No	27	24%
I don't know	15	13%
Non-response	18	16%
Awareness of health care providers who provide PPD support		
Yes	17	15%
No	59	53%
I don't know	18	16%
Non-response	18	16%
Reasons women don't access PPD support resources*		
Didn't feel like symptoms were severe enough	68	61%
Felt embarrassed/ashamed to seek help or support	65	58%
Didn't know where to find support or information	52	46%
Couldn't afford/insurance wouldn't cover PPD support	26	23%
There were no local resources for PPD support	18	16%
Did not have transportation to support services	16	14%
Desired resources more widely available*		
Postpartum screening for PPD	64	57%
Private counseling	59	53%
Health care provider support	58	52%
Support groups	54	48%
Hotlines (such as MothersCare Line)	41	37%
Home visitors	38	34%
Classes	36	32%
Community/nonprofit services	34	30%
Pamphlets and other fact sheets	30	27%
Culturally-appropriate information	27	24%

*Participants could choose more than one option.

four leading barriers to increasing access and utilization of PPD support resources were a lack of trained providers (40%); lack of PPD-specific support groups or resources (38%); cultural stigma (30%); and lack of PPD awareness among providers (30%). Providers also commented that support and treatment for PPD was lacking, noting outdated treatment protocols, the lack of availability of outpatient treatment, and insufficient referral pathways and screening tools. When asked about resources to help improve access to care, the four leading suggestions were: additional training for health care providers (50%); more counselors or providers specializing in PPD support (43%), support groups (43%), and hotlines (38%). Pamphlets (33%), enhanced insurance coverage for PPD support services (33%), and websites with local information (such as HMHB) (30%) were also mentioned as resources that would help improve access to PPD support and treatment.

Table 4. Provider Perspectives on PPD Services and Support

	Frequency of Responses	Percentage of Respondents (N = 40)
PPD support		
I do not screen for PPD, but can refer patients/clients to outside resources, if needed	12	30%
I screen patients/clients for PPD, but refer out for additional counseling and/or treatment	10	25%
I screen patients/clients for PPD and provide support, including counseling and treatment	6	15%
I do not screen for PPD, and do not refer patients/clients to any outside resources	1	3%
Non-response	11	28%
Perceptions on adequacy of training in PPD		
No	13	33%
Yes, but I could use additional training	10	25%
Yes	5	13%
I don't know	1	3%
Non-response	11	28%
Category of PPD support resources identified by providers*		
Private counseling	9	23%
Community health centers/local medical centers	9	23%
Hotlines or other support lines:	8	20%
Pamphlets and other fact sheets	6	15%
Support groups, online or in person	5	13%
Community, government, or nonprofit services	4	10%
Non-response	15	38%
Barriers to accessing and using PPD support resources*		
Lack of trained providers	16	40%
Lack of PPD-specific support groups or resources	15	38%
Cultural stigma	12	30%
Lack of PPD awareness among providers	12	30%
Patients/clients not interested or do not follow up on initial support	11	28%
Inefficient/inconsistent screening or lack of screening tools for PPD	11	28%
Funding for increasing support programs isn't available	9	23%
Materials or support not available in appropriate language (please explain in the box below)	9	23%
People live far away from health care services and don't have easy access to transportation	8	20%
Non-respondents	15	38%
Resources that would help improve access to care*		
Additional training for health care providers	20	50%
More counselors or providers specializing in PPD support	17	43%
Support groups	17	43%
Hotlines (such as MothersCare Line)	15	38%
Pamphlets	13	33%
Enhanced insurance coverage for PPD support services	13	33%
Websites with local information (such as Healthy Mothers Healthy Babies)	12	30%
Non-response	15	38%

*Participants could choose more than one option.

Breastfeeding Support Assessment

Parent Participant Results

Over 95% (n=106) of participants initiated breastfeeding and 73% of participants reported exclusively breastfeeding for at least six months (Table 5). Participants who breastfed exclusively for at least six months attributed their success to a variety of reasons, including: personal preference (70%); partner and family support (66%); knowing what to expect going into it (53%); available lactation support (33%); and having a relatively easy experience (33%). While rates of initiating and sustaining breastfeeding in this study were substantial, over half (54%) were concerned about milk supply, one-third (33%) were concerned child was not gaining enough weight, and 29% reported their milk didn't come in right away as the reasons for supplementing with formula among the 24 women that initiated and supplemented breastfeeding before 6 months.

About three-quarters (76%) of all parents reported that there were lactation consultants available at their birthing facility. About 38% said they were aware of health care providers who provided breastfeeding support (not including lactation consultants), 43% were not aware, and 19% reported not knowing or skipped the question. Of the 43 respondents who reported they knew a health provider who provided breastfeeding support, 33% had been told by a friend or family member, and 26% found out via the media. Almost two-thirds (65%, n=73) of all parents responding were aware of lactation consultants that provide breastfeeding support, 17% were not aware, and 18% did not known or didn't answer the question.

Only 53% (n=59) of respondents were aware of local breastfeeding classes, 2% were not aware, and 46% did not know or did not answer the question. Only27% (n=30) of parent respondents reported they were aware of pediatricians who provide breastfeeding support, 17% were not aware, and 56% did not know or did not answer the question. Less than half (44%) of respondents were aware of local breastfeeding websites, 46% were not aware, and 9% did not answer the question. Few respondents (17%) knew of any local breastfeeding support hotlines. Participants identified a range of barriers to accessing breastfeeding support resources, including the need for better marketing of existing resources (21%), stigma and lack of community support (18%), and the lack of parental education (15%). When asked about desired resources for breastfeeding support, 53% reported breastfeeding classes, 51% reported home visitors/breastfeeding peer counselors, 46% reported support groups, 40% reported places to rent or buy a breast pump or other equipment, 38% reported lactation consultants, and 38% reported community non-profit lactation services.

Table 5. Parent Participants Experience on Breastfeeding Behaviors and Selected Characteristics

	Frequency of Responses	Percentage of Respondents (N = 112)
Breastfeeding behavior		
Exclusively, for at least 6 months	82	73%
Reasons for breastfeeding success (n=82)*		
Personal preference	662	76%
My partner and family supported me	559	72%
I knew what to expect going into it	447	57%
Lactation support was available	229	35%
It was relatively easy	229	35%
As much as possible, but with some formula supplementation, for at least 6 months	13	12%
As much as possible, but with some formula supplementation, for less than 6 months	8	7%
Exclusively, for less than 6 months, then switched to formula	3	3%
Reasons for supplementing with formula (n=24)*		
I was concerned about my milk supply/not making enough milk	13	54%
My child was not gaining enough weight	8	33%
My milk didn't come in right away	7	29%
Medical reasons	4	17%
It was too painful	4	17%
I did not breastfeed my child	5	4%
Non-response	1	1%
Lactation consultant available at birthing facilities		
Yes	84	75%
No	24	21%
Non-response	4	4%

Table 5. Parent Participants Experience on Breastfeeding Behaviors and Selected Characteristics (con't)		
	Frequency of Responses	**Percentage of Respondents (N = 112)**
Aware of providers who provide breastfeeding support, not including lactation consults		
Yes	43	38%
Information source (n = 43)*		
Friend or family member	14	33%
Media (Internet, TV)	11	26%
Other health care provider	7	16%
Hospital	7	16%
Other	6	14%
No	48	43%
I don't know	17	15%
Non-response	4	4%
Aware of lactation consultants		
Yes	73	65%
No	19	26%
I don't know	14	19%
Non-response	6	8%
Aware of breastfeeding classes		
Yes	59	53%
No	2	2%
I don't know	41	37%
Non-response	10	9%
Aware that a pediatrician can provide breastfeeding support		
Yes	30	27%
No	19	17%
I don't know	52	46%
Non-response	11	10%
Aware of websites or online groups		
Yes	49	44%
No	52	46%
Non-response	10	9%
Aware of hotlines		
Yes	19	17%
No	81	72%
Non-response	12	11%
Identified barriers*		
Better marketing of existing resources needed	23	21%
Stigma, lack of community support	20	18%
Lack of education (parents)	17	15%
Desired resources*		
Breastfeeding classes	59	53%
Home visitors/breastfeeding peer counselors	57	51%
Support groups	52	46%
Places to rent or buy a breast pump or other equipment	45	40%
Lactation consultants	43	38%
Community/nonprofit lactation services	43	38%

*Participants could choose more than one option.

Provider Participant Results

Three-quarters (75%) of provider respondents reported discussing breastfeeding with their patients/clients as a routine part of the care, 15% reported only if the client asks for help, and 10% reported not routinely discussing it (Table 6). When asked to identify support resources that help clients breastfeed, 58% reported supportive patterns and/or families, 43% reported the availability of lactation support, 30% reported personal preferences, and 28% reported easy access to breast pumps and other equipment. Providers identified a variety of reasons that their patients/clients supplement with formula. Similar to responses from parents, the primary reason that patients/clients do not breastfeed is a perception of a milk supply issue (50%), followed by: infant not gaining enough weight (38%), disinterest in breastfeeding (23%); lack of workplace support (23%); and lack of partner and/or family support (20%). Although 14 providers (35%) indicated that they did not think women in Hawai'i had adequate lactation support, six providers (15%) *did* think lactation support was adequate, and half (50%) did not know or did not answer the question.

Providers identified a variety of barriers to increasing access and use of existing resources, including: mothers waiting too long to ask for help or not knowing where to access help (48%); lack of lactation support or resources (40%); lack of trained care providers (physicians, OB/GYNs, pediatricians; 38%); lack of insurance coverage for lactation support or equipment (35%); and employers being unsupportive of breastfeeding mothers (33%). Of note, 35% did not answer the question. 28% of providers reported there was equal access to breastfeeding support and the same proportion did not (28%), and nearly half (45%) reported not knowing or didn't answer the question. When asked about resources that providers desired to see more widely available, 53% of providers desired having lactation consultants to refer clients to, 50% desired home visitors with lactation training, 40% desired support groups, 35% desired culturally appropriate information, 33% desired classes, 33% desired places to rent breast pumps and other supplies, and 33% desired pamphlets and fact sheets.

Table 6. Provider Participants Breastfeeding Support Characteristics

	Frequency of Responses	Percentage of Respondents (N = 20)
Frequency of breastfeeding discussion		
It is a routine part of the care I provide	15	75%
Only if they ask for help	3	15%
I do not routinely discuss it	2	10%
	Frequency of Responses	**Percentage of Respondents (N = 40)**
Support resources that help clients breastfeed*		
Supportive partners and/or families	23	58%
Lactation support was available	17	43%
Personal preference	12	30%
Easy access to breast pumps and other equipment	11	28%
Preparation, such as classes	10	25%
Other	2	5%
Non-response	14	35%
Reasons for supplementing with formula*		
Perception of a milk supply issue	20	50%
Infant not gaining enough weight	15	38%
Disinterest in breastfeeding	9	23%
Lack of workplace support	9	23%
Lack of partner and/or family support	8	20%
Lack of lactation support services	6	15%
Medical problem with infant	5	13%
They didn't know the AAP guidelines of exclusive breastfeeding for 6 months	4	10%
Cultural stigma around breastfeeding	3	8%
Medical problem with mother	3	8%
Lack of access to breast pumps or other equipment	3	8%
Cultural barriers	3	8%
Other	7	18%
Non-response	14	35%

Table 6. Provider Participants Breastfeeding Support Characteristics (Con't)		
	Frequency of Responses	**Percentage of Respondents (N = 40)**
Adequacy of lactation support		
Not sufficient	14	35%
Sufficient	6	15%
I don't know	6	15%
Non-response	14	35%
Barriers to increasing access and use of existing resources*		
Mothers wait too long to ask for help/don't know where to access help	19	48%
Lack of lactation support or resources (IBCLCs or certified lactation educators)	16	40%
Lack of trained care providers (physicians, OB/GYNs, pediatricians)	15	38%
Insurance does not cover lactation support or equipment	14	35%
Employers are not supportive of breastfeeding mothers	13	33%
People don't have money or insurance to access breastfeeding support services	12	30%
Providers/health centers are not supportive of breastfeeding	8	20%
People live far away from health care services and don't have easy access to transportation	7	18%
Schools are not supportive of breastfeeding mothers	7	18%
Funding for increasing support programs isn't available	7	18%
Breastfeeding support is not offered/not available at time of birth	6	15%
Breastfeeding is not part of the culture	5	13%
Resources are not available in the right languages	4	10%
Non-response	14	35%
Equal access to breastfeeding support across incomes		
Yes it is equal	11	28%
No it is not equal	11	28%
I don't know	4	10%
Non-response	14	35%
Desired resources more widely available*		
Lactation consultants to refer patients/clients to	21	53%
Home visitors with lactation training	20	50%
Support groups	16	40%
Culturally-appropriate information	14	35%
Classes	13	33%
Places to rent breast pumps and other equipment	13	33%
Pamphlets and other fact sheets	13	33%
WIC clinics	10	25%
Hotlines (such as MothersCare Line)	9	23%
Community health centers/local medical centers	8	20%
Community or nonprofit services	8	20%
Resources/materials in languages other than English	8	20%
Lactation support training for health care providers	2	5%
Non-response	14	35%

*Participants could choose more than one option.

Discussion

A number of overarching themes emerged from these surveys, providing a strong foundation for future programmatic and advocacy efforts to improve PPD support and breastfeeding in Hawai'i. The lack of consistent screenings for PPD may be due to a lack of provider training, a lack of both providers' and parents' understanding of the importance of addressing symptoms, and cultural stigma and shame. While screening for PPD is crucial, it is also important to consider that screening should be done at multiple time periods and in different settings. As one respondent revealed, "I received a screening questionnaire on my first pediatrician visit one week after birth but I was still on adrenaline. The exhaustion and the emotions did not hit me until a few weeks later but I never got screened again or was ever asked about it in person by my OB/GYN or pediatrician." Finally, many new mothers may not be aware of available services, or might not even know that they have PPD and need help.

Participants also shared similar perceptions of the landscape of breastfeeding support resources in Hawai'i, including a lack of trained providers and inequitable access to services. Overwhelmingly, participants reported that traditional health care providers fell short in providing adequate, ongoing breastfeeding support which one respondent revealed: "The biggest gap is the lack of support from the medical community. Having lactation consultant or lactation counselor trained staff could be instrumental in helping mothers succeed (especially so with the pediatrician well baby checks)." Whereas, another highlighted the importance of availability and reinforcement of breastfeeding with the following: "There needs to be more support offered prenatal and after leaving the hospital. So many women have issues after leaving the hospital but don't have access to immediate help when it's needed." Several respondents noted that many populations are underserved and available resources in certain languages are scarce. This supports results from the Hawai'i PRAMS survey and other local studies.[3,7,9] Such studies stress the importance of culturally sensitive and appropriate approaches to promoting exclusive breastfeeding, emphasizing that high breastfeeding initiation rates among Asian subgroups may not necessarily lead to rates of high breastfeeding exclusivity.[9] Recommendations include enhanced breastfeeding support groups, better trained and more supportive medical staff, and access to comprehensive breastfeeding information, including advocacy and social marketing, as well as promoting work environments that provide breastfeeding support.

There are limitations to this study. The response rate was low, as only 152 parents and providers (4.5% of potential participants) submitted a complete survey. Using HMHB's database of contacts and social media followers for the parent survey population may have led to selection bias on several levels. Firstly, participants were limited to those who have Internet access. Secondly, the length of the survey may have narrowed the participant population, with parents of a higher-than-average SES completing it more easily than those with a lower SES. Thirdly, parent participants, by virtue of their interest in and affiliation with HMHB, have a higher-than-average commitment to breastfeeding, compared to the general population. Further, neighbor islands were underrepresented which increases uncertainty about the representativeness state wide, particularly related to support services and areas of need across all the islands. Results from parent respondents failed to capture the support needs and experiences of low-income mothers, yet responses provided unique perspectives on the topics. Responses were combined with those from provider participants, the majority of whom work with low-SES patients, to describe breastfeeding and PPD support environments. While many women who successfully breastfed attributed their success at least in part to lactation consultants (available at most Honolulu-based birthing facilities and hospitals), women who gave birth on other islands and even in certain locations on O'ahu were much less likely to have easy access to a lactation consultant.

Conclusion

To optimize both maternal and infant health outcomes, it is crucial that families access necessary postpartum support services in a timely fashion. Recommended cost-effective approaches include: enhanced breastfeeding training for healthcare providers; routine screenings for PPD symptoms; more educational classes for parents; improved access to, and awareness of, existing resources (including classes and support groups); and continued advocacy efforts. HMHB helps fulfill a valuable role, serving as a central agency for information and referrals (via website and social media, MothersCare phone line, and Text4baby), and anticipates continued growth to meet the identified postpartum support needs. The development of, and access to, more peer support groups for new mothers is one such tool being developed by HMHB to help fulfill the need for services and education. Outreach efforts to health providers are also currently being developed, and HMHB is actively looking for ways to collaborate with perinatal health providers to enhance awareness of resources to improve the health of mothers, children and families in Hawai'i.

Conflict of Interest

None of the authors identify a conflict of interest.

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Pilot Study for the Establishment of Biomarkers for Radiation Damage after Computed Tomography in Children

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Abstract

Computed tomography (CT) is an imaging modality that exposes patients to ionizing radiation (IR). We review and report findings from our pilot study evaluating whether blood markers are altered in 17 children undergoing medically indicated CT scans. Blood was drawn before ('pre-CT') and 1 hour after ('post-CT') CT scans. Plasma carotenoids, tocopherols, Q10, ascorbic acid (AA) and uric acid (UA) were analyzed by RP-HPLC with diode-array and electrochemical detection. Dehydroascorbic acid (DHAA) was calculated by subtraction from total AA. Total antioxidant capacity (TAC) was measured using the ORAC assay. Cytokines were quantified using a multiplex immunoassay. γ-H2AX foci were visualized using immunofluorescence. Mean pre- and post-CT changes were compared using t-tests; P-levels < .05 indicated significance. All major plasma lipid soluble antioxidant levels were lower post- vs pre-CT (P < .05) possibly from the scavenging of free radicals formed by CT-induced IR. Average AA levels increased (134%) while DHAA levels were decreased (29%) post-CT, probably due to intracellular recycling of AA from DHAA. TAC levels in lipophilic and hydrophilic extracts were unchanged, suggesting that other antioxidants may have assisted in free radical quenching, which would corroborate their lower concentrations post-CT. Cytokine levels were unchanged and dose-dependent increases in γ-H2AX foci, a measure of double strand DNA breaks, were observed (P = .046, n = 3 children). Our results suggest that CT-derived IR can influence the antioxidant system and may elicit detrimental responses on the cellular level of young children. When possible and if appropriate non-IR based techniques such as ultrasound or magnetic resonance imaging should be used.

Keywords

ionizing radiation, computed tomography, children, micronutrients, γ-H2AX, free radicals

Introduction

Computed tomography (CT) is an essential imaging modality that allows rapid, painless, and accurate imaging of most organ systems due to its high resolution and fast imaging capabilities.[1,2] CT use in the United States has risen substantially over the past few decades especially in the emergency department and is the largest medical source of ionizing radiation (IR) in the United States.[1] Between 1995 and 2008, the number of CT scans performed in the pediatric emergency department (ED) increased five-fold while the number of ED visits during the same time frame did not change.[3] The CT rise in children is primarily for diagnostic accuracy in conditions such as trauma, seizures, complicated pneumonias, and abdominal pain and is attributed largely to improved resolution and faster acquisition times, thereby eliminating the need for sedation.[2,4]

A dramatic increase in CT imaging of pediatric patients in the ED suffering from abdominal pain from 1998 to 2008 was reported recently[5] while a substantial increase in CT use from 1995 to 2003 in the evaluation of children with head trauma was noted.[6] A study evaluating children with suspected ventricular peritoneal shunt malfunction found that they received a median 2.6 head CT scans per year.[7]

Attributable lifetime cancer risk has been estimated at one fatal cancer per 1000 pediatric head CT scans[8,9] and it is estimated that 2% of all future cancers may be caused by diagnostic medical radiation with a higher risk for young children owing to their higher radiosensitivity and longer life expectancy than adults.[8]

Two recently published large epidemiological studies assessing IR and cancer risk in children and young adults exposed to medically indicated CT scans reported that a cumulative dose of 50 to 60 mGy received from CT scans could triple the risk of developing leukemia and brain cancers[10] and that cancer incidence was 24% greater in those exposed to CT scans than those not exposed.[11] In addition, some investigators have found that intellectual development may be adversely and permanently affected in children receiving IR to the head.[12] Furthermore, general (non-pediatric focused) hospitals are less likely to use pediatric-specific radiation reduction protocols and instead use techniques that are likely to result in children being exposed to adult-size radiation doses, which are significantly higher than those used for children.[13] This is of great concern in light of a recent report on imaging frequency that estimated 89.4% of pediatric CT scans performed in the ED were done at primary adult facilities.[3]

CT involves significant exposure to IR, which can elicit detrimental cellular responses such as DNA lesions, base

damage, and protein cross-links, all of which can significantly increase the risk of developing cancer.[1,14] DNA double strand breaks (DSBs), the principle DNA cytotoxic lesion, can induce the phosphorylation of the core histone variant H2AX (to γ-H2AX)[15-17] and the ensuing formation of γ-H2AX clusters (foci) that occurs at sites of DNA DSBs[18-20] with one focus indicating one DNA DSB.[15,21]

Carotenoids, tocopherols, and retinol are lipid-phase micronutrients (LPM) that function as important antioxidants to reduce oxidative stress and/or prevents oxidative damage.[22-27] Coenzyme Q10 (Q10) is a LPM that functions as an electron/proton carrier during cellular respiration.[28,29] Ubiquinol-10 (UL10) is the chemically reduced form of Q10 and has been shown to function as a free radical scavenger that protects against cellular oxidative injury and stress[29] and minimizes damage to low-density lipoproteins *in vitro* by dehydrogenation to ubiquinone-10 (UN10).[30] Thus, the UL10/UN10 and UN10/TQ10 ratios have been postulated as useful measures of oxidative damage.[31-34] Vitamin C (L-ascorbic acid) is a hydrophilic antioxidant that protects against free radical damage[35] by scavenging various reactive oxygen and nitrogen species.[36]

Cytokines are signaling molecules released by cells in response to noxious stimuli and act as intercellular mediators by binding to specific receptors.[37,38] Cytokines can be induced after radiation exposure and may have important regulatory roles during recovery after exposure (reviewed in[39,40]).

Here we review our previous results and report our new findings from a pilot study that aimed to evaluate whether the following compounds are altered in young children undergoing CT scans: plasma antioxidants (tocopherols, carotenoids, coenzyme Q10);[41] plasma redox status (UL10/UN10, ascorbic acid (AA) and dehydroascorbic acid (DHAA)/total AA); total antioxidant capacity (TAC), DNA DSBs (γ-H2AX foci);,[42] and levels of 10 pro- and/or anti-inflammatory cytokines.

Methods

Patient Recruitment. Seventeen pediatric patients (0.25-6 years old) undergoing medically indicated CT scans were enrolled in the emergency or radiology department at Kapi'olani Medical Center for Women and Children (Honolulu, Hawai'i) after receiving signed consent from their legal guardian. Blood draw times, CT scan times, and CT doses were documented. The Western Institutional Review Board, University of Hawai'i Committee on Human Services, and Columbia University Institutional Review Board approved this pilot study.

CT Parameters and Radiation History of each child expressed as dose in relative numbers were described previously (Table 1).[41,42]

Table 1. Demographics of Study Participants

Patient ID	Gender	Height (cm)	Weight (kg)	Age (m)	CT dose (mGy-cm)	Effective dose (mSv)	CT location	CT type	Contrast use	Multi-vitamin Intake	Radiation history (dose in relative numbers)*
1	M	88.2	11.9	24	372.85	2.50	Head	Axial	no	yes	0.02
2	M	84.0	9.8	14	372.85	2.50	Head	Axial	no	no	0.50
3	M	99.0	14.5	24	376.58	11.30	Abdomen	Helical	yes	no	1.02
4	M	95.0	13.9	36	147.37	4.42	Abdomen-Pelvis	Helical	yes	no	0.01
5	M	118.0	28.0	60	104.13	2.08	Abdomen-Pelvis	Helical	yes	no	0.05
6	F	96.0	14.0	36	340.89	2.28	Head	Axial	no	yes	0.02
7	M	65.0	12.0	17	310.71	2.08	Head	Axial	no	no	2.53
8	M	123.0	40.6	72	355.10	1.42	Orbitis	Axial	yes	no	2.05
9	F	118.0	20.0	60	195.30	0.78	Orbitis	Axial	yes	yes	0.00
10	F	102.0	14.7	48	426.12	2.86	Head	Axial	no	yes	4.37
11	M	105.0	15.5	48	426.12	2.86	Head	Axial	no	yes	0.02
12	M	102.0	18.6	72	525.55	2.10	Head	Axial	no	no	14.12
13	M	112.0	19.0	48	236.14	6.14	Mastoid bone	Axial	yes	no	1.00
14	F	114.0	18.7	48	106.48	1.28	Chest	Helical	yes	no	0.05
15	M	65.0	7.1	3	92.46	1.57	Neck	Helical	yes	no	0.03
16	M	92.0	12.1	21	426.12	2.86	Head	Axial	no	yes	1.01
17	M	68.0	11.2	15	340.89	2.28	Head	Axial	no	yes	0.00

*each head, chest, abdominal CT is 1.0 unit and pelvis 5.0 units, chest X-ray 0.01 units (posterio anterior) and 0.02 units (lateral), abdominal or plevic X-ray 0.35 units. from Ref: Mettler FA Radiology 2008: 248(1), 254-263; Valentin, J Ann ICRP 2007:37(1),1-79; American Nuclear Society Radiation Dose Chart available at: http://www.ans.org/pi/resources/dosechart/. Published 2012, accessed July 2, 2012. Table re-used with permission from Halm, 2014.[41]

Sample Collection and Processing. Peripheral whole blood was drawn by venipuncture into sodium heparin vacutainer® tubes (2.5 – 4.0 mL) from each child immediately before ('pre-CT') and one hour after ('post-CT') their scheduled CT exams as previously reported.[41,42]

Chemicals and reagents used were reported previously.[41,42] Randomly methylated beta-cyclodextrin (Trappsol) was purchased from Cyclodextrin Technologies Development Inc. (High Springs, FL)

Extraction and analyses of UL10, UN10, carotenoids, tocopherols, and retinol was performed using our well established HPLC assay with minor modifications [30,43] as previously described.[41]

Quantitative determination of Cytokines. Concentrations of plasma cytokines (IL-1β, IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, GM-CSF, IFN-γ and TNF-α) were assayed using an ultrasensitive multiplex immunoassay (Invitrogen, Camarillo, CA) per manufacturer's instructions with slight reductions in sample and reagent volumes to maximize sensitivity and minimize interferences. Median fluorescent intensities of each cytokine were obtained using the Luminex® 200™ dual-laser based fluorescent analyzer (Luminex Corp., Austin, TX) and quantified against a standard curve using GraphPad Prism 5 software (La Jolla, CA). Plasma and quality control samples were kept at -80°C, thawed immediately before use, and measured in duplicate on a 96-well magnetic plate.

Analysis of total and native AA and DHA. Total and native AA and DHA were analyzed using our previous published method.[44] Specifically, plasma was diluted 1:1 with 10% metaphosphoric acid (MPA) immediately after centrifugation of blood then vortexed followed by centrifugation at 2500 rpm for 20 min. For the analysis of total AA concentration, DHAA was reduced to AA by mixing 50 μL of the supernatant with 150 μL dithiothreitol solution (0.25 g/dL in 0.1M trisodium phosphate) followed by allowing the solution to stand for 30 min at 4°C before re-acidification with 25 μL 40% MPA; the solution was subsequently mixed with 20 μL internal standard (homogentisic acid), 10 mg/L). For native AA determinations, 50 μL of the supernatant was mixed with 150 μL 5% MPA, 25 μL 5% MPA and 20 μL HGA (10 mg/L). Two microliters were injected into an Ultra HPLC system (Model Accela; Thermo-Fisher, San Jose, CA) consisting of a Hypersil gold C18 column (2.1 x 100 mm, 2.1 μm;) preceded by a 2.1 μm filter (Thermo Scientific, Bellefonte, PA). The oven temperature was kept at 30°C and the auto-sampler was cooled to 10°C. Coulometric detection was performed with a Coulochem III detector and a 5100A analytical cell (ESA, Chemsford, MA) at E1 = -100 mV (5μA) and E2 = +450 mV (2μA). The mobile phases consisted of A: 0.15 M monochloroacetic acid (14.1 g/L), 2 mM Na_2-EDTA (0.76 g/L) 0.1 M NaOH (pH 3.0) and B: MeOH. Gradient elution was performed at a flow rate of 600 μL/min as follows: 0-0.9 min at 3%B; 0.9-1 min linear gradient to 90%B; 1.0-2.4 min keep at 90%B; 2.4-2.5 min linear gradient to 3%B; 2.5 min-3.5 min keep at 3%B. The DHAA concentration was calculated by subtraction of the native AA concentration from the total AA level.

Oxygen Radical Absorbance Capacity (ORAC) assay

Lipophilic ORAC Assay. Antioxidant activity was measured using the ORAC assay according to previously established protocols [45] with slight modifications. Briefly, 100 μL PBS-diluted plasma (20x) was mixed with 50 μl 100% EtOH and 150 μL hexane. The mixture was vortexed, left to sit for 2 min, then centrifuged at 2000 rpm for 5 min. The organic (hexane) layer was removed and the extraction was repeated. The hexane layers were combined, dried under N_2 flow, then reconstituted in 200 μL 7% randomly methylated beta-cyclodextrin (RMCD) solution in acetone:water; 50:50 v/v; 20 μL of this mix was further diluted with phosphate buffer. The final dilution of the lipophilic extract was 1:400.

Hydrophilic ORAC Assay. The remaining aqueous layer (from above) was mixed with 100 μL 0.5M perchloric acid then centrifuged at 2000 x g for 10 min. 20 μL of the supernatant was diluted with phosphate buffer. The final dilution of the hydrophilic extract was 1:200.

Deproteinized ORAC Assay. To 50 μL of the 20x PBS-diluted plasma (from above) was added 50 μL 0.5M perchloric acid. The mixture was centrifuged at 2000 x g for 10 min. 20 μL of the supernatant was diluted with phosphate buffer. The final dilution of the deproteinized plasma was 1:200.

ORAC reagent preparation. Trolox standard solutions were diluted in 75 mM phosphate buffer (pH 7) for the hydrophilic extracts and in 7% RMCD solution for the lipophilic extracts and prepared at concentrations ranging from 0.19 to 12.5 μM. A stock solution (stock #1) of fluorescein (FL), used as a fluorescence probe, was made by dissolving 0.0225 g in phosphate buffer; 50 μL of stock #1 was diluted in 10 mL phosphate buffer to make stock #2. 320 μL of stock #2 was diluted in 20 mL phosphate buffer for a final concentration of 14 μM (working solution). For the assays, 25 μL of sample or standard (trolox) were added to wells of a 96-well microplate and mixed with 150 μL FL working solution (substrate). The plate was incubated for 30 min at 37°C before addition of 25 μL AAPH (31.7 mM) to generate a peroxy radicals and initiate the reaction. The plate was shaken for 10 seconds and the fluorescence intensity (λ_{ex} = 488 nm and λ_{em} = 515 nm) was recorded at 1-minute intervals for 60 minutes at ambient temperature (37°C) using Gemini XPC fluorescence microplate reader (Molecular Devices, LLC Sunnyvale, CA). The final ORAC values were calculated using the trapezoid method equation: (X2-X1)*Y2+1/2(X2-X1)(Y1-Y2)+(X3-X2)*Y3+1/2(X3-X2)(Y2-Y3)+...+(X60-X59)*Y60+1/2(X60-X59)(Y60-Y59)

The area under the curve (AUC) of the fluorescence decay was calculated as follows:

$$AUC = (f0+f1+f2\ldots f60)/f0$$

The corresponding net AUC was obtained as follows:

$$\text{Net AUC} = \text{AUC}_{\text{sample}} - \text{AUC}_{\text{blank}}$$

The isolation of lymphocytes from whole blood, calculation of organ and blood doses, and subsequent γ-H2AX detection was described previously.[42]

Statistical Analysis

LPM+Q10, Redox status, ORAC, cytokines, and γ-H2AX. Data analyses were performed using SAS 9.3 statistical software (SAS Institute, Cary, NC) and/or Excel (Microsoft, Seattle, WA). Details were described previously.[41,42] The significance level was set at $P < .05$.

Results

Characteristics of the participants have been described previously[41] and are presented in Table 1. The children ranged in age from 3 months to 6 years. Twelve children received CT scans in the head region while the remaining children received CT scans of the abdomen (n = 3), neck (n = 1) or chest (n = 1) region. The CT and effective doses ranged from 92.46 to 525.55 mGy-cm, equivalent to 0.78 to 11.30 mSv, respectively.

In our previous report investigating *in vivo* changes in LPM levels,[41] we observed significant decreases in post- versus pre-CT plasma levels of numerous LPM, which were in contrast to the increases (albeit non significant) noted in post-CT plasma levels of UN10 and UL10. These changes are shown in Table 2.

Table 2. Pre- Versus Post-CT Changes in Plasma LPM Levels*

Analyte	Pre-CT	Post-CT	Post- to Pre-CT		
	mean±SD	mean±SD	mean %	r	*P*
UL10 (nM)	344±232	427±221	124%	0.55	.17
UN10 (nM)	62±49	68±53	108%	0.93	.35
TQ10 (nM)	406±258	495±254	122%	0.63	.16
UN10/TQ10 (%)	17±0	13±0	76%	0.56	.18
tr LUT (ng/mL)	65±33	63±31	96%	0.99	**.03**
tr ZEA (ng/mL)	21±10	21±10	97%	0.99	.09
Tot. tr LUT/ZEA (ng/mL)	87±42	83±40	96%	0.99	**.03**
Tot. cis LUT/ZEA (ng/mL)	44±22	44±22	99%	0.99	.46
tr AH-LUT (ng/mL)	29±15	27±14	95%	0.99	*.01*
cis AH-LUT (ng/mL)	18±10	17±9	96%	0.99	.10
αCRX (ng/mL)	18±8	17±8	95%	0.98	**.047**
tr ßCRX (ng/mL)	103±86	96±78	92%	0.99	**.02**
cis ßCRX (ng/mL)	28±20	27±19	97%	0.97	.54
Tot.LYCOP (ng/mL)	395±308	365±273	92%	0.99	**.03**
tr LYC (ng/mL)	119±89	111±83	93%	0.99	**.02**
5 cis-lyc (ng/mL)	183±158	167±138	92%	0.99	**.03**
DHLYC (ng/mL)	93±72	87±63	93%	0.99	**.06**
αCAR (ng/mL)	32±32	30±31	94%	0.99	**.04**
tr ßCAR (ng/mL)	126±73	116±68	92%	0.99	**.01**
cis ßCAR (ng/mL)	10±7	8±4	82%	0.72	.15
Tot.ßCAR (ng/mL)	136±78	124±72	92%	0.98	**.01**
Tot. CAROT (ng/mL)	890±473	831±428	93%	0.99	**.004**
δTOC (ng/mL)	519±35	506±38	97%	0.59	.12
ß+γTOC (ng/mL)	1256±533	1181±464	94%	0.97	**.04**
αTOC (ng/mL)	7675±2334	7218±2149	94%	0.97	**.01**
Tot.TOC (ng/mL)	9450±2452	8904±2217	94%	0.96	**.005**
tr RET (ng/mL)	294±88	285±93	97%	0.96	.19

*n=17 children. Table re-used with permission from Halm, 2014.[41]

Our study evaluating the effects of low dose IR from CT scans on lymphocytic γ-H2AX foci[42] (marker of DNA damage) led to observations of dose-dependent increases in γ-H2AX foci post-CT exam ($P = .046$) among the 3 young children examined (patient ID 15, 16 and 17; Table 1). CT-induced mean IR blood doses of 0.22 to 1.22 mGy led to mean pre- to post CT increases of 0.96 to 1.95 foci per cell (Figure 1) with an average doubling (102%) of foci per cell between the lowest and highest IR dose.

None of the 10 cytokines showed significant post- to pre-CT changes (Table 3). Average AA levels increased significantly (6.19±4.75 vs 8.32±5.00; $P = .003$) while DHAA levels were decreased (3.54±3.27 vs 2.47±1.86, $P = .057$) post-CT with borderline significance whereas the redox status (DHAA/total AA) was dramatically lowered (43% to 30%) post-CT ($P = .008$; Table 4). The ORAC assay showed non-significant post-CT changes in mean lipophilic (4.46±2.51 vs 4.33±2.32; $P = .73$), hydrophilic (7.73±2.63 vs 7.45±1.29; $P = .70$) and deproteinated plasma extracts (8.20±3.05 vs 9.44±2.73; $P = .23$, Table 5).

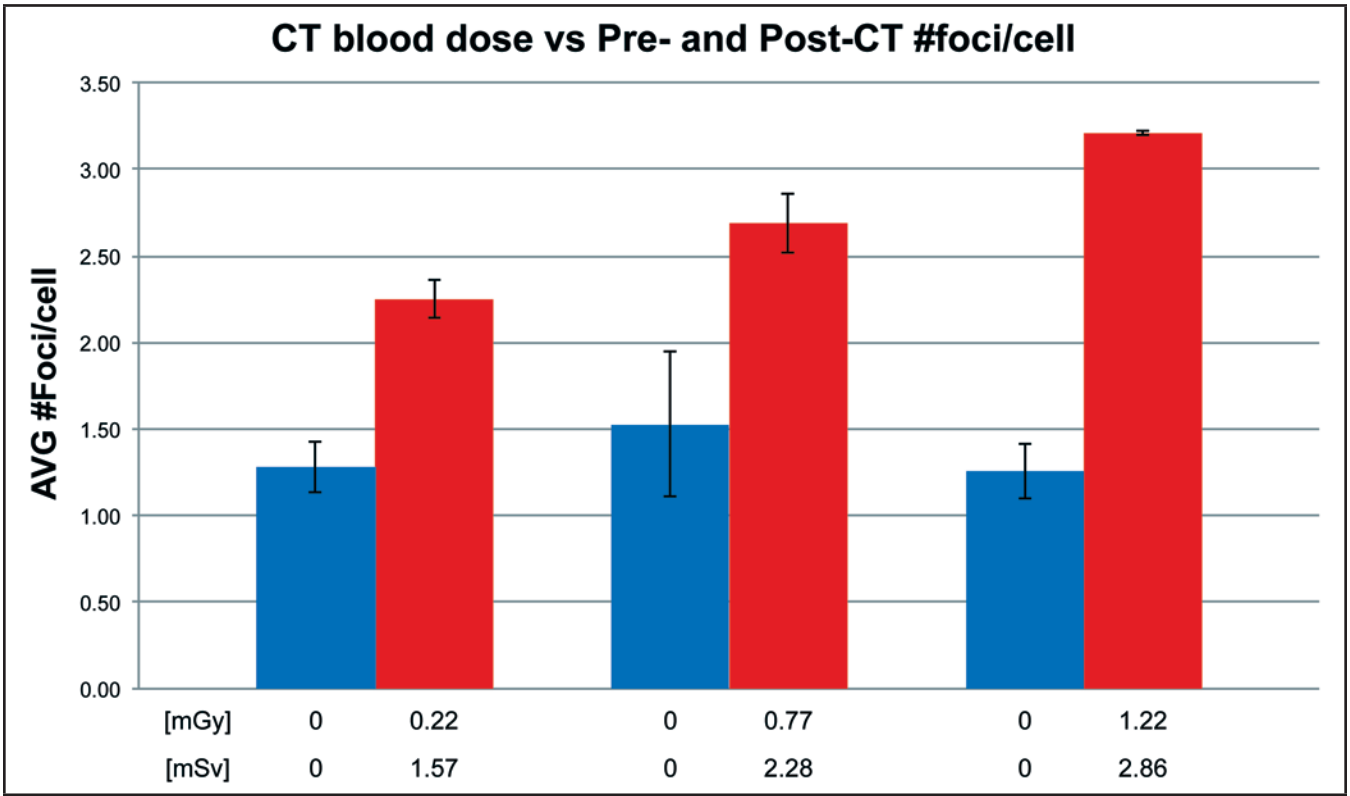

Figure 1. Post-CT (red bars) versus pre-CT (blue bars) changes in lymphocytic γ-H2AX foci from 3 young children as a function of CT-induced IR dose (expressed in blood dose [mGy] and in effective dose [mSv]); the means of the average foci per cell are presented. Error bars represent standard deviations between means of blinded duplicate analyses. Figure re-used with permission from Halm, 2014.[42]

Table 3. Post- versus pre-CT changes in inflammatory cytokines*

Analyte	Pre-CT			Post-CT			
	range	median	mean±SD	range	median	mean±SD	*P***
GM-CSF (pg/mL)	2.11-168.1	4.88	20.68±41.12	1.43-204.46	4.71	23.46±47.12	.34
IFN-γ (pg/mL)	0.3-42.85	1.17	4.09±9.86	0.22-35.03	1.14	3.26±7.63	.21
TNF-α (pg/mL)	0.44-96.89	3.50	11.78±21.81	0.10-161.48	2.67	14.71±34.57	.51
IL-1ß (pg/mL)	0.16-2.92	0.77	1.01±0.78	0.15-4.27	0.69	0.97±0.96	.53
IL-2 (pg/mL)	0.94-56.84	4.92	9.02±12.52	1.32-63.06	4.23	9.77±15.01	.82
IL-4 (pg/mL)	1.67-76.13	6.20	13.96±19.24	1.6-114.84	6.34	15.44±25.16	.68
IL-5 (pg/mL)	1.91-5.58	2.48	2.92±1.06	1.88-6.51	2.41	2.87±1.19	.44
IL-6 (pg/mL)	0.89-69.61	4.56	10.87±15.46	1.04-69.93	4.65	11.00±15.17	.77
IL-8 (pg/mL)	5.36-150.94	16.21	25.02±32.06	3.64-53.15	12.62	16.54±12.75	.14
IL-10 (pg/mL)	3.28-100.22	10.43	20.53±28.01	2.81-117.11	10.64	20.5±27.28	.22

*N=17 children. **comparison of pre-to post-CT means using student's t-test.

Table 4. Pre- versus post-CT changes in ascorbic acid, dehydroascorbic acid and total vitamin C*							
Analyte	Pre-CT			Post-CT			
	range	median	mean±SD	range	median	mean±SD	*P***
Ascorbic acid (μg/mL)	0.63-14.14	4.30	6.19±4.75	0.71-17.35	8.63	8.32±5.00	.003
Dehydroascorbic acid (μg/mL)	0.66-15.18	3.06	3.54±3.27	0.34-8.43	2.55	2.47±1.86	.057
Total Vitamin C (μg/mL)	2.83-20.06	8.06	9.74±4.81	3.25-18.06	10.00	10.78±4.57	.033
Dehydroascorbic acid/Total Vitamin C (%)	5-92%	43%	43±27%	2-78%	28%	30±25%	.008

*N=17 children. **comparison of pre-to post-CT means using student's t-test.

Table 5. Oxygen radical absorbance capacity of lipophilic, hydrophilic and deproteinated plasma pre- and post-CT extracts*										
Analyte	Pre-CT			Post-CT			Pre-/Post-CT			
	range	median	mean±SD	range	median	mean±SD	range	median	mean±SD	*P***
lipophilic plasma extract (μM)***	1.32-9.38	3.74	4.46±2.51	0.92-8.48	3.59	4.33±2.32	49-274%	91%	113±57%	.73
hydrophilic plasma extract (μM)****	5.13-16.43	6.94	7.73±2.63	5.93-10.84	7.23	7.45±1.29	77-270%	90%	106±45%	.70
deproteinated plasma extract (μM)****	3.40-15.20	6.99	8.20±3.05	5.17-14.01	10.30	9.44±2.73	47-251%	78%	95±52%	.23

*N=17 children. **comparison of pre-to post-CT means using student's t-test. ***1:400 diluted. ****1:200 diluted.

Discussion

IR from CT scans has been well documented to elicit a wide variety of detrimental cellular responses. IR such as x-rays are able to ionize surrounding atoms and molecules[1] and, in the process, generate highly reactive free radicals. In humans, hydroxyl molecules are common targets of ionization due to the abundance of water in the body. The resultant hydroxyl radicals can damage relevant biological systems and can lead to DNA lesions, base damage, and protein cross-links all of which can lead to the induction of fatal cancers.[1,14] This damage is most pronounced in children owing to their higher radiosensitivity, higher risk of cumulative exposure, and longer life expectancy than adults.[46,47]

In this report, we reviewed and reported new findings from our pilot study that investigated whether low-dose IR from medically indicated CT scans would lead to plasma biomarker changes in young children. From our previous study[41] we observed significant decreases in all major LPM levels post-CT, which we deemed may have been due to the scavenging and degradation of free radicals, a process that would help to prevent cellular and tissue damage formed by the IR. Antioxidants such as tocopherols, carotenoids (eg, lutein, β-cryptoxanthin, zeaxanthin) and CoQ10 (eg, UL10) have been shown to remove peroxyl radicals (ROO·) or prevent the formation of hydro-peroxides from radicals such as singlet oxygen ($^1O_2$) thus interrupting the propagation of lipid peroxidation[48-50] and, in the process, becoming radicals. The resulting antioxidant radicals can be considerably stabilized via aromatic delocalization and subsequently reduced back to non-radical forms by AA or other intracellular reductants.[50]

None of the 10 cytokines analyzed showed significant pre- to post-CT changes. Although low dose IR can have anti-inflammatory effects and larger doses can possibly increase serum cytokine concentrations, it is possible that in our study either cytokine release was altered more than one hour after CT or the IR dose was too low to show any detectable effects on cytokine levels.

The parallel increase and decrease in AA and DHAA levels post-CT, respectively, (Table 4) may be due to the intracellular recycling of AA from its oxidized form (DHAA) to maintain adequate AA levels as a self-protection mechanism from irreversible decomposition or as a rebound effect through increased shredding from cellular pools into the circulation after blood levels decreased or as a result of cell death.

The non-significant changes in TAC of lipophilic, hydrophilic, and deproteinated plasma extracts in post-CT samples may indicate that the CT-induced IR did not compromise antioxidant capacity in the blood and suggests that other plasma antioxidant may have assisted in the quenching of free radicals, which would corroborate their decreased concentrations post-CT. Alternatively, the ORAC assay may not be sensitive or specific enough to detect the minimal changes in these antioxidant capacities. The employed ORAC method is an inhibition assay based on the antioxidant capacity of a sample to inhibit the thermally decomposed products of AAPH, an azo-radical initiator,[45] namely alkyl-peroxy (ROO·) radicals.[51] However, quantification of AAPH generated radicals from a previous electron paramagnetic resonance study showed that the thermal decomposition of AAPH generates alkyl-oxy (RO) rather than ROO· radicals [52] thus indicating that the employed ORAC assay may not be scavenging the specific radicals.

As reported previously,[42] the γ-H2AX foci analysis of the 3 children (Table 1) revealed a significant induction of γ-H2AX foci post-CT despite the very low IR doses used - effective doses as low as 1.57 mSv corresponding to a blood dose of 0.22 mGy. The IR doses applied in our study are much lower

than other studies measuring γ-H2AX foci after CT exams [53,54] which demonstrates the high sensitivity of the employed γ-H2AX assay and indicates the reliability of the assay to evaluate the effects of low dose IR relevant to the general population.

At present, cancer risk estimations for low dose IR are based on the linear-no-threshold (LNT) model. This hypothetical model extrapolates cancer risks from well-verified moderate to high dose IR data from exposed populations (mostly Japanese atomic bomb and Chernobyl survivors) to lower IR dose ranges on the assumption that cellular effects such as DNA damage occur in direct proportion to IR exposure at all levels. In this context, the LNT model implies that no threshold level can be considered risk-free.[55,56] Although our findings support the LNT hypothesis and imply a causal role of CT for the observed changes even at very low IR doses, these results are very preliminary and need to be confirmed with larger sample sizes.

Conclusion

The results of our pilot study suggest that low-dose IR has the ability to influence the antioxidant systems and trigger detrimental responses in young children undergoing CT scans. Many of the plasma LPM levels were decreased while dose-dependent increases in γ-H2AX foci (biomarker for DNA DSB) were observed. Children exposed to IR for diagnostic medical reasons are part of a large and growing population. When possible and appropriate CT should be replaced with non-ionizing techniques such as ultrasound or magnetic resonance imaging. Our findings need to be confirmed and expanded in future studies with larger sample sizes.

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Conflict of Interest

None of the authors identify any conflict of interest.

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Academic Pharmacy Strikes Hawai'i (Part 2)

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Abstract

In partnership with the Hawai'i Journal of Medicine & Public Health, the Daniel K. Inouye College of Pharmacy (DKICP) is pleased to provide Scripts on a regular basis. In the inaugural "Script," a brief history of the profession in Hawai'i was presented up to the founding of the DKICP, Hawai'i's only academic pharmacy program. In this second part of the inaugural article, we describe some key accomplishments to date. The mission of the College is to educate pharmacy practitioners and leaders to serve as a catalyst for innovations and discoveries in pharmaceutical sciences and practice for promoting health and well-being, and to provide community service, including quality patient care. Examples are given to support the stated goals of the mission. With 341 graduates to date, and a 96% pass rate on the national licensing board exams, the college has played a significant role in improving healthcare in Hawai'i and throughout the Pacific Region. Additionally, a PhD program with substantial research programs in both pharmacy practice and the pharmaceutical science has been launched. Considerable extramural funding has been garnered from organizations such as the National Institutes of Health and Centers for Medicare and Medicaid Services. The economic impact of the College is estimated to be over $50 million each year. With over 200 signed clinical affiliation agreements within the state as well as nationally and internationally, the DKICP has helped to ameliorate the shortage of pharmacists in the state, and has enhanced the profile and practice standard of the pharmacist's role on interprofessional health care teams.

Introduction

In the second part of this two-part article, we review the current status of the Daniel K. Inouye College of Pharmacy (DKICP), University of Hawai'i at Hilo. As noted in Part 1,[1] the *Hawai'i Journal of Medicine & Public Health* and the DKICP have established a partnership that will enable faculty and affiliates of the College to submit articles dealing with contemporary issues of pharmacy education and practice. In upcoming issues, with one of the current authors serving as column editor (CSJM), DKICP *Scripts* will highlight aspects of the profession (pharmacy residency) and our College, recent drug related therapy developments (hepatitis C) and topics of controversy (drug pricing). The column editor welcomes ideas and suggestions for future publications as well as commentary.

In that the DKICP is the first and only accredited pharmacy program in the State of Hawai'i, and the Pacific Region as a whole, a brief overview of historical aspects of the profession of pharmacy were presented in Part 1.[1] The later part of the temporal sequence presented in Part 1 led us to 2006 and the launch of the DKICP. We now describe the progress and infrastructure of the DKICP.

Mission and Vision

The mission of the DKICP is: To educate pharmacy practitioners and leaders, to serve as a catalyst for innovations and discoveries in pharmaceutical sciences and practice for promoting health and well-being, and to provide community service, including quality patient care.

DKICP was founded in a manner designed to meet all of the standards for full professional accreditation. In terms of vision, the College strives for pre-eminence in two domains: (a) to be recognized among the top 25 Pharmacy programs in the world, and (b) to provide evidence of scholarship via funded research programs and innovative pharmaceutical care programs to serve individuals, families and communities. This is consistent with the Institute of Medicine (IOM) vision for academic health sciences in promoting health of people through translational research, educational reforms and practice innovations in patient care.[2]

Creation and Structure of the Daniel K. Inouye College of Pharmacy, University of Hawai'i Hilo

After many years of discussion and planning, it was decided, with the support of the late Senator Daniel K. Inouye, that a college of pharmacy would be based at UH Hilo. The Senator shared a vision of establishing centers of excellence on each of the Hawaiian Islands. As became abundantly clear after the demise of a private endeavor,[1] it is absolutely essential to obtain pre-candidate status from the Accreditation Council of Pharmacy Education (ACPE) prior to admitting any students to a pharmacy program.[3] One of the first requisite steps in submitting an application for pre-candidate status is the recruitment of a dean to serve the program, and the qualifications of the dean must meet or exceed the applicable standards established by the ACPE.[3]

In 2005, UH Hilo conducted a search, and one of the authors of this manuscript (JMP) accepted the position of founding dean in the summer of 2006, with, the objective being to accept the first class of student pharmacists and initiate the course of instruction by August of 2007.

Starting a program within a year was no small task but through a coordinated effort involving intense focus and cooperation, and the leap of faith demonstrated by the inaugural class of students who did not know their status until June of 2007, the program was off to a start in August 2007. Pre-candidate status was granted during the executive board meeting of the ACPE in June 2007.

The first five years of the program have been previously described in some detail and will not be reproduced here.[4] However, a few notable milestones follow.

- 2006 – J.M. Pezzuto leaves the position of Dean of Pharmacy, Nursing and Health Sciences at Purdue University and accepts the position of Founding Dean of DKICP

- 2006-2007 – Following ACPE designation of pre-candidate status, and a successful change of status application reviewed by the Western Association of Schools and Colleges (WASC), the first class of student pharmacists enroll and begin classes; design and construction of temporary facilities for the College begins

- 2007-2008 – College is awarded candidate status by the ACPE, accreditation is affirmed by WASC, and faculty and staff grow to about 40

- 2009-2010 – Expansion of college faculty to O'ahu and Maui hospital sites for experiential rotations, ACPE affirms candidate status, $5.5 million is approved by the State Legislature and released by Governor Linda Lingle for planning and design of a permanent building, and modular facilities are occupied

- 2010 – Expansion of the modular facilities to enable full conduct of the didactic portion of the curriculum at one site (facilitated by a $1 million gift from the J.M. Long Foundation), ACPE approves continuation of candidate status, launch of Center for Rural Health, and first DKICP residency program begins in Maui

- 2011 – Inaugural class graduates with PharmD, full accreditation is granted by ACPE, alumni association is created, programs are launched to offer the PhD in Pharmaceutical Sciences and the MS in Clinical Psychopharmacology, and accredited continuing education programs continue

- 2012-2013 – The UH Board of Regents approves naming the College the Daniel K. Inouye College of Pharmacy

- 2013-2014 – ACPE finds the College out of compliance for the standard dealing with physical facilities; in the final days of the Legislative session, funding is approved to construct a permanent building for the College; funds for construction are released by Governor Neil Abercrombie; a groundbreaking and blessing ceremony for the permanent DKICP building is held at the construction site on December 12, 2014

- 2015 – ACPE finds the DKICP in compliance with all 30 accreditation standards and continues Full Accreditation status

The Dilemma and Resolution of Physical Facility Issues

On October 31, 2009, the University received $5.5 million for design and planning of a building. The design was completed by WCIT Architecture of Honolulu by December 2011, but funding was not made available during that legislative session (2012). During the following legislative session, plans were revised and extensive interaction occurred, but again, no funding was provided.

In anticipation of future challenges with funding, the architectural plan was scaled-down. With the revised design, the DKICP would continue to use the modular facilities, but all activities would be consolidated and conducted in close proximity. At the end of the legislative session (May 2014), the State Legislature allocated $33 million for the construction of the revised facility at a site adjacent to the pre-existing modular facilities. The cost of the building was estimated to be $29-30 million, allowing for a 10% contingency fee. The funding was approved as $28 million in General Obligation bonds (to be paid by the State) and $5 million in revenue bonds (to be paid by the DKICP). A financial plan is still under development to determine exactly how the DKICP will cover the revenue bond.

Since that time, the University of Hawai'i Office of Capital Improvements has assembled a committee to oversee the project. The time-line for completion is not clear but ranges from 24 to 48 months. In addition, the plan considered by the DKICP as minimal for the advancement of our mission was unilaterally modified by the Office of Capital Improvements to a design that would reduce construction costs to $25 million. Their opinion was that the remaining $8 million should be used for contingency, equipment and furnishings, and building management. Once it became apparent this approach was unacceptable, the architectural firm returned to the second version of the plan for construction of a building comprised approximately 40,000 square feet, which is considered adequate, assuming the existing modular facilities remain in service following some remodeling. Design and construction documents are being prepared.

Clinical Affiliation Agreements: Preceptors – the Unsung Heroes

The four-year pharmacy program culminates with awarding of the profession's terminal Doctor of Pharmacy (PharmD) degree. The curriculum involves approximately two-thirds didactic and one-third experiential coursework. During the first three years of the curriculum, Introductory Pharmacy Practice Experiences (IPPE) extends over 330 hours with exposure to the various types of pharmacy practices and the role of pharmacists in hospital, retail community, long term care and ambulatory care settings. Advanced Pharmacy Practice Experiences (APPE), held entirely in the fourth year, requires clinical training in areas of hospital, community retail, acute care medicine, and ambulatory care. Pharmacy Practice faculty and volunteer preceptors (affiliate faculty) are key to the success of the experiential program. As unsung heroes, volunteer preceptors, comprised of pharmacists, physicians, nurses, psychologists, and even respiratory thera-

pists, commit additional time over and above their usual practice and work hours in order to mentor students on rotations. These types of interprofessional affiliations help us and other professions to comply with accreditation standards outlined in other health care professional program's accreditation standards.[3,5-7] The DKICP currently has over 200 clinical affiliation agreements on a state, national and international level.

Pharmacy Practice faculty hired full time by the DKICP are placed in-residence at area hospitals (The Queens Medical Center, Pali Momi Medical Center, Wilcox Memorial Hospital, Maui Memorial, and Hilo Medical Center) and at various ambulatory care clinics (Hawai'i Island Family Medicine Clinic, Bay Clinics- Hawai'i, and John A. Burns School of Medicine (JABSOM) Clinics, including the Department of Native Hawaiian Health's Lau 'Ola Clinic, and Department of Family Medicine's Physician's Center at Mililani). Faculty duties range from coordinating student teaching activities at these various sites, maintaining progressive academic clinical practices, both didactic and experiential teaching, and scholarship.

Research, Scholarship and Graduate Education

In the seven years since the opening of the DKICP, a plethora of new schools have opened for the sole purpose of filling the pharmacist gap. Scholarly innovation and discovery defines the uniqueness of DKICP. Our department of Pharmaceutical Sciences boasts an international panel of faculty that has successfully launched research programs with a respectable amount of extramural funding.

Going hand-in-hand with research and scholarship is graduate education. Since 2011, the college has admitted about 12 graduate students working toward a PhD in Pharmaceutical Sciences. This is the first science-based PhD program ever to be launched at UH Hilo, and the only such program within the entire UH System. In addition, the College established the Masters of Science (MS) in Clinical Psychopharmacology, a program to provide additional training for PhD-trained clinical psychologists. In partnership with Tripler Army Medical Center (also a training site for PharmD students and residents), our first students have graduated and now have gained prescription authority. This is the only such program offered by a college of pharmacy in the United States.

Although pharmacists are usually not formally trained in clinical research, innovative studies are currently underway. With much of the foundation built for the PharmD curriculum, the faculty in the Department of Pharmacy Practice (DPP) can dedicate more time to scholarly activities related to patient care, medication compliance and partnerships with other health professions, and entities such as the Department of Health (DOH). DOH projects include collaboration with the Asthma Initiative to provide asthma control and Antibiotic Stewardship Program (ASP) state-wide in hospitals. ASPs are programs that are designed to ensure optimal use of antimicrobial agents so that we are using the right medications to combat infections while avoiding the excessive use that leads to the development of resistance. There is a particular focus on community and critical access hospitals.

One question that invariably arises is why the DKICP was placed in a rural setting as opposed to urban Honolulu. Most recent data that describes the desperate shortage of health care professionals in rural Hawai'i justifies the placement of our program.[8,9] One of our most innovative projects is the program Pharm2Pharm, supported by a $14.3 million grant from the Center for Medicare and Medicaid Services (CMS) (Dr. Karen Pellegrin, PI). The study is being held on all islands and focuses on pharmacist liaisons to fill the gap from hospital discharge to the patient home in terms of patient medication education and adherence. Another initiative from the DPP is work in quantifying and describing the types of medications returned to the Narcotics Enforcement Department. Continued work in this area will hopefully decrease the inventory of unused medications in the home, that may lead to decreasing the incidence of home robberies and drug misadventures.[10] Ongoing studies in the ambulatory care setting include investigating the usefulness of technology such as Fitbits and monitoring of blood sugar. Projects that help patients with color-coding medication boxes may help to improve drug adherence in non-English speaking patients.

Other examples of ongoing projects and research (Table 1) at the DKICP include:

(1) The Pezzuto lab continues with ongoing projects related to resveratrol, having produced more than 100 derivatives, some of which have demonstrated better activities and more positive controls than the original compound.[11] The emphasis of the research is on the discovery and characterization of natural product cancer chemopreventive agents. Tests are conducted with natural products procured throughout the world including Brazil, China, India, Italy, Pakistan, and Thailand.

(2) Rat lungworm disease (RLWD), caused by the nematode *Angiostrongylus cantonensis*, is considered a global, emerging, infectious disease. RLWD can be considered as one of the most serious threats to human health of diseases carried by wildlife in Hawai'i, and in many other tropical and subtropical countries around the world.[12]

(3) Design and synthesis of new antibacterial agents targeting problematic bacterial infections such as *Mycobacterium tuberculosis* and *Clostridium difficile*. In collaboration with Dr. Richard Lee at St. Jude Children's Research Hospital in Memphis, TN and Dr. Julian Hurdle at Texas A&M in College Station, TX, as well as some other colleagues, we are designing and synthesizing novel small molecule and natural product-inspired chemotherapeutic agents for subsequent antibacterial evaluation.

(4) Drug discovery research is conducted for malaria and leishmaniasis, both of which are caused by parasitic organisms with extraordinarily complex life cycles and host defense mechanisms. Researchers have also been screening natural product-derived samples for antibacterial and antifungal activity on a continuous basis.

(5) Pharm2Pharm is a pharmacist-care system designed to save more than $27.1 million in health care costs in Hawai'i that has

Table 1. Research Projects and Extramural Funding, Daniel K. Inouye College of Pharmacy, 2008 – 2014					
PI Name	**Title**	**Award Sponsor**	**Award Amount**	**Award Start Date**	**Award End Date**
Andre Bachmann	Development of neuroblastoma therapeutics by optimization of polyamine inhibitor Strategy	University of Hawai'i Foundation	$40,488	09/01/10	05/31/12
Andre Bachmann	In vivo efficacy of novel proteasome inhibitors in neuroblastoma	Hawai'i Community Foundation (HCF)	$47,372	09/01/10	11/05/12
Andre Bachmann	CA-111419-04 Polyamines	NIH	$91,243	09/01/10	06/30/12
Andre Bachmann	Optimization of pediatric neuoblastoma treatment through bimodal anti-tumor therapy	Hawai'i Community Foundation (HCF)	$40,000	05/15/14	11/14/15
Robert Borris	EPSCOR	NSF	$979,510	09/01/09	08/31/14
Leng Chee Chang	BRIDGES - potential of physalis peruviaan (poha) in the treatment of breast	UH-JABSOM Cancer Center (NIH)	$25,000	09/01/12	07/31/13
Leng Chee Chang	Evaluation of vernonia cinerea (VC) in the treatment of cancer	NIH	$40,000	07/01/14	06/30/15
Mahavir Chougule	Transdermal permeation of magnesium supplement cream formulations across skin	Ctr for Magnesium Educ & Research, LLC	$16,347	10/25/11	04/25/12
Mahavir Chougule	Targeted nanocarriers of siRNA for the treatment of asthma	HCF - Leahi Fund	$35,000	08/18/11	02/18/13
Mahavir Chougule	Receptor directed nantherapeutics	Hawai'i Community Foundation (HCF)	$50,000	03/14/13	07/13/15
Mahavir Chougule	Targeted nanocarrier based gene	Hawai'i Community Foundation (HCF)	$50,000	03/29/13	09/25/15
Mahavir Chougule	Targeted combination therapy for lung cancer	NIH	$89,291	05/01/14	04/30/15
Linda Connelly	Osteoprotegerin in breast cancer cells: role in tumor growth and metastasis	NIH	$410,100	09/01/12	08/31/15
Linda Connelly	Role of endogenous osterprotegerin expression in breast cancer metastasis	Hawai'i Community Foundation (HCF)	$50,000	05/18/11	11/18/12
Linda Connelly	OPG expression in breast cancer	Hawai'i Community Foundation (HCF)	$40,000	05/15/14	11/14/15
Edward Fisher	Instruction in clinical psychopharmacology at Tripler Army Medical Center	Defense, Dept - Army Tripler Medical Ctr	$752,192	09/30/10	09/29/13
Edward Fisher	MSCP program	Defense, Dept - Army Tripler Medical Ctr	$316,928	09/01/13	08/31/14
Lara Gomez	Rural East Hawai'i workforce development network	Bay Clinic, Inc	$120,000	09/01/10	08/31/13
Lara Gomez	Immunization clinics	State of Hawai'i - Dept of Health	$2,500	07/13/14	12/31/13
Roy Goo	Antimicrobial stewardship programs	State of Hawai'i - Dept of Health	$10,000	08/28/14	07/31/15
Daniela Guendisch	Scaffolds for novel designed multiple liglands as potential therapeutics for Alzheimer's disease	Hawai'i Community Foundation (HCF)	$45,386	05/15/14	11/14/15

Table 1. Research Projects and Extramural Funding, Daniel K. Inouye College of Pharmacy, 2008 – 2014 Con't.					
PI Name	**Title**	**Award Sponsor**	**Award Amount**	**Award Start Date**	**Award End Date**
Aaron Jacobs	Involvement of HSF1 in bleomcin-induced pulmonary fibrosis	Hawai'i Community Foundation (HCF)	$25,000	04/30/14	10/29/15
Susan Jarvi	A statewide targeted pathogen surveillance study: diversity of avipoxvirus and avian malaria in native Hawaiian forest birds	Interior, Dept - Fish & Wildlife Svc	$58,414	09/01/12	03/01/14
Susan Jarvi	Efficacy of a vaccine against angiostrongylus costaricensis to a. cantonensis in rats (rattus rattus)		$40,000	07/20/12	01/20/14
Susan Jarvi	Evaluation of a vaccine for rat lung-worm (angiostrongylus cantonesis)	Agri Dept - Animal & Plant Health Insp Svc	$33,550	09/10/12	09/09/13
Susan Jarvi	Prevalence of human rat lungworm infection in East Hawaii Island	Hawai'i Community Foundation (HCF)	$50,000	05/15/14	11/14/15
Deborah Juarez	Reducing cost-related medication nonadherence in persons with diabetes	Pacific Health Research & Educ Institute	$23,823	09/01/11	08/31/12
Deborah Juarez	Cost-effectiveness of e-cigarette	Hawai'i Community Foundation (HCF)	$30,000	06/09/14	10/29/15
Eugene Konorev	Inhibition of cardiac vascular network formulation by targeted anticancer drug sorafenib	HCF Medical Research Funds	$49,993	05/16/12	11/15/13
Dana-Lynn Koomoa-Lange	MYCN-induced calcium and magnesium signaling regulates neuroblastoma progression	NIH	$134,922	09/12/12	08/31/17
Dana-Lynn Koomoa-Lange	MYCN-induced calcium and magnesium signaling regulates neuroblastoma progression	NIH	$143,311	09/01/13	08/31/14
Dana-Lynn Koomoa-Lange	ALSF DFMO-based	Foundation	$44,404	06/16/10	12/31/12
Ingo Koomoa-Lange	Therapeutic strategies targeting MY		$100,000	07/01/14	06/30/16
Carolyn Ma	Hawaii state asthma initiative	State of Hawai'i - Dept of Health	$9,500	03/20/12	12/31/12
Kenneth Morris	UHH outreach partner proposal for the NSF-ERC-SOPS	Rutgers, State University of New Jersey	$50,000	07/01/11	06/30/12
Kenneth Morris	Development PXRD method/device		$101,975	07/01/08	06/30/14
Kenneth Morris	Materials and dosage form characterization	Glaxosmith Kline	$78,688	07/01/12	06/30/13
Kenneth Morris	UHH outreach partner proposal for the NSF-ERC-SOPS	Rutgers, State University of New Jersey	$80,000	07/01/11	06/30/13
Kenneth Morris	YR3 EEC-0540855-CSOC	NSF	$30,000	07/01/13	06/30/14
Karen Pellegrin	"Pharm2Pharm" service innovation in rural Hawai'i	Health & Human Svc - Ctr for Medicare & Medicaid	$14,346,043	07/01/12	06/30/15
Karen Pellegrin	90BC0012/01 HI CTY Beacon Commconst	NIH	$14,522,189	04/01/10	05/31/13
John Pezzuto	Clniical pharmacy traning program FY 2011	Education - Dept (Federal)	$1,500,000	09/01/10	08/31/12

Table 1. Research Projects and Extramural Funding, Daniel K. Inouye College of Pharmacy, 2008 – 2014 Con't.					
PI Name	**Title**	**Award Sponsor**	**Award Amount**	**Award Start Date**	**Award End Date**
John Pezzuto	INBRE	NIH	$3,244,858	06/01/10	05/31/13
John Pezzuto	INBRE	NIH	$964,609	08/01/13	04/30/14
John Pezzuto	INBRE	NIH	$884,033	05/01/14	04/30/15
John Pezzuto	INBRE	NIH	$30,400	05/01/14	04/30/15
Dianqing Sun	Development of novel natural product-inspired antibacterial agents for treating pulmony tuberculosis	Hawai'i Community Foundation (HCF)	$50,000	08/16/12	08/15/14
Dianqing Sun	Development nof piperidinois and engelhardiones as novel antituberculosis agents	NIH	$406,257	09/01/11	08/31/15
Anthony Wright	CA-143727-03 Areca nut chemistry	UH-JABSOM Cancer Center (NIH)	$45,795	09/01/11	08/31/12
Anthony Wright	CA-143727-03 Pre-pilot project	UH-JABSOM Cancer Center (NIH)	$37,312	09/01/11	08/31/12
Anthony Wright	CA-143727-04 Guam 54 pilot project III	UH-JABSOM Cancer Center (NIH)	$29,391	09/01/12	08/31/13
Anthony Wright	CA-143727-04 Guam 54 pre-pilot project I	UH-JABSOM Cancer Center (NIH)	$24,606	09/01/12	08/31/13
Anthony Wright	CA-143727-05 Guam 54 pilot project V	UH-JABSOM Cancer Center (NIH)	$43,744	09/01/13	08/31/15
Overall - Total			**$40,464,174**		

received a $14.3 million award from the federal government. The project strives to reduce medication-related hospitalizations and emergency room visits by establishing teamwork between hospital and community pharmacists.

(6) A career development award from the National Cancer Institute (NCI) has been awarded to a professor of Native Hawaiian descent (Dr. Dana-Lynn Koomoa-Lange). This is a first within the entire UH system. Her work concentrates on finding an effective treatment strategy for advanced stage neuroblastoma (NB), an extra-cranial pediatric cancer.

(7) Development of novel natural product-inspired antitubercular agents for treating pulmonary tuberculosis. By employing approaches guided by high-throughput screening methods and inspired by natural products, researchers aim to develop small molecule piperidinol- and natural product engelhardione-based analogues as novel antituberculosis drugs.[13]

(8) Collaboration with Rutgers University on structured organic particulate systems as part of the National Science Foundation's Engineering Research Center (NSF-ERC). Researchers use materials science and engineering principles that cover a broad spectrum of uses, from basic elementary education and applications in pharmaceutical manufacturing facilities to actually producing the end product.

(9) Investigating the links between inflammation and cancer and the regulation of osteoprotegerin (OPG) expression and its role in primary tumor growth and spread (metastasis) of breast cancer. Since many patients do not respond or become resistant to current targeted therapies, identification of new therapeutic targets such as OPG will increase treatment options and improve prognosis for breast cancer patients.[14]

(10) Finding newer effective and safer therapeutics options for treatment of asthma and lung cancer using novel drug delivery approaches.[15] Researchers are evaluating the innovative encapsulation and delivery mechanisms using gelatin nanocarriers.

(11) Work from a health economist that combines investigative research, education, training and networking to study various health care issues such as the effectiveness of self-management education and financial incentives for patients and physicians compared to usual care in patients with diabetes. Other projects promote networking among researchers from minority institutions.

(12) Work to find natural product treatments for cancers with fewer side effects and lower toxicity than current therapies. One lab is focused on Stat3 as a cancer chemotherapeutic molecular target.

(13) A variety of biomedical research projects with the IDeA Networks for Biomedical Research Excellence (INBRE) program, a collaborative research program with UH Manoa and other universities in Hawai'i.

(14) Collaboration with the State of Hawai'i to help develop standards to control the quality of medical marijuana.

The Glut of New Pharmacy Programs in the United States

After 10 years in the making, the Daniel K. Inouye College of Pharmacy was established in 2007. DKICP graduates have helped to address the local pharmacist shortage. Aggregate Demand Index (ADI), as reported from the Pharmacy Workforce Center (PWC), showed Hawai'i's historic high in 2004 as 4.5 (5 = demand is much more than the pharmacist supply available,

3 = demand equal supply available, 1 = demand is much less than the pharmacist supply available).[16] August 2014 figures indicate that national level ADI figures since 2008 (ADI of 4), show a downward trend to the equilibrium point of "3" with the community pharmacy figures reported at 3.38 and institutional pharmacy at 2.78. Hawai'i's ADI (August 2014), is reported at 1.5 as compared to the Western Pacific Region's ADI of 3.54.[16] The average class of 86 graduates from DKICP is comprised of approximately 50% Hawai'i residents. Self-reported alumni data on post-graduate placement generally indicates that resident students are remaining within the state for jobs and non-residents return to the continental US. The majority of graduates gain employment in community pharmacy retail settings.[17]

The ACPE has seen rapid increases in the numbers of US schools of pharmacy. In 2000, there were 80 accredited programs of pharmacy.[18] As of 2014, a 60% increase in schools has swelled the number to 130 schools.[18]

Based on the track record so far from the DKICP, approximately 50% of graduates report having secured a position requiring the PharmD at the time of graduation, and approximately 90% of the graduates report having secured employment requiring the PharmD within one year of graduation.[12] Based on ratings provided by *US News and World Report*, the DKCIP was ranked as 74 among all pharmacy schools, and among the top five of the 40 or so schools created since 2000.[19]

The Future of Pharmacy in the United States

As described in Part 1 of this article, the profession of pharmacy has dramatically evolved since colonial times in the United States. Over the last century, educational programs have progressed from the two-year PhG (Graduate in Pharmacy) (1907), to the three-year PhC (Pharmaceutical Chemist) (1925), to the four-year BS in Pharmacy (1932), to the five-year BS in Pharmacy (1960), and finally, to the six-year PharmD (Doctor of Pharmacy). [1] As mandated by current accreditation standards, the only degree leading to professional licensure is the PharmD. Being a terminal degree, this is not likely to change in the future. But will admission standards change? Currently, even though approximately 70% of student pharmacists entering the DKICP program already hold a baccalaureate degree, and after two years of didactic work in the program they generally qualify for award of the Bachelors in Arts in Pharmacy Studies (BAPS; a new degree offered by our College), will admission requirements be changed to require the bachelor's degree prior to admission? The administration of the DKICP does not endorse such a requirement, but it will be necessary to conform with national accreditation standards if such a policy were to be implemented.

Perhaps a more eminent issue deals with residency programs. As will be described in the next article to be published in May 2015, at this time, approximately 20% of students graduating from the DKICP apply for advanced training in residency programs.[20] This upcoming graduating class of 2015 has a record 30% applying for residency. Considering the state-of-the art, will internships and residencies become a requirement for pharmacy graduates? Only time will tell, but there is a high probability this will become reality.

What is clear, at least by historical precedent, pharmacy is a resilient and malleable profession that plays a crucial role in modern day health care. Pharmacists play an integral role for interdisciplinary health care in numerous types of health care settings. Traditional duties mainly described pharmacists as chemists, and although the medicinal chemistry portion of the curriculum continues to differentiate this profession from other healthcare professionals' training, today's pharmacist can be considered the medication/drug experts who can manage therapeutic outcomes for complicated medication profiles, patient education and assure patients medication adherence and side effect management for chronic diseases. The continued movement of the Affordable Care Act requires medical organizations and third party payers to rely on pharmacist expertise in pharmacoeconomics or the study of cost effectiveness in relationship to effective drug therapy. Continued shortage of certain types of medications makes the pharmacist's knowledge critical for suggesting biosimilar medications or equivalent therapies.

Concluding Remarks

With a history of less than a decade, the DKICP has entrenched itself as an integral component of the UH System and the State of Hawai'i as a whole. Total enrollment of a remarkably diverse group of student pharmacists (Figure 1) currently stands at 337. To date, 341 Doctor of Pharmacy students have graduated with a respectable 96% pass rate for the North American Pharmacists Licensure Examination (NAPLEX), which is competitive with the national average. The infrastructure of the College has continued to grow and expand (Figure 2). An independent analysis indicated the College contributes about $50 million each year in economic activity,[21] but this was clearly an underestimate since extramural funding (which has exceeded $40 million) (Table 1) was not taken into account. With construction of a permanent facility now on the horizon, it is clear the College is well poised for preeminence as we continue to serve the people of Hawai'i as well as the entire Pacific Region.

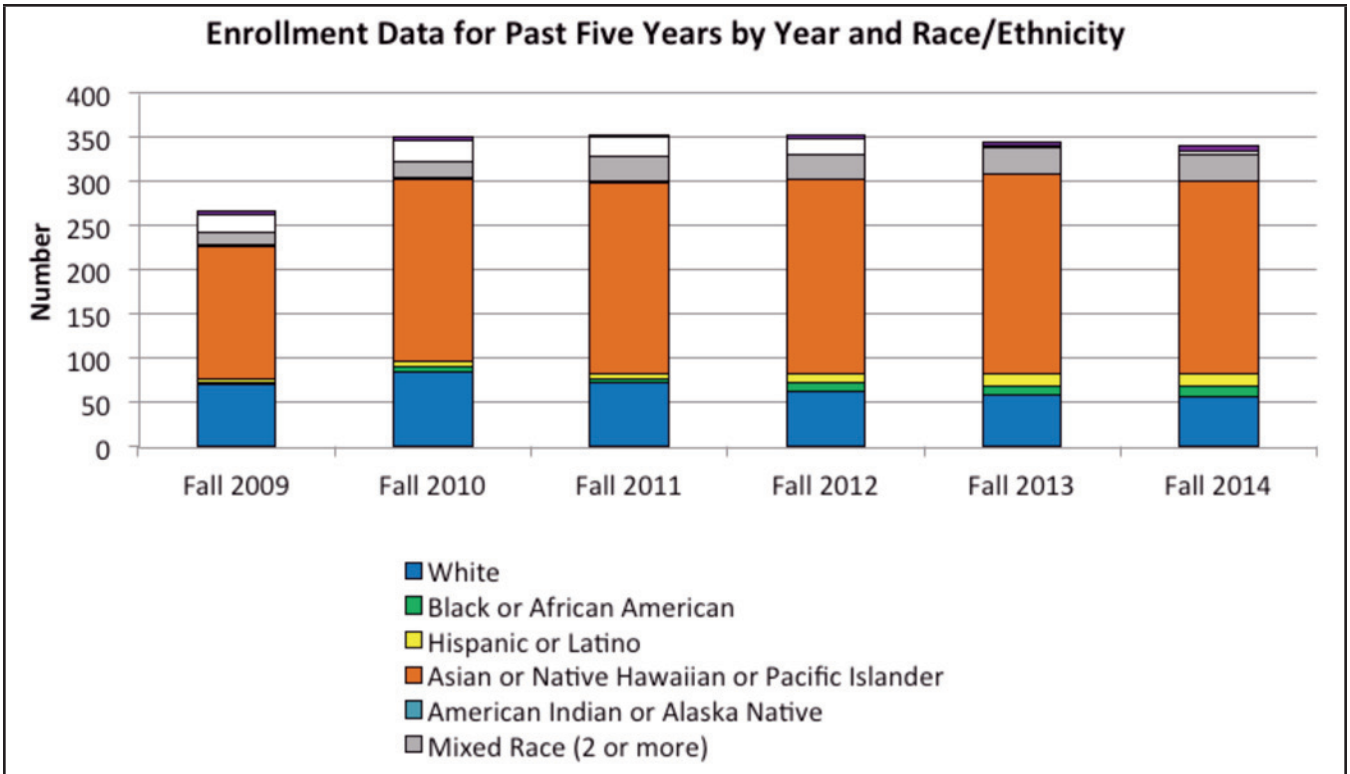

Figure 1. Enrollment Data 2009-2014, Race and Ethnicity, Daniel K. Inouye College of Pharmacy, UH Hilo

See Figure 2 on the next page.

Acknowledgements

This article is dedicated to APEx awardees Jerry Johnson, Rose Tseng, Pat DeLeon and Steven Hora. The APEx (Advancement of Pharmacy Excellence) award honors individuals who are not employed by the DKICP and have made significant contribution to the development and growth of the college.

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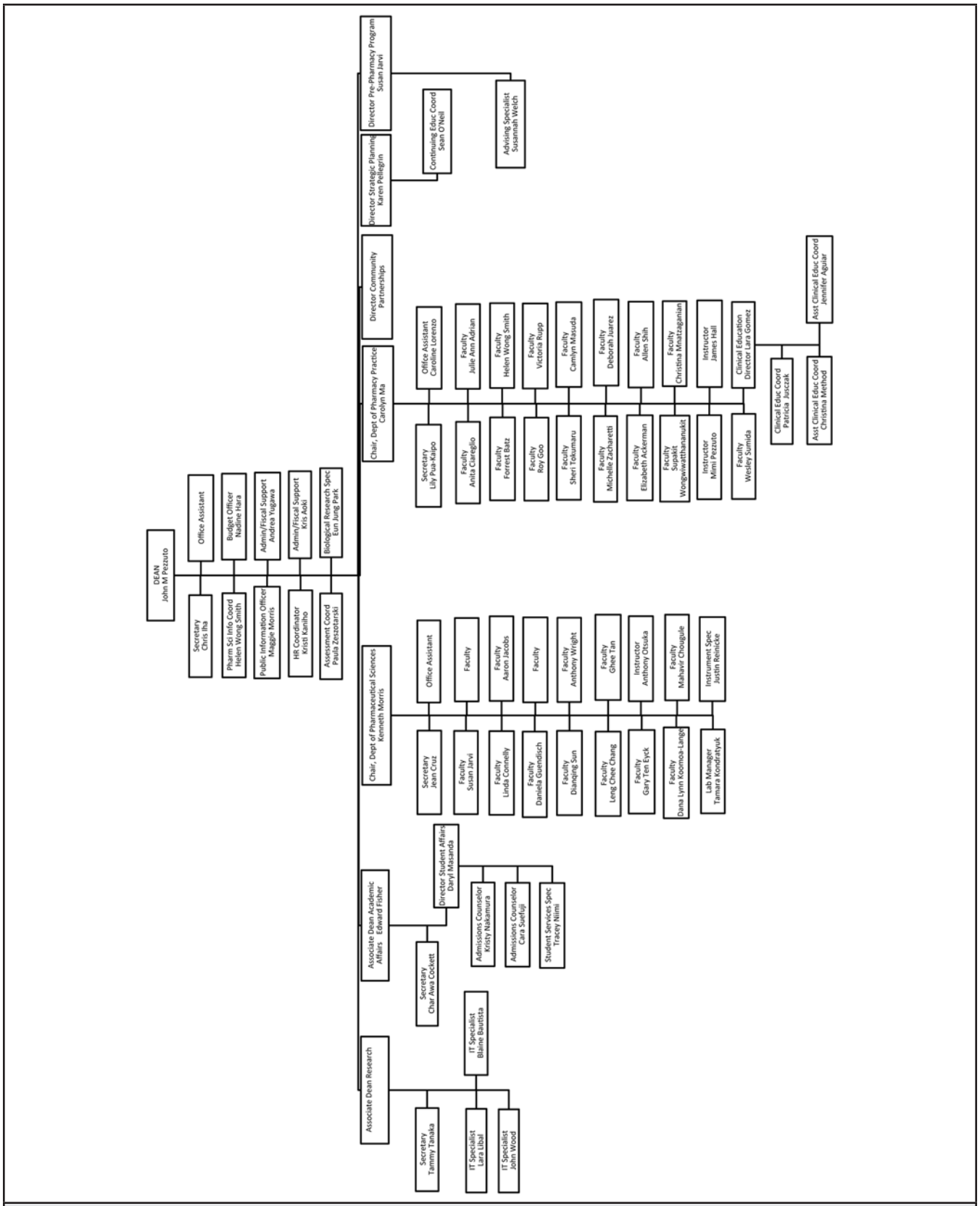

Figure 2. Current Organizational Structure for the Daniel K. Inouye College of Pharmacy

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THE WEATHERVANE

RUSSELL T. STODD MD; CONTRIBUTING EDITOR

YOU CAN'T TREAT IT UNTIL YOU KNOW IT'S THERE.

A revolutionary method of diagnosis for malaria is pending, one that would reveal the disease long before symptoms appear. Transmitted by the anopheles mosquito, malaria infects some 207 million people worldwide. Scientists reporting in Nature Medicine found in their study they could harness magnetic sensors to diagnose the parasite in 5 minutes with better accuracy than routine microscopy. Current methods require a few drops of blood on a dipstick to get an answer in 15 minutes, but miss 17% of cases. Microscopy is more accurate, but requires training, equipment and time. In this study researchers detected parasites in blood as low as 1/5th the levels perceptible with microscopes. The device relies on the inherent magnetism in the iron-containing hemoglobin in red blood cells. The parasites invade the rbc, gorge on the hemoglobin and convert it into hemozoin that boosts rbc magnetization. The red cell reveals the parasite, according to co-author Weng Kung Peng of the Singapore MIT Alliance for Research and Technology. The diagnostic device, inspired by nuclear magnetic resonance machines, could fit in a shoebox. "With malaria, a few days can be the difference between life and death," said co-author Peter Preiser at the Nanyang Technological University in Singapore. "If confirmed in humans, this technique could detect disease roughly two to four days earlier."

IT'S TIME TO GET SERIOUS ABOUT MEDICAL CARE IN HAWAI'I.

Hawai'i faces an alarming shortage of physicians. The need for both primary care and specialists, especially on the neighbor islands keeps growing, while the supply continues to shrink. Doctors are retiring without replacements, and young doctors who are recruited soon return to the mainland. The two primary factors for any doctor who might want to stay in Hawai'i revolve around reimbursement, among the lowest in the United States, and the high cost of supporting a family. Years ago a handful of Hawai'i physicians tried to impress our Washington representatives with the growing crisis in recruiting physicians. They were greeted courteously, but nothing was done. Two obvious remedies can help alleviate this problem. First, our politicians can petition Medicare to alter the Hawai'i coefficient for reimbursement to equal that of any major US city. Second, our state government can offer an incentive plan to young docs where their education debts are assumed in return for a promise of medical service for a given length of time. Old ideas true, but the time to act has arrived if we are to deter this crisis. Tell your representative, "Enough talk. Do something."

A SURGEON MIGHT SAY, "YES, WE CAN DO IT, BUT SHOULD WE?"

After 15 months of misdiagnoses Pam Pope, age 65, was told the cause of her problems. She was found to have a rare cancer "pseudomyxoma peritonei." The disease was so far advanced that the only viable action her doctors offered was removal of most of her abdominal contents. In May 2014 at Hampshire Clinic, Basingstoke, England, she survived a 13 hour operation when six surgeons removed her appendix, large bowel, gall bladder, spleen, uterus, ovaries, fallopian tubes, cervix and most of her small bowel. Post-op care required heavy doses of chemotherapy. She survives on a nightly drip for hydration, and remains very frail, according to a December report in the London Daily Mail. At this point, one might ask if the price of survival is worse the suffering?

LEGALIZING MARIJUANA, THE LAW OF UNINTENDED CONSEQUENCES.

Everyone knows about the danger of drunken driving and many states have specific parameters for law enforcement. But what about driving while high? Oregon, Alaska, and Washington DC, voted in November to join Washington state and Colorado in legalizing recreational pot. A new survey by AAA suggests that drivers and law enforcement officers have a cloudy perception of what constitutes drugged driving The potential is real for drugged driving to become commonplace. National Highway Traffic Safety Administration study found drugged driving particularly prevalent among young motorists. In a survey done in 2010, 13% of high school student respondents admitted to driving after puffing pot. Moreover, nearly a quarter of drivers in drug related crashes were younger than 25. One in six Americans say they live in an area where general perception is that it's okay to drive one hour after toking up. AAA points to federal research that shows marijuana can impair driving performance for up to three hours after use. Legalized recreational use of pot will surely spread as politicians succumb to the bandwagon effect of "all other states doing it." How to handle the projected increase of pot-using motorists is without groundwork and data. Sixteen states have banned any trace of drugs in your system while driving. According to Mothers Against Drunk Driving, alcohol related driving deaths have declined by half since 1980, but crashes still cost the United States about $132 billion a year. How will marijuana related cases impact those numbers? It's difficult to quantify the direct role marijuana plays in car crashes. Apples to apples comparisons to alcohol are not available. Beware! There's a smoky road ahead.

A $50 MILLION BREAST REDUCTION.

A shapely bosom, possibly more ample than mother nature endowed, is now a status symbol in China. Posters featuring buxom ladies promoting breast enhancements, herbal supplements, creams, underwear, and other methods to boost the bust are often seen in elevators and taxis. Due to this shift in mainstream aesthetics, the period TV drama "The Empress of China" was showing more 7th century courtesan cleavage than government censors would tolerate. The show was yanked off the air in December. The 80-episode series was produced at the extraordinary cost of $50 million, so producers quickly returned the drama to Hunan television after surgical alteration. The censor was not subtle. Necklines were moved up, and chest shots were changed to close-ups. The producers announced on social media that the delays were due to "technical problems." Whatever. This titillating subject is current and enhances Nielsen scores.

LOOK, SWEETIE, HE HAS YOUR SMILE AND — OTHER THINGS.

"Keepsake" ultrasounds are becoming popular with soon-to-be mothers as they approach the due date. These 3-D and 4-D active images often cause the mother to believe she is bonding with her unborn child. Expectant mothers can visit one of these studios, apparently on an elective basis, see the baby yawn or suck its thumb. Mothers (and fathers) can study facial features and expressions, extremities and body parts. The practice is purely for entertainment, and the studio produces a DVD and other souvenirs to take home. The Food and Drug Administration (FDA) warned that the safety of such repeated imaging is not known. Physicians agree with the FDA that the technique is not monitored and should be discouraged until studies have proven it to be safe. Of course, no one is asking the US Navy which regularly denies that its sonar is anything but benign to dolphins and whales.

ADDENDA

- Six Americans die each day from alcohol poisoning.
- The Ottoman Empire still existed the last time the Chicago Cubs won the World Series.
- Ronald Reagan said, "If we ever forget that we are one nation under God, then we will be a nation gone under."
- Eighty-seven condoms are used each second on Valentine's Day in the United States.
- On the eighth day, God found a lot of assembly parts left over.

ALOHA AND KEEP THE FAITH rts

(Editorial comment is strictly that of the writer.)

1010-1925

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