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Psychosocial and Clinical Outcomes of a Cognitive Behavioral Therapy for Asians and Pacific Islanders with Type 2 Diabetes: A Randomized Clinical Trial

Jillian Inouye PhD; Dongmei Li PhD; James Davis PhD; and Richard Arakaki MD

Abstract

Asian Americans and Pacific Islanders are twice as likely to be diagnosed with type 2 diabetes compared to Caucasians. The objective was to determine the effect of cognitive behavioral therapy on quality of life, general health perceptions, depressive symptoms, and glycemia in Asians and Pacific Islanders with type 2 diabetes. The design was a randomized controlled clinical trial comparing cognitive behavioral therapy to diabetes education and support for six weekly sessions. Participants were recruited from two endocrinology practices; 207 were enrolled. The cognitive behavioral therapy group was provided self-management tools which included biofeedback, breathing exercises, and stress relievers, while the diabetes education and support group included diabetes education and group discussions. Assessments of psychosocial and clinical outcomes were obtained before and after sessions and 12 months PostSession. Differences between the two groups were examined using linear mixed-effects models with linear contrasts. The cognitive behavioral therapy group had improved depressive symptom scores from PreSession to EndSession compared to the diabetes education and support group ($P < .03$), but the improvement did not extend to 12 months PostSession. Similar results were observed with misguided support scores in the Multidimensional Diabetes Questionnaire ($P < .03$) and susceptibility in health beliefs ($P < .01$), but no significant differences in HbA1c improvement were found between the two groups. Both interventions improved outcomes from baseline but were not sustained for 1 year.

Keywords

Cognitive behavioral therapy; self-management training; Asians; Pacific Islanders; type 2 diabetes

Introduction

Type 2 diabetes is a difficult disease with challenging behavioral requirements. In the United States, 8.3% of the population is afflicted with diabetes, with Asians and Pacific Islanders (API) having a greater prevalence of diabetes mellitus than the general population.¹ Even after adjustment for body mass index, Asians are more likely to develop diabetes than non-Hispanic whites.²

Many barriers to effective diabetes self-management exist, particularly for API. For example, ethnic and cultural differences impact diabetes non-adherence for standards of care rates, which were found to be at 65% for Asian Americans and 87% for Pacific Islanders compared to 63% for Caucasians.³ Results of a focus group with Native Hawaiians and Pacific Islanders found that participants often felt anxious, angry, and depressed as a major barrier to proper diet and exercise.⁴ Some of the themes that emerged indicated a need for family involvement in diet, exercise, and educational programs. Another study on health beliefs reported that Asian patients view insulin as a poison rather than a lifesaver and think that insulin therapy means “the end of the road” and that they will die soon.⁵ Improved strategies, therefore, that focus not just

on metabolic control but on modifying health beliefs, lifestyle behaviors, and psychological outcomes and processes such as decision making and moods, are needed for API with diabetes to enhance their self-management.⁶

Cognitive behavioral therapy (CBT) represents one strategy that may prove effective in modifying beliefs, attitudes, and behaviors to better manage diabetes among API.⁷⁻¹⁰ CBT includes the use of five strategies: (1) self-monitoring and goal setting; (2) stimulus control for the modification of behaviors and habits; (3) cognitive restructuring techniques that focus on challenging and modifying unrealistic or maladaptive thoughts or expectations; (4) stress management; and (5) social support. Studies of cognitive behavioral interventions in these groups, while few, have shown reductions in HbA1c levels, diastolic blood pressure (BP), and body mass index compared to regular education alone with a greater reduction in diastolic BP over 12 months.¹¹ No large, long-term controlled studies of CBT in API groups,¹² however, are available and consequently there is a need to examine CBT impact on API with diabetes.

The specific aim of the present study was to determine the effect of CBT in improving quality of life, general health perceptions, depressive symptoms, and glycemic control along with associated metabolic parameters. The comparison group included a Diabetes Education and Support (DES) intervention that focused on sharing experiences and reviewed diet, medications, and group suggested topics. The predictions for this study were that CBT improves psychosocial, behavioral, and clinical outcomes as compared to DES in API with diabetes.

Methods

Study Design

The study was a randomized controlled clinical trial with double blinding to condition. Patients and providers were not aware of the goals and outcomes of the study except for the interventions provided. Interventionists were unaware of what was being provided in the comparison group. The study was approved by the Committee on Human Studies (CHS #12473) and all participants signed informed consent prior to entry into this study (NCT01182701).

Participants

API patients with type 2 diabetes between the ages of 18-76 years were recruited through two practitioners in Hawai‘i. Individuals were eligible only if they had received individualized or group diabetes education and dietary counseling, performed self-monitoring of blood glucose, and maintained routine physi-

cian visits. Patients who had diabetes-related disabilities such as renal failure and blindness or were unable to ambulate and participate in an exercise program were excluded [New York Heart Assoc. Class 3 (symptomatic with daily activities) and 4 (symptomatic at rest)].¹³ Participants received sealed envelopes assigning them to either the CBT or DES group using random number sequencing generated by a psychologist. Baseline anthropometric and clinical data, medical knowledge test, and quality of life, psychosocial, and behavioral questionnaires (described below) were obtained prior to randomization and after consents were obtained. The CBT and DES group met for six successive weekly sessions that averaged 1-2 hours per session with a group size ranging between 2 and 6 individuals. Family members or a supportive friend were encouraged to attend and participate.

Cognitive Behavioral Therapy (CBT)

A six-session format was implemented to focus on behavioral practice that included modules on stress management, bio-feedback assisted relaxation, mood management, cognitive restructuring, empowerment, values clarification, problem solving, and decision making.¹⁴⁻¹⁷ The components included contracting, behavioral rehearsal, reinforcements, and a stress prevention session on anticipating and coping with the problems of stress recurrence. Learned cognitive behavioral practices were reinforced at each follow-up session as these intervention programs have been reported to be an effective way of reducing self-care behavior deficit.¹⁷ After each session, participants were asked to practice the learned behavioral interventions on their own, and reviewed and discussed their experience during the following sessions. These sessions were facilitated by research assistants who were trained on the various aspects of CBT by the investigator (JI) with unannounced fidelity checks completed at various intervals. Participants consented to these unannounced visits. Similar checks were also conducted for the DES group based on a checklist for content coverage.

Diabetes Education and Support (DES)

Participants randomized to receive DES spent an equal number of meetings and amount of time in sessions as the CBT group, but primarily focused on sharing personal experiences and receiving a review of diabetes education.¹⁸ Sessions were facilitated by different research assistants who were trained by the investigator to provide education and manage group support. Participants were asked to share their own experiences with diabetes, their problems, and what needs they had. Diabetes education was provided by the assistants based on suggestions and needs of the group. Topics covered were manualized for consistency and included "taking care of your feet, dental care, sick day management, taking your diabetes on vacation, and insurance coverage."

Health and Clinical Outcomes

Health outcomes were assessed at PreSession and EndSession, and 12 months after the end of the sessions. Anthropometric

measurements of BP, height, weight, and calculated body mass index were obtained by standard methodology.¹⁹

Diabetes Quality of Life (DQOL) Survey

Psychosocial measures included the Diabetes Quality of Life (DQOL) measure, a 46-item multiple-choice assessment for adolescents and adults with insulin-dependent diabetes mellitus. This survey rates satisfaction with quality of life, impact of diabetes, diabetes worry, and social/vocational worry on a scale from 1 (Very Satisfied or No Impact/No Worry) to 5 (Very Dissatisfied or Very Impacted/Worried). There are four subscales in the DQOL measure focusing on satisfaction, impact, social worries, and diabetes worries. The range of scores for each subscale is from 0 to 100 with higher scores indicating better quality of life.²⁰

Medical Outcome Study 36-Item Short Form Health Survey (SF-36)

The General Health subscale of the Medical Outcome Study 36-item Short-Form health survey (SF-36) which assesses self-appraised general health, was given and consists of five items ($\alpha = 0.78$) rated on a 5-point scale, designed to measure functioning and well-being in people 14 years and older. The SF-36 scores have 8 subscales including physical function, health limitations, emotional limitations, fatigue, emotional well-being, social function, pain, and general health. There is a range from 0 to 100 for each subscale with higher scores defining a more favorable health state.²¹

Center for Epidemiologic Studies-Depression (CES-D) Scale

To measure depressive symptoms, the Center for Epidemiologic Studies-Depression (CES-D) scale, a 20-item, self-report scale was given. This scale measures current depressive symptomatology including depressed mood, feelings of guilt and worthlessness, helplessness and hopelessness, psychomotor retardation, loss of appetite, and sleep disturbance, and has been validated in the Native Hawaiian population. All items were summarized to form the CES-D scores, which have a range between 0 and 60. Higher scores on the CES-D indicate higher levels of distress. A CES-D score of ≥ 16 suggests a clinically significant level of psychological distress.²²

Summary of Diabetes Self-Care Activities Questionnaire

Adherence was measured with various tools. The Summary of Diabetes Self-Care Activities questionnaire, a 12-instrument self-report measure of the frequency of completing different self-care activities over the preceding seven days, included subscales of general diet, specific diet, blood glucose, foot care, diet days, exercise, and medication taking. All subscales have scores ranging from 0 to 7, with higher values indicating better self-care activities.²³

Multidimensional Diabetes Questionnaire (MDQ)

The Multidimensional Diabetes Questionnaire (MDQ, a measure of self-efficacy), designed to provide a comprehensive

assessment of diabetes-related cognitive and social factors was used. There are 7 subscales in the MDQ measurement including interference, severity, social support, positive reinforcement, misguided support, self-efficacy, and outcome expectations. All scales have a range of 0 to 6 except self-efficacy and outcome expectations, which are ranged from 0 to 100. All scales have higher values indicating better results.²⁴

Health Belief Scale

The Health Belief Scale is a 38-item Likert scale that assesses the severity or vulnerability and cost-benefit dimensions of the health belief model, and items are rated on a 4-point agree/disagree scale and summed to provide seven sub-scores including cues to action, health motivation, severity, susceptibility, psychology barriers, treatment benefits, and structural elements with higher indication more noncompliant.²⁵

Clinical results such as the HbA1c and lipids were considered acceptable if the dates of measurement coincided with the dates of the initial session (PreSession), EndSession, and 12 months PostSession. However, a two-month allowance was made to accommodate various timing of tests ordered by the participant's physician(s). Most of the clinical measures were performed in local laboratories as requested by physicians with HbA1c levels determined by the Biorad Variance II Turbo Hemoglobin A1c Program, which is certified by the National Glycohemoglobin Standardization Program. Lipid profiles were measured on an Olympus analyzer according to National Cholesterol Education Program guidelines.

Statistical Analyses

Data analyses were performed using SAS software version 9.1 (SAS Institute Inc., Cary, NC). Descriptive statistics such as mean and standard deviations were used to describe the distributions of quantitative variables in our study. Two sample *t*-tests were used to compare the demographic and baseline quantitative variables between the CBT and DES groups and between subjects who completed the study and subjects who dropped out. Frequency distributions were used for nominal variables to show the frequencies of each category. Chi-square and Fisher's exact tests were used to examine the difference in nominal demographic variables between the CBT and DES groups, and between subjects who completed the study and subjects who dropped out to determine the missing patterns.²⁶

Linear mixed-effects models were used to examine the effects of treatment and the interaction between treatment and significant demographic covariates on each of the outcomes from PreSession to 12 months PostSession using the Proc Mixed procedure in SAS 9.1. The residuals of the linear mixed-effects models were checked and no significant deviation from normal distribution assumption was found. The covariates were selected using the stepwise selection procedure with .05 as the cutoff for both entering and dropping from the model. The linear mixed-effects models account for correlations among repeated measurements within the same subject through the repeated statement in the Proc Mixed procedure. Compound symmetry

variance-covariance structure, which was selected based on the Akaike's Information Criterion, was used to estimate the variance and covariance and account for the correlations within subjects over time. Linear contrasts for testing treatment effects at each follow-up time and for testing time trends within each intervention group were used to estimate the change of each outcome measurement over time. All significance tests were two-sided with significance level set at 5%.

Power Analysis

Estimated treatment effects used the following sample size formula: $N = [2 * (Z_{\alpha/2} + Z_{\beta})^2 * \sigma^2] / \text{delta}^2$. *N* represents the sample size per group; $Z_{\alpha/2}$ and Z_{β} represents the standard normal deviates for type I and type II errors, σ^2 represents the squared standard deviation, and delta^2 represents the squared difference between the treatment and control groups. Effect sizes were calculated on the assumptions that there would be a 5% type I error and 20% type II error, providing a power of 80%. Published effects from research on behavioral interventions estimated that the treatment group would have $\geq 15\%$ greater adherence to self-management behaviors than the control group,²⁷ and a 10-30% improvement for other dependent variables.^{28,29} Treatment effects (delta), calculated based upon published means and standard deviations as well as upon the 164 participants (82 per group) predicted to complete the trial,³⁰ estimated a $\geq 7.9\%$ change from baseline for the diabetes self-management record. For dietary fat and exercise, treatment effects were detected at 15-21% and 34-40%, respectively.

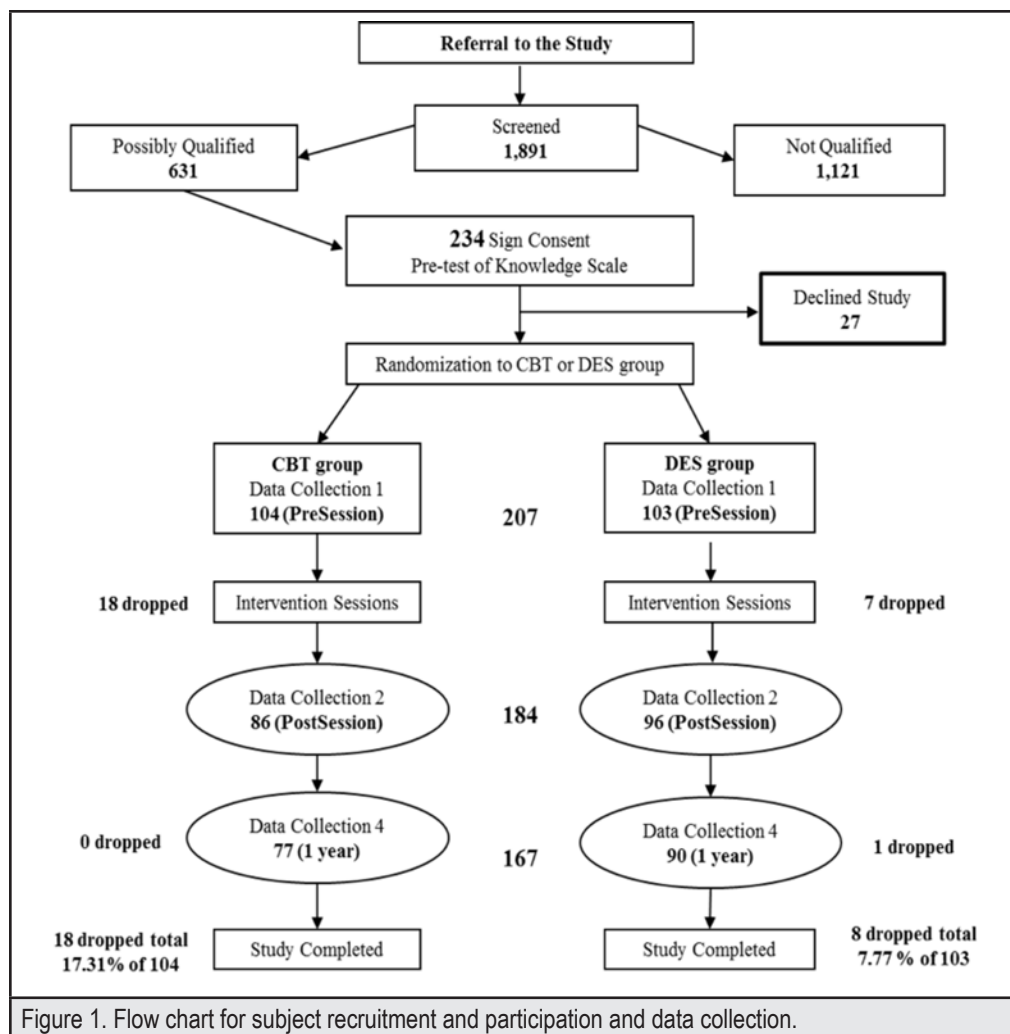
Results

The two endocrinology practices identified 1,891 individuals with diabetes of whom 631 individuals met eligibility criteria for study participation. Two hundred and thirty-four patients signed informed consent but only 207 individuals were randomized (20 individuals withdrew, 3 could not be scheduled, and 4 relocated or passed away; Figure 1).

Demographic and PreSession Characteristics

The PreSession characteristics for the 207 participants are reported in Table 1. The mean age of participants was 57.3 years with higher proportion of female (55%) and married (70%) participants. A large proportion of the participants had education level of college or higher (45%) and had professional or managerial occupations (35%). Of the 207 participants, 150 participants were Asians and the remaining 57 participants were Hawaiians or other Pacific Islanders. No significant differences were observed by gender ($P = .53$), marital status ($P = .69$), occupational status ($P = .69$), and education ($P = .34$), or by clinical measures of glycemia, weight, BP, and lipid profiles between the CBT and DES groups ($P > .05$).

Subjects who completed the study were compared with subjects who dropped out to determine missing patterns. No significant differences in gender ($P = .06$), marital status ($P = .7$), occupational status ($P = .93$), education ($P = .92$), and most clinical measures ($P > .05$) were found between subjects who



completed the study and subjects who dropped out during the study period except for triglyceride levels ($P < .01$) (Table 1). The proportions of dropouts were not significantly different between the CBT group (17.31%) and the DES group (7.77%) (Figure 1; Fisher's exact test, $P = .06$).

Health Outcomes Changes with Intervention

A significant difference between the CBT and DES groups was found for depressive symptoms via the CES-D assessment from PreSession to EndSession ($P = .03$) (Table 2). The mean reduction in CES-D score for the CBT group was greater ($8.03 - 10.48 = -2.45$ in contrast to the DES group, which was almost unchanged ($9.37 - 9.68 = -.31$). At 12 months PostSession, no significant change in CES-D score from PreSession was found between the CBT and DES groups ($P = .09$). No significant differences in diabetes DQOL and SF-36 psychosocial measures were observed between the CBT group and the DES group during the study period ($P > .05$).

For the MDQ, a statistically significant difference between the CBT and DES groups from PreSession to EndSession ($P = .03$)

was observed for the misguided support score (Table 3), with the CBT group showing an increasing trend in mean misguided support scores compared with a decreasing trend for the DES group. A statistically significant difference between the CBT and DES groups was detected for susceptibility in the health beliefs scale from PreSession to EndSession ($P < .01$). The CBT group had a decreasing trend while the DES group had an increasing trend in their susceptibility during the intervention period. At 12 months, no significant change in susceptibility from PreSession was found between the two groups ($P = .18$). No other significant differences in scores by the SDSCA, MDQ, or health belief assessment were observed between the CBT group and the DES group during the study period ($P > .05$).

Clinical Outcomes

There were no reportable adverse events. There were no significant differences in health outcomes between the CBT and DES groups at baseline for all measures except significantly lower self-efficacy scores were found in the CBT group compared to the DES group (MDQ, self-efficacy) ($P = .05$, Table 3). Results

Table 1. Baseline characteristics of participants in CBT and DES groups, completed interventions, and dropped out.							
	Total (%) N = 207	CBT (%) n = 104	DES (%) n = 103	P-value	Completed (%) n = 181	Dropped out (%) n = 26	P-value
Mean age in years	57.3±10.9	57.0±11.1	57.8±10.8	.60	57.4 ±10.5	56.7±13.7	.76
Gender							
Female	113 (54.6%)	59 (56.7%)	54 (52.4%)	.53	86 (47.5)	18 (69.2)	.06
Male	94 (45.4%)	45 (43.7%)	49 (47.6%)		95 (52.5)	8 (30.8)	
Marital Status							
Single	26 (12.8%)	15 (14.6%)	11 (11.0%)	.69	22 (12.3%)	4 (16.7%)	.70
Married	141 (69.5%)	69 (67.0%)	72 (72.0%)		124 (67.0%)	17 (72.0%)	
Post Married	36 (17.7%)	19 (18.4%)	17 (17.0%)		33 (18.4%)	3 (12.5%)	
Occupational Status							
Professional, Managerial	68 (34.9%)	32 (32.7%)	36 (37.1%)	.69	61 (35.3%)	7 (31.8%)	.93
Technical, Clerical, Sales	35 (17.9%)	18 (18.4%)	17 (17.5%)		30 (17.3%)	5 (22.7%)	
Service	21 (10.8%)	13 (13.3%)	8 (8.3%)		19 (11.0%)	2 (9.1%)	
Other#	71 (36.4%)	35 (35.7%)	36 (37.1%)		63 (36.4%)	8 (4.6%)	
Education							
Less than 12th grade	19 (9.5%)	11 (11.1%)	8 (8.0%)	.34	17 (9.7%)	2 (8.3%)	.92
High School Graduate	22 (11.0%)	10 (10.1%)	12 (12.0%)		19 (10.8%)	3 (12.5%)	
Some College/Associate	65 (32.7%)	28 (28.3%)	37 (37.0%)		58 (33.0%)	8 (33.3%)	
Bachelor's Degree	55 (27.6%)	33 (33.3%)	22 (22.0%)		47 (26.7%)	8 (33.3%)	
Graduate School	38 (19.1%)	17 (17.2%)	21 (21.0%)		35 (19.9%)	3 (12.5%)	
Clinical Measures*							
Weight (lbs)	199.7±65.2	208.1±71.5	190.2±56.4	.15	199.6±64.5	202.2±80.4	.92
BMI (kg/M²)	32.2±7.3	33.6±7.1	30.7±7.3	.11	31.9±7.1	35.7±10.5	.32
Systolic BP (mmHg)	138.7±20.0	137.9±18.6	139.6±21.6	.65	139.1±20.5	132.7±7.6	.42
Diastolic BP (mmHg)	84.3±13.0	85.4±1.5	83.1±2.0	.35	84.3±13.2	84.3±9.3	.99
HbA1c level (%)	8.0±1.6	8.1±0.2	7.8±0.2	.18	7.9±1.6	8.6±2.0	.08
Total Cholesterol (mg/dl)	167.5±41.8	165.9±4.7	168.9±4.6	.64	167.8±41.6	164.4±45.0	.77
LDL Cholesterol (mg/dl)	92.0±32.1	90.0±29.3	93.9±34.7	.46	92.0±31.9	92.6±34.9	.94
Triglyceride (mg/dl)	171.6±149.0	167.4±141.3	175.5±156.6	.73	176.9±155.8	123.8±33.7	<.01*
HDL Cholesterol (mg/dl)	43.4±11.5	43.9±12.0	43.0±11.1	.61	43.0±11.0	47.2±15.0	.17

*P-value < .05. # Other occupational status includes – agricultural, fishery, forestry, craft and repair; operators, miscellaneous.

*HbA1c and Lipid profile results were available in fewer participants than the questionnaires and anthropometric measurements: CBT group N = 75; DES group N = 84; Completed group N = 167; and Dropped group N = 26.

Abbreviations: BMI- Body Mass Index, BP- Blood Pressure, HbA1c- hemoglobin A1c, LDL- Low Density Lipoprotein, HDL- High Density Lipoprotein.

of glycemia, lipid profile, and weight were minimally changed with both interventions from PreSession to EndSession and 12 months PostSession (Table 4). Accordingly, there were no significant differences observed between the CBT and DES groups for weight, body mass index, and BP changes ($P > .05$). There was a small improvement of less than 0.3% in A1c levels at EndSession in both CBT and DES groups, but there was no change (less than 0.1%) from PreSession to 12 months ($P > .05$). Changes in lipid profile from PreSession were similar in the two groups, but not significant between groups post-intervention.

Discussion

This study was initiated to compare CBT to DES with the hypothesis that CBT would decrease depressive symptoms, increase self-efficacy, and improve quality of life and general health perceptions. The missing pattern analysis did not show any significant differences between subjects who completed the study and subjects who dropped out during the study period except for triglyceride levels. The proportion of drop outs was not significantly different between the CBT and DES groups. Thus, the missing at random assumption of the linear mixed-effects models is satisfied and the estimated coefficients from the Proc Mixed procedure in SAS 9.1 are unbiased and valid.

Table 2. Expected means and standard errors in psychosocial and clinical measures comparing the CBT group with DES group from PreSession to EndSession and 12 months PostSession.									
Variables		CBT			DES			P-value from PreSession to End-Session (CBT vs DES)	P-value from PreSession to 12 months (CBT vs DES)
		PreSession	EndSession	Twelve months	PreSession	EndSession	Twelve months		
DQOL	Satisfaction	61.10±1.66	65.20±1.76	62.77±1.85	62.46±1.65	66.63±1.68	65.20±1.72	.98	.65
	Impact	76.49±1.26	77.56±1.32	77.23±1.38	72.96±1.25	73.72±1.27	76.24±1.30	.84	.11
	Social Worries	85.24±1.59	88.81±1.71	90.38±1.82	86.86±1.62	89.35±1.64	88.80±1.70	.66	.21
	Diabetes worries	75.62±2.06	77.80±2.19	78.05±2.30	72.68±2.04	75.29±2.09	78.24±2.14	.89	.29
SF-36	Physical function	71.23±2.63	73.78±2.78	73.73±2.84	71.83±2.65	72.32±2.70	72.89±2.73	.49	.63
	Health limitations	67.30±3.95	74.11±4.24	67.56±4.39	67.27±3.92	69.41±4.03	92.97±4.08	.37	.31
	Emotional limitations	78.04±5.04	85.86±5.26	78.77±5.37	81.97±4.85	87.16±4.99	84.20±5.00	.63	.79
	Fatigue	58.15±1.88	65.01±2.02	61.94±2.09	57.71±1.87	61.31±1.92	62.16±1.94	.18	.80
	Emotional well being	79.11±1.44	83.52±1.55	81.22±1.61	78.68±1.44	80.26±1.47	79.82±1.49	.15	.63
	Social function	82.98±2.20	86.60±2.39	83.00±2.50	80.14±2.19	82.17±2.25	81.75±2.29	.63	.64
	Pain	73.82±2.31	75.02±2.46	69.07±2.54	67.86±2.29	73.83±2.34	68.37±2.38	.10	.08
	General Health	54.34±2.07	57.46±2.18	57.80±2.23	52.96±2.05	57.02±2.09	58.61±2.11	.68	.35
CESD		10.48±0.83	8.03 ±0.88	9.33 ±0.90	9.68 ±0.83	9.37 ±0.85	10.21±0.86	.03*	.09

*P-value <.05. Abbreviations: DQOL- Diabetes Quality of Life Measure, SF-36- General Health subscale of the Medical Outcome Study 36-Item Short-Form Health Survey, CES-D- Center for Epidemiologic Studies-Depression. The least squares means and standard errors of the means for each subscale of those measurements were estimated from the linear mixed effects models at each test point. P-values were obtained from linear contrasts of testing differences in means from PreSession to EndSession, and from PreSession to 12 months between CBT and DES group.

Implications

Both CBT and DES improved (at least in the short-term) PostSession quality of life and adherence measures and HbA1c levels from baseline. There were also improvements in CES-D scores at the end of the sessions in the CBT group as compared to the DES group, but this difference did not persist to 12 months PostSession. Another study found that CES-D scores were lower among specific Asian groups such as mixed Asians as compared to Japanese,³¹ and differences in depressive symptoms measures were noted between API.^{22,32} Differences in CES-D scores among API at baseline could have impacted the effect of CBT on depressive symptoms score changes in this study. However, a separate analysis of the intervention effect could not be performed between API with diabetes due to small sample size. Changes in misguided support scores and susceptibility in the Health Beliefs Scale, components of adherence measures also improved with CBT as compared to DES at EndSession, but again failed to be maintained long-term at 12 months. The CBT interventions in this study attempted to focus on patient-centered models and included social support, behavioral skills training, attitudinal change, and cognitive interventions for change which could have impacted depressive symptoms scores and measures of adherence. However, other multilevel factors of CBT such as social and environmental resources were not addressed³³ and should be included in future studies. In general,

all changes measured showed initial improvement at EndSession with recidivism occurring further away from the intervention.

Collectively, the results of this study demonstrate that among API participants with type 2 diabetes, CBT reduces depressive symptoms scores and improves multiple components of adherence measures, but the improvements are short-lived. Unfortunately, the changes were not associated with long-term improvements in quality of life, depressive symptoms, and adherence scores beyond comparator intervention of DES. Moreover, changes in clinical parameters of glycemia and weight were similar between the two groups, despite perceived improvements in psychosocial and behavioral aspects with CBT at EndSession.

Limitations and Implications for Future Studies and Practice

A significant limitation was the decrease in contact for both groups after the initial intervention. While all participants were seen in group sessions at the 12-month time period, no other interactions took place. “Booster” sessions that assist with long-term benefits and better outcomes have been recommended by others, and perhaps may have provided more positive results at 12 months in this study.³⁴

Other limitations and a possible explanation for the lack of difference between interventions may be due to the interven-

Table 3. Expected means and standard errors in measures of adherence comparing the CBT group with DES group from PreSession to EndSession and 12 months PostSession.

Variables		CBT			DES			P-value from Pre-Session to EndSession (CBT vs DES)	P-value from to Pre-Session to 12 months (CBT vs DES)
		PreSession	EndSession	Twelve months	PreSession	EndSession	Twelve months		
SDSCA	General diet	3.61±0.12	4.15±0.13	3.83±0.14	3.79±0.12	3.98±0.13	4.00±0.13	.07	.96
	Specific diet	3.52±0.12	3.58±0.13	3.61±0.14	3.47±0.12	3.42±0.12	3.64±0.13	.57	.67
	Blood glucose	4.24±0.23	4.69±0.25	4.65±0.26	4.68±0.24	5.21±0.24	5.05±0.25	.80	.89
	Foot care	3.57±0.15	4.23±0.16	4.34±0.17	3.60±0.15	4.46±0.16	4.51±0.16	.30	.49
	Diet days	3.52±0.21	4.14±0.23	3.60±0.24	3.78±0.21	4.13±0.22	3.90±0.22	.43	.91
	Medications	4.93±0.20	4.81±0.22	5.57±0.23	4.81±0.21	4.85±0.21	5.39±0.22	.61	0.88
MDQ	Interference	3.06±0.11	3.08±0.11	3.01±0.12	3.08±0.11	3.08±0.11	3.00±0.11	.82	.81
	Self-Efficacy#	58.47±2.30	67.54±2.49	62.60±2.61	65.26±2.33	70.09±2.39	66.06±2.44	.23	.36
	Severity	1.22 ±0.15	1.14 ±0.16	1.16 ±0.17	1.29 ±0.15	1.32 ±0.16	1.16 ±0.16	.57	.73
	Social support	2.22 ±0.23	2.31 ±0.24	2.19 ±0.24	2.28 ±0.23	2.31 ±0.24	2.20 ±0.24	.75	.81
	Positive reinforcement	2.46 ±0.18	2.21 ±0.19	2.41 ±0.20	2.50 ±0.18	2.68 ±0.19	2.70 ±0.19	.06	.29
	Misguided support	2.07 ±0.17	1.79 ±0.18	1.92 ±0.19	2.09±0.18	2.27 ±0.18	2.35 ±0.18	.03*	.07
Health Beliefs	Outcome expectancies	90.00±1.36	94.69±1.49	92.72±1.58	93.70±1.38	95.71±1.43	93.17±1.46	.25	.18
	Cues to action	12.12±0.29	12.50±0.31	12.08±0.32	12.26±0.29	12.48±0.30	12.60±0.30	.70	.37
	Health motivation	10.22±0.23	10.51±0.24	10.59±0.25	10.70±0.23	11.09±0.23	11.06±0.24	.77	.97
	Severity	12.96±0.40	13.38±0.43	13.36±0.45	13.24±0.40	13.16±0.41	13.56±0.42	.40	.89
	Susceptibility	19.51±1.01	18.23±1.03	19.21±1.04	18.67±1.02	19.38±1.03	19.28±1.03	<.01*	.18
	Psychology barriers	8.74 ±0.23	8.61 ±0.25	8.50 ±0.26	9.03 ±0.23	8.83 ±0.24	8.37 ±0.24	.85	.24
	Treatment benefits	26.51±0.32	27.05±0.35	26.66±0.37	26.70±0.33	27.15±0.34	27.13±0.34	.86	.55
Structural elements		12.64±0.25	13.35±0.27	12.93±0.28	12.95±0.25	13.46±0.26	13.51±0.27	.58	.45

*P-value <.05. Abbreviations: SDSCA- Summary of Diabetes Self-Care Activities, MDQ- Multidimensional Diabetes Questionnaire. The least squares means and standard errors of the means for each subscale of those measurements were estimated from the linear mixed effects models at each test point. P-values were obtained from linear contrasts of testing differences in means from PreSession to EndSession, and from PreSession to 12 months between CBT and DES group. # Significant difference at PreSession in Self-efficacy between CBT and DES groups; P = .05.

Table 4. Comparison of clinical outcomes among participants in the CBT and DES groups from PreSession to EndSession and 12 months.

Variables	CBT (N)			DES (N)			P-value from PreSession to EndSession (CBT vs DES)	P-value from to PreSession to 12 months (CBT vs DES)
	PreSession	EndSession	Twelve months	PreSession	EndSession	Twelve months		
Weight (lbs)	185.6 (91)	190.1 (74)	191.8 (75)	188.8 (91)	190.1 (83)	191.2 (81)	.36	.17
BMI (kg/M ²)	31.3 (87)	31.7 (73)	32.0 (72)	31.4 (90)	31.2 (81)	31.7 (81)	.59	.13
Systolic BP (mmHg)	136.0 (91)	141.3 (74)	135.4 (75)	136.5 (92)	135.2 (84)	136.2 (81)	.07	.82
Diastolic BP (mmHg)	84.1 (91)	84.2 (74)	81.3 (75)	80.1 (92)	80.6 (84)	81.4 (81)	.66	.08
A1c level (%)	7.93 (75)	7.64 (58)	7.84 (71)	7.79 (84)	7.61 (61)	7.79 (57)	.91	.66
Total Cholesterol (mg/dl)	165.5 (70)	160.0 (53)	174.1 (63)	167.6 (78)	165.6 (55)	172.8 (55)	.38	.91
LDL Cholesterol (mg/dl)	89.3 (68)	80.6 (51)	86.9 (60)	93.3 (74)	90.1 (51)	87.8 (51)	.97	.60
Triglyceride (mg/dl)	162.7 (70)	146.3 (52)	163.7 (62)	175.2 (78)	166.0 (54)	177.2 (55)	.50	.65
HDL Cholesterol (mg/dl)	44.4 (70)	42.4 (53)	43.5 (62)	42.5 (78)	42.1 (53)	45.8 (55)	.42	.24

tion properties of the DES group. They were given time for group support and discussions as well as review of previous diabetes self-management classes not specifically related to self-management but more towards their care. Studies have found that social support has a positive impact on changing motivation to change health outcomes such as quality of life.³⁵ Another explanation was the high satisfaction measures and a low dropout rate for both intervention groups indicating a selection bias with motivated participants in both groups.

One study found Asians had the least difficulty with physical activity and blood sugar monitoring, worried least about their future, and had good control of their disease compared to the other groups.³⁶ These behavioral and psychological factors could play an important role in influencing treatment adherences and was not taken into account in this study. However, this could be addressed in the future with a larger sample of the different ethnic groups.

Finally, this program of six weeks may not have met the threshold necessary for more dramatic change to occur. Still, the results suggest CBT and mediators such as depressive symptoms and self-efficacy do influence health outcomes.³⁷ Another paper in review reports on the effects depressive symptoms have on responses to interventions as well as the association with glycemic control (VU, JI, JD, & RFA, unpublished data, 2015). This has implications for clinical practice as addressing depressive symptoms may have a positive effect on management of their disease. For the investigation of CBT on diabetes self-management for long-term effects, future studies could examine disaggregated ethnic groups to address the differences between API, which will require a larger cohort of participants. Additionally, future studies could include a true control group, assess motivation to change, tailor a longer intervention period to specific ethnic groups, and include environmental influences on attempts to self-manage.

In conclusion, API patients with type 2 diabetes who were recruited from endocrinologist's practices and have had diabetes for many years, initially thought that they would receive very little benefit from participating in this study. Yet, improvements in psychosocial and clinical outcomes albeit small and short-term, suggest that motivated individuals produce outcomes (self-selected, a bias) regardless of the intervention. Clinicians could take heart in the results of this study and support their patients' participation in diabetes education and self-management training programs offered in the community. Understanding the difficulty in maintaining improvement for a year as shown in our study raises the need to provide ongoing support to improve overall psychosocial, adherence, and clinical outcomes in their patients.

Conflict of Interest

None of the authors identify a conflict of interest.

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Levonorgestrel Intrauterine Device Use in Overweight and Obese Women

Lynne Y. Saito-Tom MD, MS; Reni A. Soon MD, MPH; Sara C. Harris MD; Jennifer Salcedo MD, MPH, MPP; and Bliss E. Kaneshiro MD, MPH

Abstract

The levonorgestrel intrauterine device (LNG-IUD) is a safe, effective, long-acting, reversible contraceptive that reduces unintended pregnancy and decreases heavy menstrual bleeding. Many procedures such as IUD insertion are more challenging in overweight and obese women. The objective of this study was to describe LNG-IUD insertion, continuation, and complications in overweight and obese women in an ethnically diverse population in Hawai'i. A retrospective cohort study of women who had a LNG-IUD inserted at the University of Hawai'i, Department of Obstetrics and Gynecology Resident and Faculty practice sites between January 2009 and December 2010 was performed. A total of 149 women were followed. The most commonly reported races were Asian (32%), Native Hawaiian (26%), and non-Hawaiian Pacific Islander (20%). The mean BMI of the study population was 28.4 (standard deviation 7.2) with 37% classified as normal weight, 30% as overweight, and 33% as obese. Overall, 76% of women continued the LNG-IUD 12 months after insertion. No statistically significant difference emerged in 12-month IUD continuation between the BMI groups. Difficult (5%) and failed (3%) IUD insertions were rare for all BMI groups. IUD complications occurred in 9% of women and included expulsion and self-removal. In this diverse population, the majority of women continued to use the LNG-IUD one year after insertion with low rates of difficult insertions and complications.

Introduction

Among women of reproductive age in the United States, 59.5% are considered overweight or obese.¹ In Hawai'i, approximately 46% of adult women 18 years and older are overweight or obese.² Overweight and obese women have higher rates of menstrual irregularity and complications related to pregnancy.³ Studies suggest rates of unintended pregnancy may vary by body mass index (BMI) with rates being higher in obese women.⁴ Though unwanted pregnancy is an important health concern for all women, the health risks to obese women may be greater.⁵

Providing contraception to obese and overweight women to help them achieve their reproductive life goals raises specific challenges. Combined hormonal contraceptive methods like the pill may be less effective.^{6,7} The contraceptive patch has been shown to be less effective in women weighing more than 90 kilograms (198 pounds).⁸ Although venous thromboembolism is rare in reproductive age women, studies suggest obese women taking combined hormonal contraceptives have an increased risk of venous thromboembolism compared to normal weight women.⁹ Compliance with an oral contraceptive pill differed by body weight in the research setting with obese women being less likely to adhere to the study regimen than normal weight women.¹⁰

The intrauterine device (IUD) is safe and highly effective regardless of body weight due to its direct progestogenic effect on the endometrium, making it an ideal method for many women.¹¹ IUDs are easy to use, have few absolute contraindications, and

result in few side effects beyond changes in menstrual bleeding. The levonorgestrel IUD (LNG-IUD) results in decreased menstrual bleeding which many women find desirable.¹²

Cochrane Reviews in 2010 and 2013 of hormonal contraceptive use in overweight or obese women found no studies describing hormonal IUD use in obese women.^{13,14} Subsequent to the 2010 Cochrane Review, three studies evaluating IUD use in obese women have been published. One study examined acceptance rates of IUDs in obese adolescents,¹⁵ and two studies looked at choice of contraception in women of different BMIs.^{16,17} None of these studies evaluated IUD insertion, complications, or continuation rates. Given that insertion of IUDs may be more challenging in overweight and obese women, studies evaluating these outcomes are needed to understand whether IUDs are an effective form of contraception for this population. Additionally, data on IUD use in a significant number of Native Hawaiian and Pacific Islander women has not been previously published. The objective of this study was to describe LNG-IUD use in overweight and obese women based on different BMI categories. Specific measures included difficulties with IUD insertion, complications, and 12-month continuation rates.

Methods

Study Population

We conducted a retrospective cohort study of female patients of all ages who had an IUD-related medical visit at the University of Hawai'i (UH), Department of Obstetrics and Gynecology resident and faculty practice sites between January 1, 2009 and December 31, 2010. Eligible patients were identified through the electronic medical record using International Classification of Disease, 9th revision (ICD-9) codes for IUD use [V25.1, V25.11, V25.12, V25.13, V25.42, 69.7, 97.71] and IUD complications [996.32, 996.65, 996.76] and Current Procedural Terminology (CPT) codes for IUD insertion and removal [58300, 58301]. Our study population was further refined to patients who had a LNG-IUD inserted at a UH resident or faculty practice site and had a follow-up visit documented in the medical record more than 365 days after the insertion date. During the study period, only the LNG20-IUD (releases 20 mcg LNG per day, Mirena®, Bayer HealthCare Pharmaceuticals Inc.) was available. Therefore, the LNG14-IUD (releases 14 mcg LNG per day, Skyla®, Bayer HealthCare Pharmaceuticals Inc.) was not included in this study. Two authors [LST, SH] reviewed all of the medical records. For quality purposes, data were compared between the two chart reviewers.

Main Independent Variable

The main independent variable was body mass index (kg/m^2) at the time of IUD insertion. The patient's measured weight on the day of IUD insertion and the measured or self-reported height were used to calculate the BMI. It was decided *a priori* to evaluate BMI as a dichotomous variable (normal weight [$\text{BMI} < 24.9$] vs overweight and obese [$\text{BMI} \geq 25$]). During data analysis, clinical differences between the overweight and obese groups became apparent. Therefore, the results are presented as three BMI categories (normal weight [$\text{BMI} < 24.9$], overweight [$\text{BMI} 25\text{--}29.9$], and obese [$\text{BMI} \geq 30$]).¹⁸

Dependent Variables

Dependent variables including successful IUD insertion, difficult IUD insertion, 12-month continuation, and complications related to the LNG-IUD. IUD insertion were evaluated based on the IUD insertion procedure note. Successful IUD insertion was defined as placement of the LNG-IUD at the first IUD insertion visit without use of additional instrumentation (ie, cervical dilators), anesthesia, or cervical ripening agents. Difficulty with IUD insertion (yes/no) was defined as successful placement of the IUD at the initial visit, but with the use of additional instrumentation, anesthesia or cervical ripening agents. Failed IUD insertion was defined as the inability to insert the IUD on the day of the procedure.

The 12-month continuation rates and complications of the LNG-IUD were determined by reviewing all the office or emergency room visit notes in the electronic medical record after the IUD was inserted. The 12-month continuation of the IUD was categorized as "yes" if the IUD was still in place 12 months or more after insertion and "no" otherwise. The IUD was determined to be in the uterus by visualization of the IUD strings through the external cervical os or any diagnostic imaging report describing an IUD in the uterus. Once a patient had her IUD placed, it was assumed that the same IUD remained in situ unless the patient reported removal and/or replacement of her IUD at an outside facility.

Complications from the LNG-IUD included infection, expulsion, perforation, or failure. Infection was defined as signs or symptoms of pelvic inflammatory disease after the IUD was placed. Expulsion of the IUD was defined as the patient or provider reporting visualization of the IUD outside the uterus or if no strings were visualized through the cervical os, an ultrasound confirmed absence of the IUD in the uterus and an x-ray confirmed absence of the device in the abdominopelvic cavity. Perforation was defined as imaging reports with the IUD through the myometrium or in the abdominal cavity. IUD failure was defined as a diagnosed pregnancy with the IUD in situ.

Statistical Analysis

Bivariate analysis was used to evaluate the relationship between the main independent variable and the outcomes using the Chi-square test for categorical variables and the Student's t-test for continuous variables. Data on potential confounders

were collected including age, marital status, insurance type, ethnicity, race (the electronic medical record allows patients to identify with only one race, obtained verbally during registration at the clinic or hospital), gravity and parity, history of abortion, history of sexually transmitted infections (STIs) or pelvic inflammatory disease, reason for IUD insertion, training level of inserting provider, postpartum insertion, and breastfeeding. A multiple logistic regression model was created with body mass index and any potential confounders and predictor variables that were associated with the outcome using a $P < .20$ cutoff for inclusion in the model. Through backward elimination, confounders or predictor variables were removed from the model at a significance of $P > .05$.

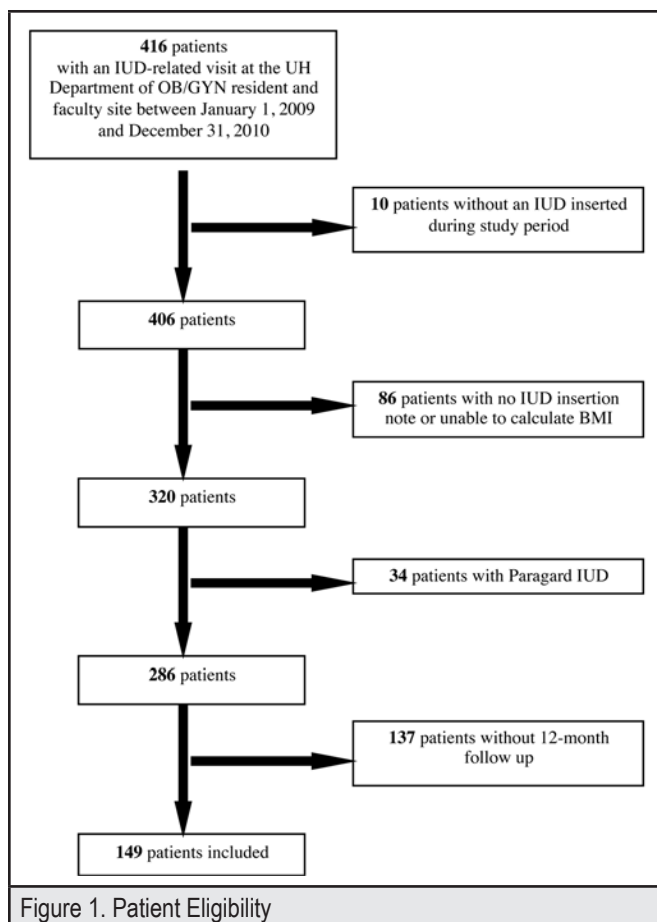
A sample size calculation was used to determine the number of charts to review based on the assumption that 85% of normal weight women would be using the LNG-IUD after 12-months.^{19,20} To detect a 10 percent difference in 12-month continuation between normal weight versus overweight and obese women with 80% power and a one-sided alpha of 0.05, a total of 280 charts were to be reviewed (140 charts in the normal weight group and 140 charts in the obese and overweight group).

The data was analyzed using SPSS 16.0 (SPSS Inc., Chicago, IL). The statistical significance was set at $P < .05$. The Western Institutional Review Board approved this study.

Results

Of the 416 potentially eligible patients identified by ICD-9 and CPT codes, 149 met our inclusion criteria (Figure 1). Most of the patients were between 21 and 30 years old (47%), single (69%), and used public insurance (61%) (Table 1). The most commonly reported races were Asian (32%), Native Hawaiian (26%), and non-Hawaiian Pacific Islander (20%). The majority of the patients had given birth to at least one child (88%), did not have a previous abortion (70%) or a history of sexually transmitted infection (75%) or pelvic inflammatory disease (98%). Most women used the LNG-IUD for contraception (91%) rather than for menstrual irregularity (9%). Resident physicians inserted seventy-five percent of the LNG-IUDs. Of the women who had the LNG-IUD inserted postpartum, 78% had the LNG-IUD placed more than 6 weeks after delivery and 72% of these women were breastfeeding.

The mean body mass index for the study population was $28.4 \text{ kg}/\text{m}^2$ (SD 7.2) with 37% ($n=55$) classified as normal weight, 30% ($n=45$) as overweight, and 33% ($n=49$) as obese. BMI varied significantly by race ($P < .01$) (Table 1). A higher proportion of Asian (24/43, or 56%) and Caucasian (10/17, or 59%) women were of normal BMI, while Native Hawaiian (25/35, or 71%) and non-Hawaiian Pacific Islanders (25/26, or 96%) were more likely to be overweight or obese ($P < .01$). Only one non-Hawaiian Pacific Islander woman had a normal BMI. BMI also varied by level of inserting provider as resident physicians were more likely to insert LNG-IUDs in the overweight and obese women, while attending physicians and nurse practitioners inserted more of the LNG-IUDs in the normal weight women ($P < .01$).



Most LNG-IUDs (92%) were inserted without difficulty (Table 2). Difficulty with IUD insertion, though not statistically significant, was more common in the normal weight (5%) and obese groups (8%) than the overweight group (2%; $P = .47$). Failed IUD insertion occurred in two patients in the normal weight group secondary to cervical stenosis and two patients in the obese group, one due to cervical stenosis and the other due to inability to visualize the cervix.

The majority of patients (76%) had their IUD in place 12 months after insertion (Table 2). No statistically significant difference emerged in 12-month IUD continuation between the BMI groups ($P = .73$). Complications were higher in the normal weight (11%) and obese (11%) groups compared to the overweight group (4%), but were not statistically significant ($P = .47$). Reported complications included expulsion (11/145, 8%) and self-removal (2/145, 1%), patients deliberately and successfully removing their own LNG-IUD. Both self-removals occurred in normal weight women. No perforations, infections, or failures occurred in the study population.

In the final multiple logistic regression model, adjusting for age and insurance, overweight women had a 33% higher odds (adjusted OR 1.33, 95% CI 0.48-3.66) of continuing the LNG-IUD 12 months after insertion compared with normal weight women, while obese women had a 25% lower odds (adjusted

OR 0.75, 95% CI 0.29-1.92) of continuing the LNG-IUD for 12 months after insertion compared to normal weight women (Table 3).

Discussion

A higher than expected loss to follow up resulted in this study being underpowered to demonstrate statistically significant differences in IUD continuation based on BMI. However, we provide estimates of 12-month IUD continuation by BMI group, which ranged between 74% and 80% and is similar to general continuation rates that have been reported in the literature (70% to 88%).¹⁹⁻²¹ Difficult (2% to 8%) and failed (0% to 4%) IUD insertions were rare for all groups and were similar to rates reported in a recent study of LNG-IUD and Copper IUD insertion in nulliparous women, which classified 9.3% as difficult and 1.2% as failed IUD insertions.²²

IUD expulsion and self-removal occurred in a minority of women. The overall IUD expulsion rate of 8% was higher than expected when compared to 3 to 5% which is typically reported in the medical literature.^{19,21} However, a study by Teal et al. of IUD use in primiparous teenagers reported a LNG-IUD expulsion rate of 13.3%, likely due to the younger patient age.²³ Additionally, Madden, et al, noted a 12-month expulsion rate of 6.3 per 100 LNG-IUDs and a 36-month cumulative expulsion rate of 10.1 per 100 LNG-IUDs.²⁴ Larger studies of an ethnically diverse population with adequate power are needed to better understand our findings.

As noted earlier, half of the women did not follow up 12-months after IUD insertion. Lower than expected follow up rates may be reflective of patients who are satisfied with a long-term contraceptive and do not need to return for birth control refills. Additionally, decreases in the recommended frequency of cervical cancer screening may have contributed to lower than expected follow up.

Despite our racially diverse population, we used the National Institute of Health (NIH) standard BMI classification to define obesity. Race-specific BMI cutoff points have been proposed for the Asian population in general, but have not been determined for each subset of Asians (ie, Japanese, Chinese, Korean).²⁵ Since we do not have race-specific BMI cutoffs for each race in our population, the NIH BMI classification was used for consistency among the population. Once race-specific BMI cutoffs are defined, it would be useful to evaluate IUD use by these BMI categories.

BMI misclassification is a potential limitation as self-reported height was used to calculate the patient's BMI if a measured height was not available. Studies have documented that self-reported height and weight provide a reasonable representation of women's BMIs, particularly when BMI is categorized.²⁶ We used BMI on the day of LNG-IUD insertion because, unlike BMIs measured on other days, this BMI could affect the success of IUD insertion. Once the LNG-IUD is inserted into the uterus, a change in the patient's weight does not affect the LNG-IUD's mechanism of action and therefore would unlikely affect continuation and complications.

Table 1. Patient characteristics of women with LNG-IUDs by BMI category					
	Body Mass Index Category				
Characteristics	Normal weight n=55	Overweight n=45	Obese n=49	Total N=149	P-value ^a
Age					.10
≤20	19 (35)	7 (16)	7 (14)	33 (22)	
21-30	22 (40)	23 (51)	25 (51)	70 (47)	
>30	14 (25)	15 (33)	17 (35)	46 (31)	
Marital Status					.06
Single	40 (75)	25 (56)	37 (76)	102 (69)	
Married	13 (25)	18 (40)	11 (22)	42 (29)	
Divorced	0 (0)	2 (4)	0 (0)	2 (1)	
Widowed	0 (0)	0 (0)	1(2)	1(1)	
Insurance					.02
Public	30 (55)	22 (49)	39 (80)	91 (61)	
Private	19 (35)	19 (42)	8 (16)	46 (31)	
No Insurance	6 (11)	4 (9)	2 (4)	12 (8)	
Race					<.01
African American	3 (6)	1 (3)	0 (0)	4 (3)	
American Indian	0 (0)	0 (0)	3 (7)	3 (2)	
Asian	24 (47)	13 (33)	6 (14)	43 (32)	
Caucasian	10 (20)	5 (13)	2 (5)	17 (13)	
Hispanic	3 (6)	1 (3)	1 (2)	5 (4)	
Native Hawaiian	10 (20)	11 (28)	14 (33)	35 (26)	
Pacific Islander	1 (2)	9 (23)	16 (38)	26 (20)	
Parity					.10
0	9 (16)	2 (4)	6 (12)	17 (11)	
1-2	32 (58)	30 (67)	22 (45)	84 (56)	
3 or more	14 (26)	13 (29)	21 (43)	48 (32)	
Previous Abortion					.63
Yes	18 (33)	14 (31)	12 (24)	44 (30)	
No	37 (67)	31 (69)	37 (76)	105 (70)	
Previous Sexually Transmitted Infection					.35
Yes	14 (25)	8 (18)	15 (31)	37 (25)	
No	41 (75)	37 (82)	34 (69)	112 (75)	
Previous Pelvic Inflammatory Disease					.42
Yes	2 (4)	1 (2)	0 (0)	3 (2)	
No	53 (96)	44 (98)	49 (100)	146 (98)	
Reason for IUD Insertion					.29
Contraception	53 (96)	41 (91)	42 (86)	136 (91)	
Menstrual Irregularity	1 (2)	1 (2)	4 (8)	6 (4)	
Both	1 (2)	3 (7)	3 (6)	7 (5)	
Inserting Provider					<.01
Resident	33 (60)	33 (73)	46 (94)	112 (75)	
Attending	16 (29)	10 (22)	3 (6)	29 (20)	
Nurse Practitioner	6 (11)	2 (4)	0 (0)	8 (5)	

Table 1. Patient characteristics of women with LNG-IUDs by BMI category (Con't.)					
More than 6 weeks postpartum					.82
Yes	28 (82)	21 (78)	24 (73)	73 (78)	
No	6 (18)	6 (22)	9 (27)	21 (22)	
Breastfeeding					.58
Yes	18 (67)	15 (79)	20 (71)	53 (72)	
No	9 (33)	4 (21)	8 (29)	21 (28)	

*P-values were determined by Chi-square test. Column percentages may not add up to 100 percent due to rounding.

Table 2. Twelve-month LNG-IUD continuation, Difficult with IUD insertion, and Complications by BMI category					
	Normal weight	Overweight	Obese	Total	P-value ^a
Difficulty with IUD Insertion					.47
Yes	3 (5)	1 (2)	4 (8)	8 (5)	
No	50 (91)	44 (98)	43 (88)	137 (92)	
Failed Insertion	2 (4)	0 (0)	2 (4)	4 (3)	
IUD in place at 12 months					.73
Yes	39 (74)	36 (80)	35 (74)	110 (76)	
No	14 (26)	9 (20)	12 (26)	35 (24)	
Complications					.47
Yes	6 (11)	2 (4)	5 (11)	13 (9)	
No	47 (89)	43 (96)	42 (89)	132 (91)	

*P-values were determined by Chi-square test.

Table 3. Unadjusted and Adjusted OR for 12-month LNG-IUD continuation rates (OR, 95% CI)		
	Unadjusted OR	Adjusted OR*
BMI Category		
Normal weight	Reference	Reference
Overweight	1.34 (0.43-2.57)	1.33 (0.48-3.66)
Obese	0.73 (0.27-1.95)	0.75 (0.29-1.92)

*Adjusted for Age and Insurance. Other confounders (eg, race) were not included in the model because the P-value was $\geq .20$ in bivariate analysis.

The study population was racially diverse with the majority of patients being Asian, Pacific Islander, and Native Hawaiian, which is reflective of Hawai'i's demographics. Although not exactly comparable to our study, Thompson, et al, described the demographic characteristics and the proportion of IUD users in a diverse population in California.²⁷ They found that a smaller proportion of US-born Asian women, compared to other ethnic groups, used intrauterine contraception.

Overall, this is the first known study to evaluate LNG-IUD use by BMI in Asian and Pacific Islander women. Additional studies are needed with a larger baseline population and less loss to follow up. A larger sample will allow for stratification by classes of obesity and other demographic variables and will provide more information on this understudied research topic. Also, to adequately understand IUD effectiveness in preventing unintended pregnancy, we need to collect information on

important potential cofounders such as frequency of sexual intercourse, use of alternative forms of birth control (eg, condoms, female condoms, dental dams, male sterilization), and underlying infertility or other medical conditions. Nevertheless, this study provides estimates of IUD continuation and complications which may inform future research and guide recommendations for its use in the clinical setting.

Conflict of Interest

None of the authors identify a conflict of interest.

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A Case of Wound Infection with *Providencia rettgeri* and Coincident Gout in a Patient from Guam

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Abstract

Providencia rettgeri (*P. rettgeri*) is a ubiquitous organism that is infrequently associated with human disease. Here we report the isolation of this organism from a polymicrobial wound infection resulting from ruptured tophi on a 54-year-old male patient from Guam. We describe the identification and confirmation of this organism, and propose metabolic synergy as a possible mechanism of pathogenesis. To our knowledge, this is the first published report of a wound infection colonized by *P. rettgeri* from Guam, and the first report to speculate upon the role of bacterial synergy in *P. rettgeri* pathogenesis.

Providencia rettgeri (*P. rettgeri*) is a motile, gram-negative rod shaped organism and a member of the *Enterobacteriaceae* family.¹ It is capable of growth on MacConkey agar, capable of catalyzing the dissociation of urea into ammonia and carbon dioxide, capable of deaminating phenylalanine, and capable of producing gas from glucose fermentation. However, most strains are incapable of fermenting lactose, a defining feature of the genus *Providencia*.² The first members of this genus were isolated by Leo F. Rettger of the Sheffield Laboratory at Yale University. These isolations were undertaken as part of an epidemiological investigation into a 1904 fowl cholera epidemic.³ However, the organisms were not characterized until about 1918 when Phillip Hadley performed a cursory evaluation of the genus and proposed the name *Bacterium rettgeri* to refer to an unusual urease producing strain. In 1943, Rustigian and Stuart recommended that *Bacterium rettgeri* be assigned to the genus *Proteus* based on biochemical characteristics.³ However, a series of DNA-DNA hybridization studies by Brenner and others in 1978 demonstrated a clear relationship between certain members of the genus *Proteus* and certain members of the genus *Providencia*. This recognition resulted in the reassignment of *Proteus rettgeri* to the genus *Providencia*.³

The first report of a human infection with *P. rettgeri* was published in 1951. This report, by Goldfarb and De Bakey, described a case of *P. rettgeri*-associated empyema.⁴ Antibiotic resistant strains of this organism were reported as early as 1971. These reports were initiated by Traub, Craddock, and others who reported an outbreak of a lactose fermenting, highly antibiotic resistant strain of *P. rettgeri* among surgical ward patients.⁵ A second large outbreak of *P. rettgeri* (urinary tract infection) was reported by Edwards, and others, in 1974.⁶ Furthermore, this organism had been implicated in the etiology of gastrointestinal illness in 1986, traveler's diarrhea in 2004, and ocular infection in 2006.⁷⁻⁹ It is of interest to note that *P. rettgeri* has been identified as the causative agent of "purple bag syndrome," an unusual and striking condition in which purple-tinted urine is produced as a result of bacterial enzymatic activity.¹⁰ A 2014 report on the isolation of *P. rettgeri* from a cluster of surgical

infections in Nepal illustrates the presence and significance of this organism in the Asia-Pacific region.¹¹ With regard to antimicrobial susceptibility, *P. rettgeri* is typically resistant to gentamicin and tobramycin but susceptible to amikacin. There have been reports of extended spectrum beta lactamase (ESBL) producing *P. rettgeri* in Eastern Europe and New Delhi, and metallo-beta lactamase (NDM-1) producing *P. rettgeri* isolates in South America and Asia.¹¹⁻¹⁵

We describe a case of an ampicillin-resistant *P. rettgeri* wound infection coincident with tophaceous gout in a polymicrobial wound on a patient from Guam. This is the first published report of this organism in association with gouty tophi. This report may represent a sentinel case that indicates the presence of an antibiotic-resistant, human-colonizing strain of *P. rettgeri* circulating in the Marianas and it may represent the first indication of this organism participating in a synergistic relationship with other bacterial species colonizing a wound site.

Case Report

A 54-year-old man from Guam with no significant travel history, no indication of insect bites, or immunosuppression, and a medical history significant for hypertension, chronic kidney disease, and tophaceous gout was referred to our facility due to the presence of multiple wounds resulting from ruptured tophi, and worsening symptoms. Upon presentation, the wounds were found on the left shin. A punch biopsy was performed and samples were sent to the laboratory for histological analysis and bacterial culture. Histology was negative for neoplasm and bacterial isolate analyses utilizing the Vitek 2 (bioMérieux, Hazelwood MO) phenotypic identification system revealed the presence of 2+ *Staphylococcus aureus* (*S. aureus*), 2+ *Pseudomonas aeruginosa* (*P. aeruginosa*), and 2+ *P. rettgeri*.¹⁶ Due to the fact that *P. rettgeri* is an unusual cause of wound infection, the identity of this isolate was confirmed by matrix-assisted desorption/ionization time of flight mass spectrometry using the Vitek MS (mass spectrometry) system.¹⁷

Sensitivity studies revealed that the isolate was resistant to ampicillin, ampicillin/sulbactam, cefazolin, gentamicin, and trimethoprim/sulfamethoxazole. It was found to be susceptible to ceftriaxone, cefepime, ciprofloxacin, and piperacillin/tazobactam. The patient was initially treated with clindamycin (300mg QID x 10 days) and ciprofloxacin (500mg BID x 10 days) to cover both gram negative and gram positive pathogens as the *Pseudomonas* isolate was susceptible to ciprofloxacin and the *Staphylococcus* isolate was susceptible to clindamycin. Local wound care was initiated with topical polymem silver foam. This treatment was continued daily. At 10 days post-

presentation, creatinine levels were elevated to 2.09 mg/dl and potassium levels were elevated to 5.7 mEq/L. The patient also complained of diarrhea. He was therefore advised to stop both ciprofloxacin and clindamycin therapy. Topical treatments with polymyx silver foam were continued. At this time, his wounds were greatly improved and without signs of active infection. At a two week follow-up, the initial wounds were in a state of resolution and repeat cultures were positive only for an antibiotic sensitive strain of *Pseudomonas aeruginosa* and *Corynebacterium* species (most likely representing a skin contaminant). These results suggest that the abbreviated antibiotic therapy in combination with the topical application of polymyx silver foam was effective in eliminating both *Providencia* and *Staphylococcus* infections and that it was sufficient to initiate the process of wound resolution.

Discussion

Wound infections with *P. rettgeri* are rarely reported in the literature. To date, there has been no confirmed association between *P. rettgeri* and tophaceous gout. A PubMed search using the Boolean search terms “wound” and “*Providencia rettgeri*” yielded only seven results.¹⁸ Three of those were in reference to the flora recovered from snakes and snake bites, one was in reference to horse wounds, two were a study of the attraction of certain insects to volatile compounds released from wound infections, and one was a study on catheter-associated urinary tract infections.¹⁹⁻²⁵ In contrast, a search using the Boolean search terms “wound” AND “*Staphylococcus*” yielded 7,375 results, the majority of which were directly related to skin and soft tissue infection.²⁶

The fact that *P. rettgeri* is not often associated with wound infection is rather surprising given that this is an organism with an almost ubiquitous presence in the environment. It has been isolated from such diverse locations as fresh water sources, run-off wastewater, and explosive-contaminated soil.^{27,28} In addition, this organism has been found living as either a commensal or a pathogen in several invertebrate and vertebrate species including the fruit fly (*Drosophila melanogaster*), the Black Cobra (*Naja naja karachiensis*), the snake *Bothrops jararaca*, and several species of waterfowl, horses, and alligators.^{19-22,30-32} Interestingly, screwworm flies (*Calliphoridae*) appear to be attracted to organic compounds generated by fresh cultures of *P. rettgeri* indicating that mechanical vector transmission may be possible.^{23,24}

In the present case, it is unclear where the organism was acquired. However, it is significant that the patient had a history of tophaceous gout and presented in the clinic with multiple ruptured tophi. Superinfection of gouty tophi is a well-known complication of the condition and it is one of the most common reasons for surgical intervention.³³ It is possible that *P. rettgeri* was inoculated into ruptured tophi during water or soil exposure. It is also possible that prior colonization with *Pseudomonas* and *Staphylococcus* set the stage for *P. rettgeri* superinfection by triggering local attenuation of the immune response and by initiating the formation of a protective biofilm. However, given

that the pathophysiology of gout involves the accumulation of uric acid crystals at the site of tophi formation, the fact that *P. aeruginosa* produces urate oxidase, which initiates the hydrolysis of uric acid to urea and the fact that *P. rettgeri* is capable of the hydrolysis of urea to ammonia and carbon dioxide, it is tempting to speculate that the colonization of a site with multiple tophi was the result of a urea-based chemotactic response initiated by the degradation of uric acid by *P. aeruginosa*.³⁴⁻³⁶ Indeed, certain strains of *Helicobacter pylori* have shown both a urease dependent and a urease independent chemotactic response to urea.³⁶⁻³⁸

If the local decomposition of uric acid to urea initiated by *P. aeruginosa* was sufficient to drive secondary colonization by *P. rettgeri*, the decomposition of urea to ammonia by this organism may have been partially responsible for the tissue damage at the wound site. Indeed, scenarios in which pathogenesis is augmented by metabolic synergy has been described for several oral pathogens and such a scenario would explain the initiation of wound resolution following the antibiotic-mediated elimination of *P. rettgeri*.^{39,40} However, further studies will be required to determine whether *P. aeruginosa* and *P. rettgeri* synergize *in vivo*, whether this activity increases pathogenesis and whether this activity is accelerated in cases of gout.

The contribution of *P. rettgeri* to the pathology of wound infection has yet to be determined. It is often difficult to differentiate between those organisms that merely colonize a wound site and those organisms that are truly pathogenic.⁴¹ No definitive virulence factors have been described for *P. rettgeri*. Nonetheless, there is mounting evidence to suggest that, under certain conditions, urease can act as a general virulence factor.⁴² The reported toxicity of bacteria-produced ammonia to epithelial cells supports the notion of wound-site pathology catalyzed by bacterial urea and uric acid degradation.^{42,43} This hypothesis is especially attractive with respect to the present case, given the role of uric acid in the pathology of gout, the ability of *P. aeruginosa* to decompose uric acid, and the ability of *P. rettgeri* to convert the resulting end products to ammonia. A 2001 report by Murray and Comeau describes a case of hyperammonemia resulting from a *P. rettgeri* infection.⁴³⁴ This case was so severe that the patient suffered a coma that only resolved with the elimination of *P. rettgeri* by antibiotic therapy.³⁶ This report clearly demonstrates that the urease activity of *P. rettgeri* is significant, and that it is capable of altering clinical outcomes.

Conclusion

Although *P. rettgeri* is rarely reported as the sole cause of wound infection, the isolation of this organism from a wound site should not be summarily dismissed. *P. rettgeri* maintains two traits that may serve to aggravate tissue injury. These are the possession of antimicrobial resistance mechanisms and the ability to produce ammonia from urea. Either of these traits can potentially influence the ecology of the wound site and alter the kinetics of wound healing. In the present case, antibiotic therapy appeared to eliminate both the *P. rettgeri* infection and the *S. aureus* infection and elimination of these two organisms

appeared to correlate with the initiation of wound resolution. Despite the fact that *P. rettgeri* is a known producer of ammonia, it is impossible to determine the extent to which this organism contributed to overall wound pathology. A greater understanding of the pathophysiology of *P. rettgeri* (including the role of metabolic synergy as a mechanism of virulence) will be required to develop the means to reliably discriminate between cases of colonization versus cases of infection, to identify and eliminate bacterial synergy, and to facilitate the development of proper treatment guidelines.

The views expressed in this manuscript are those of the authors and do not reflect the official policy or position of the Department of the Army, Department of Defense, or the US government.

Conflict of Interest

None of the authors identify a conflict of interest.

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MEDICAL SCHOOL HOTLINE

Liaison Committee on Medical Education Accreditation: Part II: The Graduation Objectives

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An essential accreditation requirement of the Liaison Committee on Medical Education, is Standard 6: *"The faculty of a medical school define the competencies to be achieved by its medical students through medical education program objectives and is responsible for the detailed design and implementation of the components of a medical curriculum that enables its medical students to achieve those competencies and objectives. The medical education program objectives are statements of the knowledge, skills, behaviors, and attitudes that medical students are expected to exhibit as evidence of their achievement by completion of the program."*¹ The program objectives must be defined in outcome-based terms that allow the assessment of medical students' progress, and are made known to all medical students, faculty, residents, and others with responsibility for medical student education and assessment.

In June 2008, the John A. Burns School of Medicine (JABSOM) Curriculum Committee developed the current set of institutional graduation objectives. The committee took into account objectives and competencies defined by the Association of American Medical Colleges (AAMC) in 1998 and the Accreditation Council for Graduate Medical Education (ACGME) in 1999. The former stated the learning objectives for undergraduate medical student education, aimed to elucidate the essential attributes needed by physicians to fulfill their duties to society.² These essential attributes are:

- Physicians must be altruistic.
- Physicians must be knowledgeable.
- Physicians must be skillful.
- Physicians must be dutiful.

The ACGME stated the following general competency categories to guide medical schools to prepare graduates³:

- Patient care
- Medical knowledge
- Practice-based learning and improvement
- Interpersonal and communication skills
- Professionalism
- System-based practice

These graduation objectives were communicated with the broader community through the Hawai'i Medical Journal.⁴ Since then, the Curriculum Committee has annually reviewed these objectives, with the last review in March 2015. This article outlines JABSOM's Graduation Objectives and describes how they are used by faculty to monitor student progress. These objectives and detailed evaluation indicators can be found on the JABSOM website.⁵

The JABSOM Graduation Objectives are organized under the following seven major headings:

1. Life-Long Learning Skills

*JABSOM graduates are life-long learners who are capable of identifying their learning needs, searching for and retrieving biomedical information, critically appraising this information and applying it appropriately to patient care.*⁴

This objective is assessed by the student "achieving a grade of 'credit' in all required courses and 4th year electives, and achieving a satisfactory evaluation in all Pre-clerkship PBL tutorials and the Triple Jump Examination."⁵ (The Triple Jump Examination evaluates competency in the problem-based learning (PBL) process).

2. The Biological Sciences

*JABSOM graduates will be able to apply the biological sciences to the practice of medicine. They can explain normal structure and function of each major organ system and alterations that occur in various illnesses.*⁴

Successful completion of this objective is "measured by achieving a grade of 'credit' in all required courses and 4th year electives, and achieving a passing score on the USMLE Step 1 Examination."⁵

3. The Care of Patients

JABSOM graduates care for their patients by applying clinical reasoning and problem-solving skills in performing a complete or

*organ-specific history and physical exam, ordering appropriate diagnostic tests, performing procedural skills under appropriate supervision, and developing an appropriate therapeutic plan.*⁴

Successful completion of this objective is “measured by achieving a grade of ‘credit’ in all required courses and 4th year electives, and achieving a passing score on the MDED 541 Comprehensive Clinical Skills Assessment, the USMLE Step 2 Clinical Knowledge Examination and the USMLE Step 2 Clinical Skills Examination.”⁵

4. Oral and Written Communication Skills

*JABSOM graduates will communicate effectively by greeting their patients warmly, eliciting relevant information, understanding their perspective, responding to their feelings, educating them about their condition, and explaining further management.*⁴

This objective is assessed by the student “achieving a grade of ‘credit’ in all required courses and 4th year electives, and achieving a passing score on the MDED 541 Comprehensive Clinical Skills Assessment, the USMLE Step 2 Clinical Knowledge Examination and the USMLE Step 2 Clinical Skills Examination.”⁵

5. Populational and Community Health

*JABSOM graduates contribute to the health of communities by applying their knowledge of the epidemiology of disease, non-biological determinants of health, common biostatistical tools, and important public health measures in their role as physicians.*⁴

Successful completion of this objective is “measured by achieving a grade of ‘credit’ in all required courses and 4th year electives, and achieving a passing score on the MDED 541 Comprehensive Clinical Skills Assessment, the USMLE Step 2 Clinical Knowledge Examination and the USMLE Step 2 Clinical Skills Examination.”⁵

6. Professionalism

*JABSOM graduates are professional and ethical. They act with integrity, altruism, respect, and accountability while delivering compassionate care to their patients.*⁴

This objective is assessed by the student “achieving a grade of ‘credit’ in all required courses and 4th year electives, and achieving a passing score on the MDED 541 Comprehensive Clinical Skills Assessment, the USMLE Step 2 Clinical Knowledge Examination and the USMLE Step 2 Clinical Skills Examination.”⁵

7. Personal Health and Well-Being

*JABSOM graduates know how to maintain their personal health and well-being and can state strategies to cope with stress and access resources available for treating depression, substance abuse, and other forms of physician impairment.*⁴

This objective is measured by the students’ “creation of a personal health and well-being plan for the preclerkship, clerkship, and postgraduate periods of their medical education and the

ability to role play safety and wellness practices in the clinical setting.”⁵ For the latter, students are observed applying skills such as debriefing critical incidents and trained to recognize potentially unsafe patient encounters.

Incoming medical students are informed of the program objectives during orientation week. They are displayed prominently on posters lining the hallway leading to classrooms on the third floor of the Medical Education Building. Similar posters are displayed at JABSOM clinical departments. The graduation objectives are also placed on the JABSOM website, within the “General Guide to the MD Program,” and in course handbooks. Finally, all JABSOM course and clerkship student evaluation forms contain rating items that reflect the graduation objectives, providing further reinforcement for faculty and students.

Courses have learning objectives aligned with the graduation objectives that advance students towards their achievement. The following, excerpted from the MDED 552 (Cardiovascular and Pulmonary Problems) handbook for first year medical students, illustrates the course objectives that are aligned with Professionalism.

OBJECTIVE 6: MDED 552 students will be professional and ethical, demonstrate an enthusiasm for medicine, and value honor, integrity, altruism, respect, accountability, excellence, scholarship, and leadership while delivering compassionate care to their patients.

Students will exhibit the highest standards of professional and ethical behavior by demonstrating to the satisfaction of faculty:

- A. Knowledge of the theories and principles that govern ethical decision-making including those related to the major dilemmas in medicine, with special attention to:
 - Ethical issues surrounding gifts from patients
 - Refusal of blood transfusions
 - Dealing with medical errors
 - Physician-assisted suicide
 - Leaving against medical advice
- B. The ability to interact with patients such that each patient feels they have been treated by a compassionate and competent physician in whom they trust, with special attention to:
 - Writing a condolence letter
- C. Respect for others, honesty, integrity and an absence of arrogance, rudeness, and coercion in all interactions with patients, their families, colleagues, and others with whom physicians must interact with in the practice of medicine.
- D. Altruism and a commitment to advocate at all times for the interests of one’s patients over one’s own interests, with a special attention to:
 - The physician’s duty to care for patients with infections even if it increases their chances of getting a deadly illness
- E. A professional appearance and demeanor.
- F. Self-awareness of personal limitations and the need for life-long learning.
- G. Performance that continually improves as a result of honest self-reflection and an openness to feedback.
- H. Punctuality and the completion of assignments, duties, surveys, forms, immunizations, and other school and professional requirements on a timely basis.
- I. A willingness to teach and support others.

On an annual basis, the JABSOM Curriculum Committee reviews both internal and external outcomes that reflect student achievement of the graduation objectives and the overall quality of the educational program.^{6,7} The JABSOM Program Evaluation plan consists of a set of specific surveys.

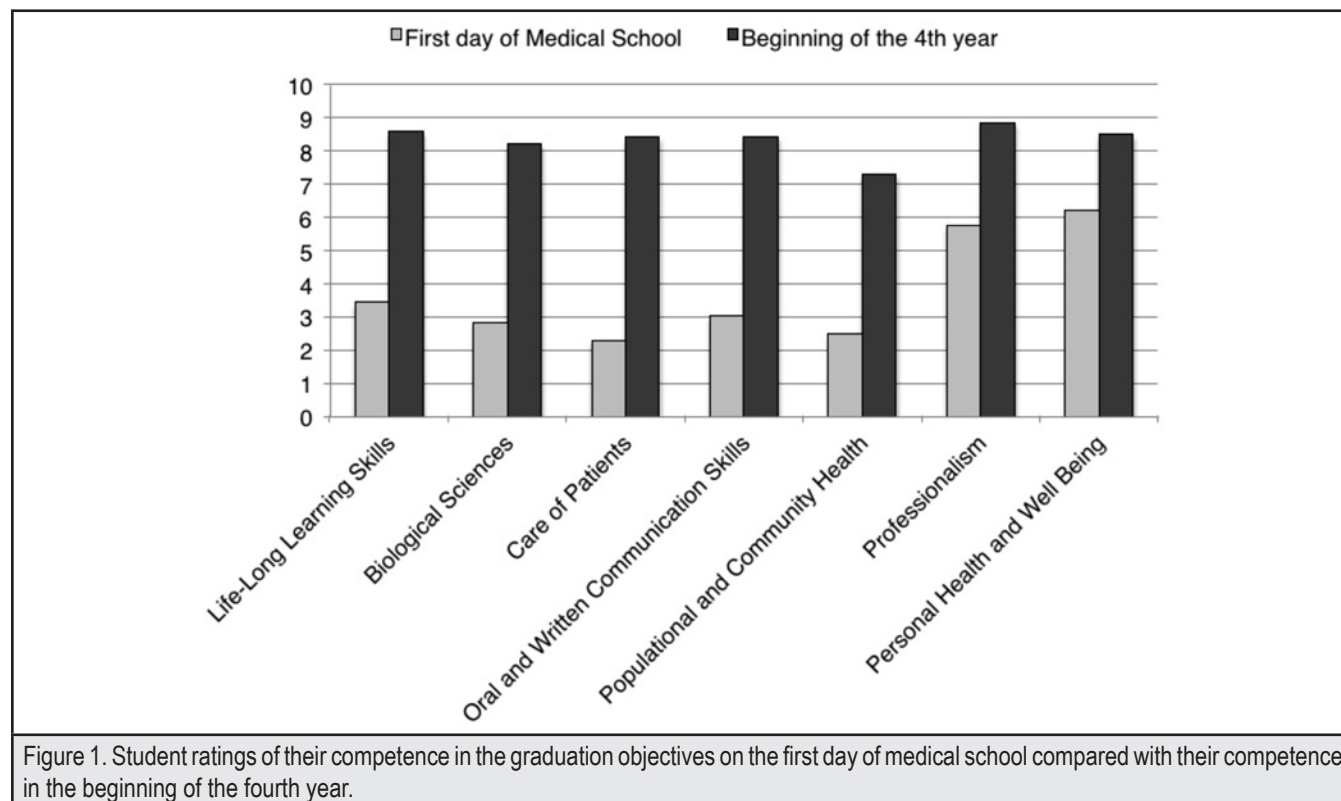
- Students complete surveys of all required courses and segments of the curriculum.
- The “Intern Survey” asks JABSOM graduates nearing the end of their intern year, how well their education prepared them for residency training.
- The “Program Director” survey asks residency program directors supervising JABSOM graduates how well they performed in comparison to residents who graduated from other schools.
- The “Alumni Survey” asks JABSOM graduates to reflect on the value of their education six years after graduation.
- The Curriculum Committee monitors student responses on the AAMC Graduation Questionnaire completed by all graduating seniors.
- Internal reviews of required courses and clerkships occur every three years that incorporate LCME accreditation standards serve a valuable peer-review purpose for educational quality improvement.

Whenever a deficiency or concern is identified in any survey, a quality improvement plan is initiated and monitored by the Curriculum Committee. JABSOM also monitors student per-

formance in the National Resident Matching Program, board certification of graduates, and other outcomes that measure program quality.

The information collected to date indicate that JABSOM students are successful in achieving the school’s Graduation Objectives.

- The average score of JABSOM students on the USMLE Step 1 Exam has exceeded the national average in nine of the last ten reported years (2005-2014).
- All JABSOM graduates pass an internally-developed standardized patient exam assessing their clinical skills.
- JABSOM students are successful in obtaining competitive residency positions in a variety of specialties through the National Resident Matching Program.
- The percentage of JABSOM students who strongly agreed or agreed with the statement, *Overall I am satisfied with the quality of my medical education* on the AAMC Graduation Questionnaire exceeded the national average for all schools in nine of the last eleven years (2005-2015).
- All JABSOM graduates, in the Class of 2013, responded either *Good* or *Excellent* on the Intern Survey when asked to rate their preparation *To provide competent medical care to my patients*.
- For the Class of 2013, 97% of the Program Directors (32/33) responded *Good* or *Excellent* when rating JABSOM graduates as *Providing competent medical care to patients*.



At the beginning of their senior year, students complete a survey to ascertain how well JABSOM's Graduation Objectives are being met. Sixty-two items from the Graduation Objectives are rated on a ten point scale on which 1 = "Not at all" to 10 = "Very much". In addition students are asked to think back to "Day 1" at JABSOM and rate the same items. A composite of the findings from the Class of 2012 is presented in Figure 1.

There were gains in all seven graduation objectives as rated by the students, and items that pertained to medically-specific objectives had the largest increases (objectives 1-5), while interpersonal items had smaller increases (objectives 6-7).

Summary

JABSOM's graduation objectives have seven years of proven success since they were first developed in 2008. These objectives serve as the organizing principles for curricular content, student evaluations, and program assessment. The school's Curriculum Committee and its sub-committees monitor student achievement of the objectives as a measure of program quality. Outcome data to date suggest that JABSOM students meet the objectives of the medical school curriculum and are prepared to undertake the challenges of their chosen profession as physicians.


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INSIGHTS IN PUBLIC HEALTH

For the Love of Data! The Hawai'i Health Data Warehouse

Julia Chosy PhD; Katherine Benson; Dulce Belen; Ranjani Starr MPH;
and Tonya Lowery St. John MPH

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

Abstract

Data form the framework around which important public health decisions are made. Public health data are essential for surveillance and evaluating change. In Hawai'i, public health data come from a multitude of sources and agencies. The Hawai'i Health Data Warehouse (HHDW) was created to pull those data into a single location and to present results in a form that is easy for the public to access and utilize. In the years since its creation, HHDW has built a second consumer-focused web site, Hawai'i Health Matters, and is now introducing new functionality on the original site that allows users to define their own enquiry. The newly adopted Indicator-Based Information System (IBIS) uses a web interface to perform real-time data analysis and display results. This gives users the power to examine health data by a wide range of demographic and socioeconomic dimensions, permitting them to pinpoint the data they need.

Keywords

Public health data, BRFSS, YRBS, PRAMS, Vital statistics, Indicator-based information system

Introduction

In public health, there's no denying that data are critical. Not only do public health data inform practitioners, researchers, and policy makers about the health of the community, they also monitor trends, identify prevention targets, and provide a baseline against which to measure change. Public health data can be used to assess healthcare costs and to identify the largest causes of morbidity and mortality among a specific group. The data can also be used to characterize determinants of health, such as behavioral, social, and environmental factors. With this information, actions can be taken to help individuals live longer, healthier lives.

There are many sources of public health data, including surveys, hospital records, and vital statistics. However, finding specific data can be a complicated task. Even within a single organization, there may be many different data streams. Unfortunately, they frequently remain in separate silos, often based on ownership of the data. These silos can sit around gathering dust and helping no one simply because the person who needs the data doesn't know they exist.

If public health data were more accessible to people like researchers, policy makers, and students, there would be a larger return on investment and a greater chance for discoveries resulting in better health outcomes. In addition to making them accessible, public health data need to be easy to find and use. There can be a great deal of complexity when working with data, especially if the user wants to compare different data sources or incorporate multiple years of data for more robust estimates. For example, a survey question's wording may change, requiring a close examination of the data to determine if the item can be trended over time or if a new variable must be made. In some surveys, the same question may have different variable names depending on the year of collection. In this case, great care must be taken to correctly combine multiple years of data. Furthermore, if the data sources are from different sources, multiple data sharing agreements would need to be processed. It can take a considerable amount of time for an individual to receive and prepare the data he or she wants. In an effort to bring together these silos into a one-stop data shop and to standardize the data for ease of use, the Hawai'i Health Data Warehouse (HHDW) was formed.

Hawai'i Health Data Warehouse

In 2004, the Hawai'i Health Data Warehouse (HHDW) was created through a collaboration between the Hawai'i State Department of Health (DOH) and the University of Hawai'i at Manoa's John A. Burns School of Medicine (JABSOM). Currently, it is affiliated with DOH and the Office of Public Health Studies at the University of Hawai'i at Manoa. The goal of its creation was to build a centralized source of public health data for the state of Hawai'i, making it easier for people to find and use the data so essential for understanding the health of our residents. This involved gathering all the data, identifying and addressing changes to the surveys over time, and conforming the data so users can make better comparisons across datasets. Once the data warehouse was created, the next step was building a web site, HHDW.org, to disseminate the data to the public.

In addition to managing these data, HHDW was tasked with monitoring the progress of the state toward the *Healthy People 2010* goals established by the U.S. Department of Health and Human Services. As time progressed, HHDW advanced to track the *Healthy People 2020* (HP2020) goals.

HHDW currently pulls data from six state and national sources within the DOH, including some that had not previously been available to the public (Table 1). In its original configuration, the HHDW web site provided data in the form of static PDF documents. Users could search the data by category or topic and pull reports across all the data sources, or search by topic within a specific data source. The HHDW web site continues to evolve and now contains a separate section that displays data for the HP2020 objectives, by category. Additionally, two series of reports have been created that focus on the HP2020 Leading Health Indicators (LHI), which are objectives considered to be high-priority health issues in the country. Each series of 10 reports displays multiple indicators around a given topic area, such as access to health care or tobacco use. One series presents the data for the state and each of the four major counties, while the second shows the data by race-ethnicity for four major groups represented in Hawai'i (Native Hawaiian, Japanese, Filipino, and Caucasian).

All downloadable PDF reports have a trend page that shows the data values over the previous years and data tables with each year of data broken out by a range of demographic and socioeconomic dimensions. For example, the report for the prevalence of diabetes among adults gives the data by state, county, island, community, age group, race-ethnicity, gender, education, employment, income, poverty level, marital status, and health care coverage. Youth reports are broken out by state, county, gender, race-ethnicity, and grade level, and the pregnancy-related reports include additional dimensions such as birthweight, infant gender, tobacco usage, and participation in Women, Infants, and Children Special Supplemental Nutrition Program (WIC).

While these reports are incredibly data-rich, they can also be lengthy and cumbersome for users to gather the specific data they need. They also lack the contextual information that can help newer users navigate public health data. For these reasons,

HHDW decided to create a second web site that would be more user-friendly and provide contextual information along with data.

Hawai'i Health Matters

HawaiiHealthMatters.org (HHM) was launched in 2008 with data from the six sources in HHDW. As time progressed, data were pulled from additional sources to give a broader view of public health in the state. Currently, HHM contains over 450 health indicators from 39 different data sources. Depending on the source, the data may also be shown by county and by some demographic factors. Contextual information and links to additional resources make HHM more meaningful to the general public. In addition to the health data, HHM also houses a report center, socio-needs index, and a nationwide collection of promising practices and funding opportunities.

HHM also offers data trackers to monitor the state's movement toward established goals. The Healthy People 2020 tracker on HHM is following the progress of Hawai'i on over 300 HP2020 objectives. The Chronic Disease Prevention and Health Promotion Division of the Hawai'i DOH currently has trackers for two of the state plans: the Hawai'i Physical Activity and Nutrition Plan and the Hawai'i Asthma Plan. Additional trackers, such as the Hawai'i Tobacco Use Prevention and Control Plan, are forthcoming.

Although HHM provides data and resources in a more user-friendly format, HHDW wanted to make it easier for users to find and explore data specific to their needs. One limitation of the original HHDW web site was that the user could not look at a health indicator by more than one dimension at a time. For example, a researcher might want to look at asthma among women living below the poverty line. On the public web site, this person could only determine the prevalence of asthma among women or among all persons below the poverty line, but not the intersection of both. At this time, these data can only be obtained by sending a data request through the web site. A HHDW staff member can then fulfill the specific request using the record-level data stored on a private, secured server. Growing use of the web sites and a rapidly increasing number of data requests received through HHDW supported the idea that there

Table 1. Data sources available through HHDW.

Behavioral Risk Factor Surveillance System (BRFSS) ■ Health-related behaviors, chronic health conditions, and use of preventive services among adults.
Hawai'i Health Survey (HHS) ■ Health and socio-demographic conditions among residents of Hawai'i.
Pregnancy Risk Assessment Monitoring System (PRAMS) ■ Maternal attitudes and experiences before, during, and shortly after pregnancy.
Vital Statistics ■ Births, deaths, infant deaths, fetal deaths, and intentional terminations of pregnancy (ITOPS).
Youth Risk Behavior Survey (YRBS) ■ Health risk behaviors among youth that contribute to the leading causes of death and disability.
Youth Tobacco Survey (YTS) ■ Attitude, exposure, and use of tobacco products.

was a need for these data to be more readily available (Table 2). Between 2013 and 2014, visits to the web sites increased by over 60% and the number of data requests nearly doubled. In response, HHDW began to explore options for creating a more interactive web site that would give users the flexibility and freedom to examine the data by their parameters of interest. After researching existing possibilities and gathering information from users and stakeholders, HHDW adopted the Indicator-Based Information System for Public Health (IBIS-PH).

Table 2. Usage statistics for HHDW.org and HawaiiHealthMatters.org (HHM) from October 1, 2014, to September 30, 2015.		
Metric	HHDW	HHM
Unique visitors	9,000	18,400
Visits	15,300	26,000
Page views	62,000	74,600
Data requests	123	NA

Data acquired with Google Analytics. NA- Not Applicable; data requests are only received through HHDW.

Hawai'i-IBIS

IBIS-PH, or simply IBIS, is a set of open-source, license-free applications originally created by the Utah Department of Health, with funding from the Centers for Disease Control and Prevention (CDC). The IBIS query system is based on Statistical Analysis Software (SAS) and provides a web interface that allows users to do real-time SAS data queries. As of October 2015, IBIS has been adopted by 9 states and 2 Federal agencies, including the National Center for Health Statistics (NCHS). The IBIS Community of Practice, comprised of adopters, works to continually improve the software and address users' concerns. Staff of HHDW have become contributing members of the community since HHDW adopted the software.

The power of IBIS comes from its user interface, which allows the user to select a number of parameters for the data they are examining (Figure 1). Once a health indicator has been chosen (eg, alcohol use, colorectal cancer screening, or body mass index), IBIS presents a range of possible filters so the user can access the exact data he or she is seeking. In Hawai'i-IBIS, these filters include:

Query Builder for Hawaii's Behavioral Risk Factor Surveillance System (BRFSS) Data - Asthma - prevalence

Use the following optional steps to modify your query and to select how to display your results.

When you are finished, click the "Submit" button below to see your modified query result.

Step 1: INDICATOR: Have you ever been told by a doctor or other health professional that you had asthma?; Yes versus No.
(Yes)

+

Step 2: TIME PERIOD: Select Year
(2013, 2012, 2011)

+

Step 3: GEOGRAPHIC AREA: NOTE: Only the County geographic area will produce a map

+

Step 4: POPULATION: Select age group(s)

+

Step 5: POPULATION: Select sex

+

Step 6: POPULATION: Select other demographic characteristics

+

Step 7: How to display the data
(Grouped By: Geography, Chart: Horizontal Bar, Map: Default)

+

Submit

Reset

Figure 1. Hawai'i-IBIS user interface displaying filter options for data queries.

Year

- The default query shows an aggregated report of all available years of data. Users may select individual years or a combination of years resulting in an aggregated report.

Geography

- The default query shows the data for the state and the four major counties of Hawai'i. Depending on the data source, users may also look at the data by the 6 major islands, 23 communities based on zip code groupings, or 40 school area complexes.

Age

- The default query shows the data for all ages. However, the age filter includes five additional options for age groupings.

Sex

- The default query shows the data for both genders; this filter allows users to examine the data by males or females separately.

Other

- The default query shows the data for all individuals. But the filters available in this section offer a wide variety of demographic and socioeconomic dimensions. Depending on the data source, there are up to 3 different race-ethnicity groupings: Census categories (6 options), DOH categories (10 options), or Program categories (36 options). This section also includes filters for education, employment, income, marital status, sexual orientation, and health care coverage. As HHDW continues to build out the system, other options will be added.

Hawai'i-IBIS also offers multiple ways to display the results from a query. The default query returns a horizontal bar chart for the counties, a data table, and (where available) a map. There are multiple options for the chart type, including the option to group and display the data by selected dimensions. The 'Display by' option allows the user to display the data by a given dimension. For example, choosing 'Sex' would result in a chart and data table displaying the information for males and females separately. An additional 'Group by' feature allows the user to

choose a second dimension, such as 'Age Group'. In this case, the user would receive a chart and table data displayed by gender and age group. With the multitude of options available, users can tailor their queries to exactly what they need. Once they have what they want, they can export the data to Excel or use a screen grab to make an image of the chart or map. In addition to this impressive dynamic data query system, Hawai'i-IBIS also provides static resources, including information on basic statistical and epidemiologic concepts, a system tutorial, and guides on interpreting data.

In summary, HHDW offers three ways to access public health data directly: through the data-heavy, detailed HHDW.org; through the more-compressed data and contextual content of the HawaiiHealthMatters.org; or through the interactive query and reporting capability of the Hawai'i-IBIS application. HHDW also continues to respond to individual requests for data and on-site or on-line demonstrations of the web sites.

Future Directions

Currently, Hawai'i-IBIS only contains a subset of data from the Behavioral Risk Factor Surveillance System. However, HHDW established a plan to continue adding new indicators and data sources to Hawai'i-IBIS. As the Hawai'i-IBIS application expands, the PDF reports on the main HHDW web site will no longer be necessary and will be removed. In the future, HHDW will also evaluate new data sources for inclusion into the warehouse and into the Hawai'i-IBIS application.

HHDW hopes to continue receiving suggestions and feedback from its users and the public, so it can continue to improve and be a valuable resource for public health practitioners, researchers, policy makers, and community groups. Please take a look at these valuable resources for health data in Hawai'i: HHDW.org and HawaiiHealthMatters.org.

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Hepatitis C in 2015: Recent Advancements and Current Challenges

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Background

Approximately 130–170 million people worldwide are infected with chronic hepatitis C virus (HCV).¹ Of those infected, 3.2–3.7 million reside in the United States, or approximately 1.3% of the population.^{1,2} Furthermore, up to 75% of individuals who are infected with the virus are unaware of their infection.³ Hepatitis C virus is the most common blood-borne infection in the United States and will infect and kill more patients than those affected by the human immunodeficiency virus (HIV).⁴ Risk factors for transmission of HCV include previous injection drug use, receipt of blood transfusions or solid organ transplants before 1992 or clotting factors before 1987, hemodialysis, and being born to a HCV-positive mother. In 2012, the Centers for Disease Control and Prevention (CDC) recommended that all patients born from 1945–1965, regardless of risk factors, should receive a one-time screening for HCV. This specific birth cohort was selected because approximately 75% of all HCV-infected patients were born during those years.³ Currently, HCV is the leading cause of end-stage liver disease, liver-related death, and hepatocellular carcinoma in the United States. Unlike hepatitis A or B, there is no vaccination to protect against hepatitis C infection.⁵

Six genotypes of HCV have been identified, with genotype 1 (GT 1) accounting for approximately 75% of HCV infections in the United States, followed by genotypes 2 (GT 2) and 3 (GT 3), which represent about 20%.⁴ In Europe, genotypes 1–3 are also most common, while genotype 4 (GT4) is found primarily in the Middle East, genotype 5 (GT5) in South Africa, and genotype 6 (GT6) in Asia.

Within genotype 1, there are sub-genotypes 1a and 1b, with 1a being harder to treat, comparatively. Genotypes 2 and 3 are historically “easier-to-treat” than genotype 1, however studies have demonstrated that patients with GT3 may have lower response rates compared to patients with GT2.⁶ In addition to treatment response variability based on genotype, several other factors may increase the risk for treatment failure. Such characteristics include patients who have failed previous treatment attempts, those with advanced liver disease, and those with comorbidities, such as advanced kidney disease or co-infection with HIV. Patients with these characteristics have traditionally been classified as “harder-to-treat.”

Chronic HCV infection progresses slowly, with complications of the virus often taking several decades to be clinically manifest.⁵ Therefore, conducting clinical trials that identify disease-related morbidity and mortality as a primary outcome would be unrealistic given the time required to reach these outcomes. Instead, conducting efficacy and safety trials for HCV agents that achieve a sustained virologic response (SVR) is deemed acceptable by regulatory agencies that decide on approvals of upcoming therapies. Historically, SVR has been defined as the absence of HCV RNA in the blood 24 weeks after completion of therapy. Recently, however, there has been data to support measuring an SVR as early as 12 weeks after the completion of therapy. Reporting data on what is referred to as an “SVR12,” to indicate measurements recorded 12 weeks after the completion of therapy, is considered an appropriate primary endpoint for drug companies seeking regulatory approval for new HCV therapies.⁷ Achieving an SVR has demonstrated a reduction in mortality in those infected with HCV and is considered curative.^{8,9}

In the past several years, there has been an increasingly heightened focus on drug research and development for new HCV agents. This trend is prompted by the emerging liver-related complications of those who have now been infected with HCV for several years or even decades as well as the increasing need for treatment options that are effective with minimal adverse effects. This review article identifies the progress that has been made in hepatitis C treatment options and discusses the challenges that patients with HCV continue to face.

List and Definitions of Abbreviations	
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
GT	Genotype
SVR	Sustained virologic response
CYP450	Cytochrome P450 enzymes
NS3/4A protease	Protease required for hepatitis C viral replication
NS5B polymerase	Polymerase required for hepatitis C viral replication

History of Treatment Options

Table 1 provides a synopsis of previously and currently approved HCV treatment options.

Prior to 2011, the first-line treatment of HCV was dual-therapy with ribavirin, an oral capsule dosed twice daily, and polyethylene glycol encapsulated interferon (peginterferon), a once weekly subcutaneous injection.⁵ Ribavirin works by inhibiting the replication of viral RNA and DNA and has also demonstrated efficacy against influenza and adenoviruses.¹⁰ Peginterferon has antiviral and immune-regulating activity and was historically also been used to treat hepatitis B infections in addition to HCV.^{11,12}

For the treatment of HCV, the duration of therapy with ribavirin and peginterferon was 24 or 48 weeks, depending on the genotype being treated.⁵ In addition to long treatment durations, a number of significant adverse events posed medication adherence challenges. Peginterferon has been associated with flu-like symptoms, depression, anxiety, alopecia, neutropenia, thrombocytopenia, and several other significant adverse reactions. Ribavirin frequently leads to the development of anemia, which may require treatment with an erythropoiesis stimulating agent when hemoglobin levels decrease below 10g/dL, despite dose reductions in ribavirin. In some instances, adverse events may become severe enough to warrant treatment discontinuation. Additionally, the SVR rates with this treatment were only 40%-50% in patients with HCV genotype 1.

In 2011, two novel first-generation NS3/4A protease inhibitors, boceprevir and telaprevir, received FDA approval for the treatment of HCV genotype 1 infections as a part of combination therapy with ribavirin and peginterferon.^{13,14} Unlike ribavirin and peginterferon, these protease inhibitors specifically target

the replication of the hepatitis C virus.^{15,16} As a result, when combined with ribavirin and peginterferon, the replication of HCV and the host immune response to the virus were impacted through multiple mechanisms.

Treatment with ribavirin, peginterferon, and either boceprevir or telaprevir became known as “triple-therapy”. Compared to dual-therapy, triple-therapy revealed improved SVR rates ranging between 63-79% for treatment-naïve patients and 32-86% for treatment-experienced, depending on the type of previous treatment response.^{17,18} Despite improvements in SVR rates, HCV treatment with triple therapy still presented a number of less than ideal characteristics, including continued lengthy treatment durations (24 – 48 weeks, based on initial response), extensive adverse events, high daily pill burdens with strict timing of administration given the incidence of resistance, and several drug-drug interactions with the protease inhibitors, both of which are strong inhibitors of cytochrome P450 (CYP450) enzymes.

In late 2013 two more agents, simeprevir and sofosbuvir, were approved for treatment of HCV.^{19,20} Simeprevir, a second-generation NS3/4A protease inhibitor approved for use in HCV genotype 1, demonstrated similar SVR rates as boceprevir and telaprevir but offered the advantage of being administered once daily, compared to three times daily with the first-generation agents.²¹ Sofosbuvir, an NS5B polymerase inhibitor which acts similarly to the protease inhibitors to interrupt hepatitis C viral replication, was also approved for once daily administration and yielded improved SVR rates of 56-100%. In addition, sofosbuvir also offered several beneficial characteristics that included treating multiple HCV genotypes and patients co-infected with HIV, thereby increasing the treatment opportunities for

Table 1. Characteristics of Previous and Current HCV Treatment Options					
	Approved GT	Treatment Duration (weeks)	SVR (%)	Peginterferon-Free	Ribavirin-Free
1990s – 2011 (“Dual-therapy”)					
Peginterferon & ribavirin	1 – 6	24 – 48	40 – 50*	No	No
2011 – 2013 (“Triple-Therapy”)					
Boceprevir or telaprevir, plus peginterferon & ribavirin	1	24 – 48	32 – 86	No	No
2013 Approvals					
Simeprevir	1	24 – 48	53 – 80	No	No
Sofosbuvir	1 – 4	12 – 24	56 – 100	Depends on regimen	No
2014 Approvals					
Ledipasvir/sofosbuvir combination tablet	1	12 – 24†	94 – 100	Yes	Yes
Ombitasvir/paritaprevir/ ritonavir combination tablet & dasabuvir	1	12 – 24	89 – 99	Yes	Depends on regimen
Simeprevir; to be used in combination with sofosbuvir	1	12 – 24	95 – 100	Yes	Yes
2015 Approvals					
Daclatasvir; to be used in combination with sofosbuvir	3	12	58 – 98	Yes	Yes

* = SVR rates with dual-therapy for genotype 1 (most common form of HCV in the United States); genotypes 2 and 3 experienced SVR rates of 80% or more with dual-therapy

† = A shortened treatment duration of 8 weeks may be considered in treatment-naïve patients without cirrhosis who have a pre-treatment HCV RNA less than 6 million IU/mL

a large group of patients who previously had limited options. Furthermore, sofosbuvir was approved for a shorter treatment duration (12 – 24 weeks based on treatment history), as well as the possibility of an all-oral/peginterferon-free regimen, which was a novel concept for chronic hepatitis C treatment.^{21,22} As a result, the shortened treatment duration and elimination of peginterferon-related side effects allowed for the opportunity for improved adherence.

Recent Approvals

Since the Fall of 2014, the FDA approved three new HCV therapies and expanded the indication for the use of simeprevir in combination with sofosbuvir.²³⁻²⁶ These recently approved agents work by distinct but related mechanisms, all of which target specific pathways within the HCV life cycle.

The first approved combination therapy, ledipasvir/sofosbuvir is a fixed-dose combination oral tablet that is dosed once daily and is approved for treatment of HCV genotype 1.²⁷ The approved treatment duration is 12 – 24 weeks, based on prior treatment experience as well as the degree of disease progression. A shortened treatment duration of 8 weeks may be considered in treatment-naïve patients without cirrhosis who have a pre-treatment HCV RNA less than 6 million IU/mL. Subjects in clinical trials, including traditionally harder-to-treat patients with advanced liver disease, experienced SVR rates of 94%-100%.

The second approval, which is marketed as Viekira PakTM includes a combination tablet consisting of ombitasvir, paritaprevir, and ritonavir and an additional tablet consisting of dasabuvir.²⁸ The combination tablet is dosed once daily and dasabuvir is dosed twice daily. Viekira PakTM is approved with or without ribavirin for the treatment of HCV genotype 1, including patients with compensated cirrhosis. The treatment duration is 12 – 24 weeks based on genotype subtype (1a versus 1b) and the presence of cirrhosis. Pre-marketing clinical trial data revealed SVR rates between 89%-99%.

The third and most recent approval, daclatasvir, is indicated for use with sofosbuvir for the treatment of chronic HCV GT3 infections.²⁹ It is the first drug approved for GT 3 infections that does not require co-administration of peginterferon or ribavirin, which is a considerable advance for the treatment options for this genotype. Daclatasvir is administered once daily for a treatment duration of 12 weeks. Clinical trial results evaluating the use of daclatasvir showed that patients without cirrhosis achieved SVR 92%-98% of the time, based on treatment history. This compares to SVR rates of 58%-69% in patients with cirrhosis, thus highlighting an area for future improvement.

The decision to approve the combined use of simeprevir and sofosbuvir was largely based on results of a study that demonstrated SVR rates of 95%-100% in patients, including those with cirrhosis. Like ledipasvir/sofosbuvir, the combined use of simeprevir and sofosbuvir is dosed once daily and is recommended for a treatment duration of 12 – 24 weeks.²¹

Compared to the adverse effects that frequently hindered previous treatments with peginterferon and ribavirin, the common side effects reported with the newer HCV agents include headache, fatigue, nausea and diarrhea.^{21-22, 27-29}

Implications and Economic Considerations

Hepatitis C virus was discovered less than three decades ago and during that time, an extraordinary amount of progress has been made, most of which has occurred in the last 24 months. Less than five years ago, the treatment for HCV warranted almost 12 months of therapy, intolerable adverse effects and was successful in fewer than 50% of cases. Since that time, recently approved therapies have allowed for improved SVR rates above 90% for a large majority of patients, a drastic reduction in treatment-related adverse effects, considerably shorter treatment durations, and improved ease of administration.

As a result of these advancements, the approach and attitude towards HCV from the medical community has also changed. Previously, only patients with advanced liver disease may have been considered for therapy when the potential benefits of the less than ideal treatment may have outweighed the likely risks of receiving no treatment. Currently, however, while the most recent guidance still recommends “urgent initiation of treatment” for patients with advanced liver disease, the general recommendations support treatment of all HCV-infected individuals, with the exception of those expected to live less than 12 months.³⁰

Despite vast amounts of clinical evidence supporting the benefits of treating all patients infected with HCV, therapy for many patients has been denied or delayed due to the high prices of recently approved treatment options.³¹ The wholesale acquisition costs, or “sticker prices” of these new drugs range from \$1,000 USD per day for sofosbuvir to a staggering \$1,750 USD per day for daclatasvir when prescribed concomitantly with sofosbuvir.³² Based on treatment history and genotype, total treatment costs may reach and exceed \$150,000 USD for some patients.

The high costs of these therapies have come under high scrutiny from lawmakers, insurance companies, medical providers and patients. One argument in defense of these high prices is that treating HCV now will offset the economic burden of untreated disease and subsequent complications in the future. A recent economic analysis, however, found conflicting data.³³ The authors of this analysis found that treating eligible patients with HCV over the course of the next 5 years would cost the United States \$65 billion USD, whereas the economic burden of not treating the same patients would be \$16 billion USD.

Over the past several months, much action has been taken in order to examine the legality and ethics of such high prices as well as encourage improved access to care. Healthcare experts from the Public Health Service and the president’s Advisory Council on HIV/AIDS have requested for Medicaid officials to widen access to new HCV agents by lessening current restrictions to treatment, citing that they “defy clinical guidelines and best practices.”³⁴ Members of the HCV Guidance Panel have even weighed in on the issue, recognizing that access to care is as much of a challenge as developing effective therapies. In response to this challenge, a new section on cost, reimbursement, and cost-effectiveness was added to the clinical guidelines, which encourages insurers, government and pharmaceutical companies to work together in order to make HCV treatment affordable and accessible.³⁰

Focusing on Chronic Hepatitis C in Hawai'i

Hepatitis C is estimated to affect approximately 23,000 residents in Hawai'i, or 1.6% of the population. The true prevalence, however, may be closer to 2.1% of the population as the survey used to estimate disease prevalence does not include prisoners, illegal immigrants, homeless or institutionalized patients (N. Tsai, personal communication, June 29, 2015).

Currently, the State of Hawai'i Department of Health (DOH) and Hep Free Hawai'i, a local coalition of over 80 partner agencies, have been making strides to increase awareness and screening efforts for hepatitis C from both the patient and provider perspective (H. Lusk, personal communication, July 10, 2015). The DOH established 16 free testing sites, the majority of which are located in community health centers or non-profit organizations, where patients can be screened. The DOH also sent letters to all licensed providers encouraging them to screen their patients for hepatitis C, along with hepatitis B and HIV (T. Pham, personal communication, July 13, 2015).

Additionally, Hep Free Hawai'i provides downloadable forms on its website that patients can bring to their healthcare providers (H. Lusk, personal communication, July 10, 2015). These forms provide information about who should be screened and billing codes for various screening procedures. This is especially helpful for those providers who may not be as familiar with the screening recommendations or how to implement them into their individual practices.

The efforts of the Department of Health and Hep Free Hawai'i have largely contributed to increasing awareness and screening for hepatitis C for both patients and providers. This progress, however, is still limited by the challenges surrounding the approval process for patients to receive recently approved treatment options, as described previously.

Conclusion

As treatment options for chronic hepatitis C virus emerge, the approach to this disease continues to develop. Recent and upcoming treatments focus on improving SVR rates for "harder-to-treat" patients and decreasing the duration of therapy. Despite this clinical progress, the high price of new therapies poses an unfortunate treatment barrier that greatly limits access to care.

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SOMETIMES THE SYSTEM WORKS.

A 57-year-old trucking company executive from New Jersey and his wife were headed for Hawai'i on vacation. Three hours from the mainland, the man became unresponsive and his wife realized he was in desperate straits. The flight attendant called for medical help and four nurses appeared, one an intensive care nurse. They realized the man was in cardiac arrest, moved him to the floor of the plane and began CPR. An IV line was established, epinephrine was injected and the automatic defibrillator was brought into action. After multiple shocks the patient awakened and the flight was diverted to Maui where an ambulance was waiting. At the hospital, a cardiologist inserted a bi-lead defibrillator and prescribed oral medications. The patient was entirely normal with no evidence of any neurologic deficit, and ready to return home in four days. And that is textbook on how cardiac arrest in an unusual setting can be managed.

MOVING TOWARD COED FOXHOLES.

Orders from Secretary of Defense Chuck Hagel in May 2015, mandate that all gender restrictions in the military end by January 1, 2016. All branches must be open to combat positions to women — from basic infantry battalions to elite special operations units such as Navy SEALs and Army Rangers. In an attempt to gauge what the Marine Corps might look like with women in combat roles, the USMC tested an integrated task force in Twentynine Palms, California. Previously closed positions include infantry, artillery and armored divisions. Only two of the roughly two-dozen women that started remained at the conclusion of the nine-month program. Most dropped out due to physical and mental stress that comes with combat roles. Women had a difficult time, like moving a 200 lb. dummy off the battlefield, or operating from the turret of a “damaged” vehicle. Both men and women reported a breakdown in unit cohesion. Should a politically correct attitude overrule military function?

HOW LOUD WAS THAT BELL?

Athletes refer to a concussion as “getting their bell rung.” Indeed, sports-related brain trauma sends 248,000 American kids and teens to emergency rooms each year. Allowing a return to play after a concussion increases the risk of more severe damage. Shu Yang, materials science and engineering professor at the University of Pennsylvania, has devised a method to measure impact of a collision. The force can be measured with a chemical strip that changes color based on the effect on tiny embedded crystals. The goal is to incorporate the material into the helmets of athletes and soldiers to know when a concussion occurs. Richard Figler MD, a surgeon at the Cleveland Clinic and former team physician for the NFL's Cleveland Browns, states that Yang's crystal reliably measure force, but head injuries are very difficult to evaluate given that “no one's been able to predict in clinical cases how much force it takes to cause a concussion.”

HERE; HAVE A BAR OF GREEN GOO.

Pond scum, a term in urban use meaning lower than a dog deposit, is the green algae swirling around in swamps, lake margins and similar venues. Euglena, a Tokyo based company is selling pond scum for big bucks at \$37.8 million last fiscal year. The mixture, part plant, part animal, is packed with nutrients and has a slightly bitter taste similar to kale. Euglena converts it to protein powders, health bars, noodles and other foods it markets to high-end supermarkets in Japan. Their health drinks sell for twice the price of regular fruit juice. In business for just 10 years, the company has branched out into cosmetics and fertilizer. The big-time dream of owner Mitsuru Izumo is biofuel. Like a plant, Euglena gracilis can sustain itself through photosynthesis that can result in the production of lipids. Lipid-based additives can be mixed with regular diesel to power buses, already used in a year-old test project.

All Nippon Airways has signed on to help develop a fuel for planes. Chevron has agreed to help build a special refinery to be built by 2018. Izumo expects that in 5 to 10 years biofuel will overtake health food as the primary product. Still, it will take at least that long before “pond scum” replaces suave and debonair to describe James Bond.

YOU WANT A SECOND OPINION? YOUR NOSE IS TOO BIG.

Medical studies show that as many as 20% of patients seek a second opinion when given a new diagnosis. Specialties like oncology rate a figure of 50%. Research has found that second opinions often result in different diagnoses or treatments. Some medical centers, including Massachusetts General Hospital and Cleveland Clinic sponsor second opinion services. Best Doctors Inc., offers online second opinions. Patients can request their medical records be sent to an online second opinion service. Requests may cost between \$500 and \$5,000 depending on the case, including people from overseas, and from companies that include the service as part of employee benefits. For patients faced with a serious or life-threatening illness, second opinions might direct them to various treatment opportunities that are less invasive or have fewer side effects. Patients often feel their physician might be offended when seeking a second opinion, but caring doctors welcome other eyes or brains examining a serious disorder.

GIVE ME THE CAR KEYS, DAD. YOU TOO, JUNIOR.

The Insurance Institute for Highway Safety reported in a study that older Americans are driving more, but are less likely to be killed or injured in a car crash than 20 years ago. Older drivers are still more likely to die in a crash than 30, 40 or 50 year-olds, but the gap is narrowing. For drivers 80 and older the rate has fallen 55% and the rate for 70 to 74 year-olds fell 32% in the same period. The study doesn't offer explicit causes, but Institute senior VP Anne McCartt who co-wrote the report believes cars are safer and older drivers are more robust. Motorists ages 35 to 54 fatality rates dropped 26%, and rates for the 55 to 69 fell also. Those drivers age 25 to 29 death rates rose nearly 38%. The data fall at a time when policy makers and families are wondering what to do about the fast growing population of elderly drivers reluctant to give up the car keys. Close friends and family members will have to act as controllers when they know a loved one must stop driving.

A SUPERHEROE'S SECRET IDENTITY. A NURSE BY DAY...

A thief grabbed the purse of an elderly woman as she and her husband exited a Fred Meyer store in Spokane, Washington. They had no chance to catch him as he ran through the parking lot. His escape route took him by a nearby hospital where a 42 year-old nurse surmised what was happening and gave chase. He soon realized he could not outrun her and surrendered the purse that she returned to the woman. Later the nurse revealed her alter ego: she competes in the roller derby for the Spokannibles where she is known as Ms. Ida B. Choazz.

ADDENDA

- Nearly 25% of American adults did not read a book in the past year, a percentage that has tripled since 1978.
- Antarctica is the only continent without reptiles.
- Outside every thin woman is a fat man trying to get in.
- Parenting can only be understood and taught by people who have no children.
- All men make mistakes, but married men find out about them sooner.

ALOHA AND KEEP THE FAITH **rt**s

(Editorial comment is strictly that of the writer.)

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