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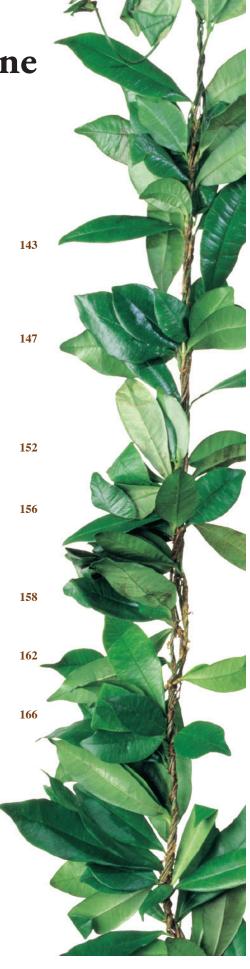
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# University of Hawai'i John A. Burns School of Medicine Medical Students' Attitudes Towards Obese Patients

Kristen M. Chin HSDG; Mary Tschann MPH; Jennifer Salcedo MD, MPH, MPP; Reni Soon MD, MPH; Kasey Kajiwara MD; and Bliss Kaneshiro MD, MPH

#### **Abstract**

Studies have shown that healthcare professionals often demonstrate obesity biases, which in turn reduce the quality of care obese patients receive. The purpose of the current study was to describe third and fourth year University of Hawai'i, John A. Burns School of Medicine medical students' attitudes towards obese patients. Data were collected using previously validated questions from a pilot study assessing how healthcare providers react and recommend medical care to patients with varying characteristics. The responses of 114 medical students were analyzed. Overall, the majority of students' responses reflected the belief that obesity may be a behavioral issue. There were no statistically significant differences between the third and fourth year students' responses. Important areas of future research include assessing students' awareness of the social determinants of health and ability to self-identify possible biases in caring for obese patients.

#### **Keywords**

obesity, obese patients, bias, attitude, medical students

#### **Background**

Obesity is a chronic disease that affects more than one-third of the adults living in the United States. In Hawai'i, 22.1% of adults are obese and 36.0% are overweight. Despite obesity's high prevalence, many healthcare professionals struggle with treating obesity<sup>3-5</sup> and studies suggest providers often harbor negative attitudes towards obese patients. Additionally, physicians have been shown to demonstrate strong implicit and explicit "anti-fat" biases independent of their own BMI, race/ethnicity, and gender. A significant proportion of physicians believe obese patients are less likely to adhere to medications, lack the discipline and motivation to lose weight, and are difficult to treat. Subsequently, physicians report experiencing negative reactions towards obese patients during visits as well as a lowered desire to help them. 5.10

Negative attitudes towards obese patients can reduce the quality of medical care obese patients receive with respect to effective communication, time allocated, and relationship building. One study reported that physicians are less likely to build emotional rapport with obese patients, and another study demonstrated that physicians are more likely to avoid servicing them altogether. Accordingly, obese patients receive fewer diagnostic screening services and less injury, stress, and tobacco education. Physicians' overall obesity bias may result in obese patients feeling mistrust, avoiding medical care, experiencing stress and decreased satisfaction, and struggling to adhere to medical guidance.

A study evaluating medical education regarding obesity yields discouraging results. In general, medical schools provide

minimal hours of nutrition education and obesity instruction.<sup>4</sup> Additionally, students in the medical disciplines are engaged in learning environments that do not actively discourage obesity bias.<sup>6</sup> Students have reported that their peers, healthcare providers, and instructors make negative comments about obese patients.<sup>6</sup> The pervasiveness of obesity stereotypes and the lack of adequate obesity care training for medical students results in physicians struggling to discuss weight loss with obese patients or avoiding the topic entirely.<sup>3</sup> Many physicians report feeling unprepared to initiate conversations about weight loss and provide treatment for obesity confidently.<sup>3-5,10</sup>

At the University of Hawai'i John A. Burns School of Medicine (JABSOM), topics including the physiology and treatment of obesity are interspersed through the pre-clinical years and taught through a combination of lectures and Problem-Based Learning sessions. During the clinical years, students observe preceptors and engage in weight management directly with patients. The purpose of this study was to assess JABSOM medical students' attitudes towards obese patients. We hypothesized that the majority of JABSOM medical students would demonstrate attitudes that are consistent with obesity bias.

#### Methods

Data for this study were generated from a study which sought to gain preliminary data on how patient race affected reproductive health recommendations. The majority of the questions in the survey addressed attitudes regarding race and gender. In an attempt to minimize social desirability bias, survey participants were also presented with a subset of five questions derived from a previously validated survey by Foster, et al. 5 Foster, et al, used these validated questions to better understand physicians' attitudes towards obese patients, obesity itself, and the treatment of obesity. We selected five questions from Foster's original 20 questions that were pertinent to medical education. We did not address areas that medical students would not have experience with (ie, questions about provider time or reimbursement). The data collected from the five questions relating to obese patients were analyzed for the present study ("I believe it's necessary to educate obese patients on the health risks of obesity.", "It is difficult for me to feel empathy for an obese patient.", "Most obese patients are well aware of the health risks of obesity.", "Most obese patients could reach a normal weight (for their height) if they were motivated to do so.", "I feel uncomfortable with examining an obese patient."). Participants answered questions using a 6-point Likert scale (very strongly disagree, strongly disagree, disagree, agree, strongly agree, very strongly agree). Though the study by Foster, et al, used a 5-point scale (strongly disagree, disagree, neutral, agree, strongly disagree), we decided to use a 6-point.

Participants were third and fourth year medical students who were at least 18 years old attending JABSOM. Students were recruited through email solicitations between June 2014 and July 2015 and were provided a link to an anonymous online questionnaire. No personally identifiable information was collected. The participants received a \$5 gift card if they started the study. This study was granted exempt status by the University of Hawai'i Committee on Human Studies. Descriptive statistics were calculated using Statistical Package for the Social Sciences (version 24.0, New York, US). We compared the responses of third and fourth year students using Fisher's Exact tests.

#### **Results**

All third and fourth year students (n=180) received an email with a link to the online questionnaire. A total of 124 JABSOM medical students began the survey and 114 students completed all questions that pertained to obesity, resulting in a response rate of 63.3%. Table 1 summarizes the overall responses to the five obesity questions. Nearly all (98.3%) of the students were in favor of educating obese patients about the health risks of their condition. Only 1.8% (n=2) disagreed that it was important to educate patients about the health risks of obesity. Most students (79.9%) did not find it difficult to feel empathic

towards obese patients though it was concerning that 10.5% of students strongly and very strongly agreed that it was difficult to feel empathy towards obese patients. Over half (57.0%) believed that obese patients are not necessarily aware of the health risks of their condition, and 69.4% of students thought that obese patients could reach a normal weight if they were properly motivated. Seven in ten students (71.1%) indicated that they were comfortable with examining obese patients. Of concern, nearly three in ten students expressed some discomfort with examining obese patients.

Over half of the respondents (61.4%) were third year medical students (n = 70), 30.7% were fourth year students (n = 35), and 7.9% did not disclose their level of training (n = 9). Figures 1 to 5 compare the third and fourth year student responses for each of the five questions. No statistically significant differences emerged between the third and fourth year medical students' responses. Responses to three of the questions ("I believe it's necessary to educate obese patients on the health risks of obesity.", "It is difficult for me to feel empathy for an obese patient.", "I feel uncomfortable with examining an obese patient.") indicated sensitivity towards and comfort with caring for obese patients. We found that 59.6% of respondents gave sensitive responses to all three questions and only one respondent (0.9%) indicated they were not comfortable in examining an obese patient, did not think it was necessary to educate obese patients on the health risks of obesity, and found it difficult to feel empathy towards an obese patient.

Table 1. Responses of Study Population (n = 114)							
Question	Very Strongly Disagree n (%)	Strongly Disagree n (%)	Disagree n (%)	Agree n (%)	Strongly Agree n (%)	Very Strongly Agree n (%)	
I believe it's necessary to educate obese patients on the health risks of obesity.	1 (1)	0 (0)	1 (1)	18 (16)	36 (32)	58 (51)	
It is difficult for me to feel empathy for an obese patient.	15 (13)	39 (34)	37 (33)	11 (10)	9 (8)	3 (3)	
Most obese patients are well aware of the health risks of obesity.	3 (3)	12 (11)	50 (44)	37 (33)	11 (10)	1 (1)	
Most obese patients could reach a normal weight (for their height) if they were motivated to do so.	1 (1)	3 (3)	31 (27)	54 (47)	19 (17)	6 (5)	
I feel uncomfortable with examining an obese patient.	9 (8)	19 (17)	53 (47)	26 (23)	3 (3)	4 (4)	

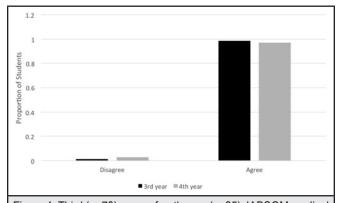


Figure 1. Third (n=70) versus fourth year (n=35) JABSOM medical students' responses to: I believe it's necessary to educate obese patients on the health risks of obesity (P = 1.00).

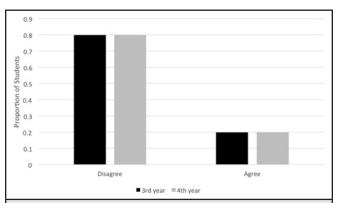


Figure 2. Third (n=70) veresus fourth year (n=35) JABSOM medical students' responses to: It is difficult for me to feel empathy for an obese patient (P = 1.00).

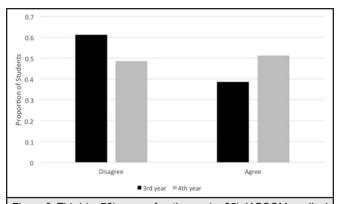


Figure 3. Third (n=70) versus fourth year (n=35) JABSOM medical students' responses to: Most obese patients are well aware of the health risks of obesity (P = 0.22).

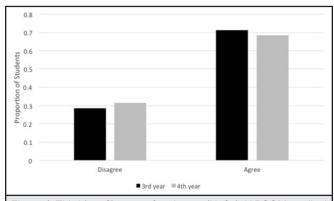


Figure 4. Third (n=70) versus fourth year (N=35) JABSOM medical students' responses to: *Most obese patients could reach a normal weight if they were motivated to do so* (P = 0.82).

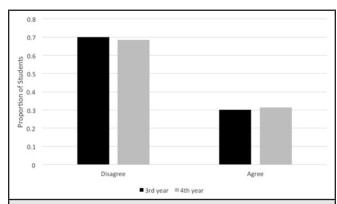


Figure 5. Third (n=70) versus fourth year (n=35) JABSOM medical students' response to: I feel uncomfortable with examining an obese patient (P = 1.00).

#### **Discussion**

Obesity is a complex health care issue for both patients and physicians. We found nearly all students were in favor of educating obese patients about the health risks of their condition. Most students did not find it difficult to feel empathic towards obese patients though it was concerning that 10.5% of students strongly and very strongly agreed that it was difficult to feel empathy towards obese patients. Most students reported that obese patients could reach a normal weight if they were motivated to do so, suggesting that medical students place importance on the behavioral aspects of weight management. We did not find any significant differences between the third and fourth year students' responses because medical education on obesity occurs heavily during their first two years of medical school.

Our results were similar to those noted in the study by Foster, et al.<sup>5</sup> In the Foster study, 95.0% of physicians agreed about the importance of educating obese patients about their condition, 80.2% did not feel difficulty in empathizing with obese patients, and 74.5% felt comfortable with examining obese patients.<sup>5</sup> In addition, Foster asked several other questions regarding obesity and concluded that physicians primarily view obesity as a behavioral issue, attribute negative stereotypes to obese patients, and lack confidence in treating obesity. Because we asked a limited number of questions, we cannot comment on these aspects of caring for obese patients. Our findings suggest that students at JABSOM have a strong appreciation for the importance of weight in overall health but could benefit from additional instruction on educating patients about the health risks and obesity and examining the obese patient.

Several other studies have identified medical student's biases against obese patients. One study reported one-third of medical students had significant implicit anti-fat bias though few were aware of that bias.<sup>23</sup> A study by Phelan, et al, found that medical students' implicit weight bias against obese individuals improved over the first two years of medical training.<sup>24</sup> Less positive contact with patients with obesity and more exposure to faculty role modelling of discriminatory behavior towards patients with obesity was associated with more obesity bias in another study.<sup>25</sup> Our study had several important limitations making it impossible for us to provide a complete assessment of obesity bias. As noted previously, data for this study were generated from a pilot study which sought to gain preliminary data on a different topic. Though the five validated questions we posed to participants were unlikely to precisely capture a medical student's comfort and aptitude in caring for obese patients, our results provide a preliminary, though important, glimpse into this complex area. We are unable to determine if our findings are reflective of medical education at JABSOM or if our findings simply represent the attitudes of typical medical students. We also lacked the flexibility to gather more data on participant demographics that may have been meaningful when interpreting our results, such as student gender, BMI and age. Additionally, our sample size may have been too small to find any statistically significant differences between third and fourth year medical students. Since this study was conducted on a group of students from one medical school, we cannot generalize our results to all medical students. Future studies should take a qualitative approach to elicit student's in-depth thoughts on the adequacy of medical education addressing obesity. Counseling patients on sensitive topics like weight can be challenging for health care providers and providing educational opportunities through simulation and professional patients may also be of value in increasing the comfort of students in providing care for obese patients.

#### **Conclusion**

The data from this study suggest attitudes expressed by JAB-SOM medical students may be consistent with those of other healthcare professionals with regard to obese people. Educational interventions to help students understand and address the social determinants of health could better the treatment of obesity and improve the quality of physician-patient relationships. Although norms that reinforce obesity biases are prevalent, other interventions could increase students' awareness of their own attitudes so that they can improve patient care. Future studies are needed to formulate education programs that can potentially be integrated into the medical school curriculum. Additionally, studies and interventions should be designed with the knowledge that team-based, patient-centered care is increasing in prominence. Caring for patients is often the responsibility of an entire health care team rather than an individual physician. Assessment of the adequacy of education and the development of future interventions to improve the care obese patients receive should take this into account.

#### **Conflicts of Interest**

No conflicts of interest were identified for this study.

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### Primary Care Integration of Psychiatric and Behavioral Health Services: A Primer for Providers and Case Report of Local Implementation

Anthony P.S. Guerrero MD; Cori L. Takesue PsyD; Jared H.N. Medeiros APRN-Rx; Aileen A. Duran APRN-Rx; Joseph W. Humphry MD; Ryan M. Lunsford MD; Diana V. Shaw PhD, MBA, MPH; Michael H. Fukuda MSW; and Earl S. Hishinuma PhD

#### **Abstract**

Mental health conditions are common, disabling, potentially life-threatening, and costly; however, they are mostly treatable with early detection and intervention. Unfortunately, mental healthcare is in significantly short supply both nationally and locally, and particularly in small, rural, and relatively isolated communities. This article provides physicians and other health practitioners with a primer on the basic rationale and principles of integrating behavioral healthcare — particularly psychiatric specialty care — in primary care settings, including effective use of teleconferencing. Referring to a local-based example, this paper describes the programmatic components (universal screening, telephone availability, mutually educational team rounds, as-needed consultations, etc) that operationalize and facilitate successful primary care integration, and illustrates how these elements are applied to population segments with differing needs for behavioral healthcare involvement. Lastly, the article discusses the potential value of primary care integration in promoting quality, accessibility, and provider retention; discusses how new developments in healthcare financing could enhance the sustainability of primary care integration models; and summarizes lessons learned.

#### **Keywords**

Primary care integration, mental health, telepsychiatry, sustainability

#### **Abbreviations**

U.S. = United States

BHI = behavioral health integration

FQHC = federally qualified community health center

SBIRT = Screening, Brief Intervention, and Referral to Treatment

VTC = video-teleconferencing

SSRIs = serotonin-selective reuptake inhibitors

HIPAA = Health Insurance Portability and Accountability Act

#### Introduction

In the United States (U.S.), mental health conditions — defined as those conditions that affect mood, thinking, and/or behavior — affect 20% of the general population.¹ Unfortunately, because of significant mental health provider shortages and stigma, only a fraction of this 20% receives appropriate and timely care. Untreated mental health conditions tend to get worse with time, and they significantly contribute to disability and mortality. Of note, the top leading causes of death among children, adolescents, and young adults in the U.S. and Hawai'i are unintentional injuries (accidents) and suicide.²³ Furthermore, untreated mental health conditions (including addictions, maladaptive health behaviors, and non-adherence secondary to depression and other behavioral health conditions) contribute

to approximately one third of excess cost and waste in the U.S. healthcare system.<sup>4</sup>

In Hawai'i, even conservative, demand-based estimates of psychiatric workforce needs indicate a shortage in absolute number of psychiatrists as well as a significant mal-distribution of services, such that there are very small numbers of psychiatrists on certain neighbor islands, 5 and some of the smallest islands do not have any resident psychiatrists. The prevalence of certain youth and adult mental health conditions and substance use in Hawai'i appear to be similar to those found nationally,6 but there are ethnic and socioeconomic health and mental health disparities<sup>7</sup> that may reflect limitations in cultural appropriateness or accessibility of care. As an example, Andrade, et al, found that Native Hawaiian youth had significantly higher rates of any psychiatric disorder (32.7%) than non-Hawaiian youth (23.7%) and that these differences were largely the result of significantly different anxiety disorder rates.<sup>7</sup> On the other hand, Hawai'i has been a national leader in terms of primary care accessibility via the "medical home," which is a concept founded by Dr. Calvin Sia as early as the 1970s.8

While primary care providers may be optimally positioned to ensure early detection and care for mental health conditions, they may be either unprepared or pressured for time in their practice. It is also important to note that in the U.S., most prescriptions for psychotropic agents (such as antidepressants and anxiolytics, including benzodiazepines) are written by primary care providers. In view of the prime importance of accessible behavioral healthcare for the future of U.S. healthcare reform, agencies such as the Substance Abuse and Mental Health Services Administration (SAMHSA), and the Health Resources and Services Administration (HRSA) have strongly advocated for models of behavioral health integration in the primary care medical home. Such models are particularly important for island states where the only way to access appropriate care is by paying for and flying to another island.

This article aims to provide the reader with a primer on the concept of behavioral health integration (BHI) for an island state by describing one local-based example of BHI. In studying this example, certain programmatic elements may be identified that improve access to mental healthcare and that could be potentially applicable for other remote and/or sparsely populated locations

#### Methodology

#### **Program Overview**

The program described in this article was based in a rural neighbor island federally qualified community health center (FQHC) that served a population of approximately 1,500 patients, predominantly of Asian, Native Hawaiian, and Other Pacific Islander ancestry. In this community, there were significantly fewer than 8,400 people, which is a number cited to feasibly support a full-time psychiatrist. There were not any locally based psychiatrists in this community, which was remotely located and accessible only by air or sea.

The program's leadership felt that BHI was arguably the only viable option for sustainable and accessible psychiatric care. Without BHI, access to psychiatry and psychiatric sub-specialties (child, addictions, geriatric, pain medicine, etc) would be only a remote possibility for small isolated communities.

The program had, at its foundation, a grant-funded behavioral health/primary care integration project. The project's general activities included: awareness of behavioral health conditions presenting in primary care; behavioral health screening by multidisciplinary healthcare providers, who have received basic training in such protocols as Screening, Brief Intervention, and Referral to Treatment (SBIRT); trauma-informed care; promotion of healthy behaviors and adherence, and practical application of motivational interviewing approaches; and overall promotion of mental health in the community.

The program included an on-site, primary care-embedded clinical psychologist/behavioral health specialist (1.0 full time equivalent [FTE]), as well as funding for a part-time psychiatrist (0.13 FTE), physically located in an urban setting, but readily available by video-teleconferencing (VTC) or telephone. In this project, the psychiatrist's time was devoted to the following roles: guidance on screening tools for behavioral and developmental conditions throughout the lifespan; provider-to-provider consultation around selected patients, including those who screened positive; telephone availability during the working week for questions relevant to primary care management of psychiatric conditions; scheduled VTC consultations with selected patients, together with their primary care team providers; ongoing collaboration and discussion with the primary care/psychology team around selected patients; monthly participation at team conferences; and in-services as requested - particularly around high-yield topics, such as pain management and common geriatric psychiatric conditions. In-person visits from the psychiatrist were periodically scheduled (approximately semi-annually), guided by needs for on-site team-building, problem-solving, and developing familiarity and relationships with community resources.

# Process of Comprehensively Describing the Pilot Program and Identifying Key Components

The authors — inclusive of all members of the FQHC's primary care, embedded clinical psychology, and psychiatry teams (collectively the BHI team) — contributed to a comprehensive description (assembled by the first author) of the BHI model as

it evolved over the previous year-and-a-half since the team's formation.

The Institutional Review Board of the University of Hawai'i at Manoa provided approval for dissemination of program information (Committee on Human Studies #24022), as did the leadership of the project's community health center. No consents were utilized given the nature of this retrospective study.

#### **Results**

#### **Description of Program Components**

The model used for matching services to population needs is depicted in Figure 1 and Table 1 and is based on the clinic's intent to provide accessible health and preventive services for the community. The model illustrates how the aforementioned psychiatric services are integrated with the clinic's practice in providing care for patients with differing levels of need for mental healthcare. To demonstrate how the model is implemented in practice, four fictitious case vignettes are provided below. The case vignettes illustrate the important operational details of the model:

Fictitious/Hypothetical Case Vignette #1 (representing the general population aiming to stay mentally healthy): An early adolescent male patient presents for a routine school physical. The primary care clinic staff utilize a behavioral health screening tool that had previously been recommended by the BHI team and that (through training) they felt comfortable administering. They further feel confident that, should the screening be positive for depression or any other psychiatric condition, the embedded behavioral health specialist would be available on-site either to provide advice to the primary care providers or to meet the patient for additional screening and services, if appropriate. The screening is negative for any mental health concerns. Resources for mental health promotion (e.g., exercise, mindfulness, etc) are available through the community center.

Fictitious/Hypothetical Case Vignette #2 (representing the population of patients with transient behavioral health conditions and/or maladaptive behaviors impacting health): A young adult female is newly diagnosed with Type II diabetes mellitus, along with obesity and elevated blood pressure. Routine mental health screening reveals sub-threshold symptoms of depression, which the primary care provider feels are important to address nonetheless to improve adherence with lifestyle changes that are necessary to manage the patient's chronic conditions. The behavioral health specialist sees the patient for a few sessions and provides suggestions to the primary care provider on how to optimize motivation and address psychosocial barriers to change. The primary care provider and behavioral health specialist are aware that they have multiple forums — including the monthly team meeting and availability — to seek input from the psychiatrist should there be any need to seek consultation regarding the development of a major depressive episode possibly requiring treatment with psychiatric medication.

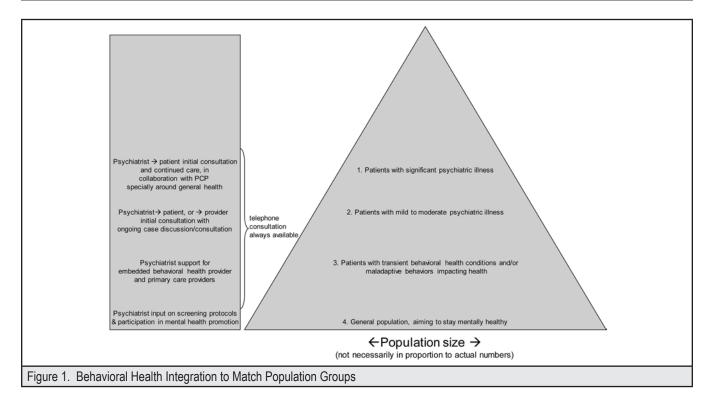
**Fictitious/Hypothetical Case Vignette #3** (representing the population of patients with mild to moderate psychiatric illness): An adult female patient has a history of Major Depressive Disorder and Generalized Anxiety Disorder. She has not fully responded to the various serotonin-selective reuptake inhibitors (SSRIs)

prescribed by the primary care provider nor to regular psychotherapy from the behavioral health specialist. The primary care provider and behavioral health specialist arrange for a call with the psychiatrist. The psychiatrist subsequently sees the patient for a VTC consultation and recommends updated laboratory tests (including a thyroid function test) to rule out other medical causes for the psychiatric symptoms and pharmacogenomic testing, the results of which subsequently guide the selection of a new antidepressant/anxiolytic medication. The primary care provider and psychiatrist jointly see the patient for a few sessions while the medication regimen is stabilized, and subsequently, the primary care provider (with the psychiatrist readily available for re-consultation or additional advice if needed) once again resumes the medication follow-up.

**Fictitious/Hypothetical Case Vignette #4** (representing the population of patients with significant psychiatric illness): An adult male, relatively new to the clinic, has a history of a Schizophrenia Spectrum Disorder with past exacerbations requiring psychiatric hospitalization. He also has chronic pain from a previous injury. His psychotropic medication regimen consists of an antipsychotic medication, an SSRI, and an anxiolytic. The psychiatrist (via

VTC, or on-site if able to coincide with a periodic site visit) and primary care provider see the patient together for several sessions and take the opportunity to mutually educate each other on the care they provide. In follow-up, the primary care provider, who sees the patient more frequently than the psychiatrist does, assists the latter in identifying early warning signs of relapse, in monitoring recommended labs (eg, fasting blood glucose, lipids, etc) in a timely fashion, and in monitoring for abnormal involuntary movements using standardized assessments. Periodically, the psychiatrist also sees the patient jointly with the behavioral health specialist, who provides supportive psychotherapy and assistance with stress management (to minimize the risk of symptom exacerbations). Working collaboratively, the entire BHI team can assist the patient with other issues that are optimally addressed via a combined primary care/behavioral health approach, ie, weight loss (particularly in the context of atypical antipsychotic medications with a side effect of weight gain and associated metabolic consequences), smoking cessation, and appropriate pain management. Because the lattermost issue is a particularly challenging one for the whole team, the psychiatrist provides, during one of the monthly team meetings, an in-service on nonnarcotic management of chronic non-malignant pain.

Table 1. Hypothetical and Fictitious Examples of Patients in Each Population Group						
Population group	Hypothetical/fictitious clinical example, with description of services provided (please see text for further examples and further elaboration)					
Patients with significant psychiatric illness	Adult or adolescent needing treatment with atypical antipsychotic medication and needing ongoing psychiatric follow-up and metabolic side effect monitoring from the primary care provider					
2. Patients with mild to moderate psychiatric illness	Adult with major depression, amenable to and responsive to standard medication (eg, serotonin-selective reuptake inhibitor)					
Patients with transient behavioral health conditions and/or maladaptive behaviors impacting health	Adult with diabetes or other chronic illness needing assistance with improving health behaviors and/or adjusting to illness					
General population, aiming to stay mentally healthy	Adolescent or parent of a new baby, presenting for health maintenance care and receiving depression screening					



#### **Preliminary Findings and Impressions**

Over the course of the project, regular check-ins were made with staff to review the model and the implementation, and to make necessary adjustments. Overall, the BHI team maintained a very positive view of the project, and while describing the project's model, they spontaneously identified several perceived strengths. They felt that most of their patients were served well and even optimally — because of enhanced continuity — by the primary care team, with readily available backup from the consulting psychiatrist. The psychiatrists' telephone availability allowed for timely feedback and advice when uncommon, but potential medication side effects were encountered in primary care. In addition, the team felt that mutual education and collaboration allowed psychiatry, psychology, and primary care team members to become partners in assuring that patients were on-time for recommended blood draws and other screens. The BHI team also felt that, particularly for patients with chronic psychiatric conditions needing periodic psychiatric (and not just primary care) visits, it was extremely beneficial to have regular team dialogue and collaboration around weight management, smoking cessation, and coexisting medical conditions (see Case Vignette #4). The on-site primary care providers and behavioral health specialist felt that it was very helpful and essential to the project's success to have all psychiatric documentation (in this case, via notes faxed soon after the psychiatric consultations) available in their health records.

The BHI team recalled various scenarios where they, by necessity, developed experience in stabilizing acute symptoms that, if not treated early, could potentially have led to emergency room visits or off-island acute hospitalizations that (besides being unsustainably costly) could further have fragmented the care.

The BHI team did not recall any encounters where VTC was either not accepted by patients or families, or technologically unfeasible. The BHI team authors observed that VTC consultations allowed for more accessibility and scheduling flexibility than is usually experienced in a comparable urban (non-VTC) practice. The team's experience was consistent with literature reviews supporting VTC's reliability and favorable outcomes.<sup>11</sup>

Thus far, lessons learned are as follows. In anticipation of long-term sustainability, it would have been ideal to have, from the beginning, a more detailed tracking of all professional activities and communications, including those pertaining to patients in the 3rd and 4th tiers of the pyramid and those not currently attached to billing codes (but potentially attached to billing codes in the future). Also, in retrospect, it would have been ideal to involve psychiatric or primary care physician trainees in the process of establishing and maintaining a behavioral health integration program, which could very well be an important component of future practice that would address workforce issues.

An additional lesson is one that is probably already well known; however, it bears repeating: Collaborating closely to provide coordinated care to patients is efficient and results in high-quality care. Especially in a remote, rural area, these types of specialty services and coordination are often non-existent — yet this program provided both to this rural community. It was very important to have, from the beginning, a team approach to care fostered at the FQHC and a strong commitment from primary care and clinical psychology to expand existing practices (such as SBIRT) and to positively engage psychiatry into planning and work-flow. It was also very important to have a reliable user-friendly VTC platform that could ensure buy-in from staff, consultants, and patients. The FQHC had an existing license for Zoom version 4.0.2258.0125, 9 (San Jose, CA) which is a cloud-based, Health Insurance Portability and Accountability Act (HIPAA)-compliant VTC/telehealth application that made scheduling and connecting easy by any member of the FQHC team.

#### **Discussion and Future Directions**

An important limitation of this paper was the absence of any quantitative or semi-quantitative data to measure outcomes. Notwithstanding this limitation, we believe that the impact on quality of behavioral health care was significant and recognized by all of those directly involved. On any given month, the primary care team has five to ten active patients with direct psychiatric intervention. The ability to provide medication management, particularly for patients with severe mental illness, dramatically improved with BHI, The primary care providers are currently safely using a much broader spectrum of psychotropic medication, monitoring for side effects, appropriately titrating and adjusting doses, and at times using combinations of medication. For several patients, the addition of psychiatric services has aided in establishing correct diagnoses for such conditions as adult Attention-Deficit Hyperactivity Disorder (ADHD), Autism Spectrum Disorder, Schizophrenia Spectrum and Other Psychotic Disorders, and Personality Disorders. With the obvious improved quality in our care delivery system, we felt that it would be helpful for local and regional healthcare providers to learn about the authors' experiences with behavioral health/primary care integration. To our knowledge, this was the first published paper (data-driven or descriptive) focused on a Hawai'i-based program's experience with behavioral health/ primary care integration.

Professional isolation is a constant challenge in rural settings. It often leads to significant stress in doing the right thing for complex patients and eventually to provider burn out. Based on our experience with this project, the authors believe that vertical integration with multi-specialty psychiatric support and backup has had a positive impact on both primary care and behavioral health providers in the rural setting. The BHI model dramatically expanded the care team and has subjectively improved the structured treatment plan and quality of medication management. Furthermore, we believe that, by reducing isolation in rural communities, BHI has the potential to improve provider job satisfaction and retention, which is a constant struggle in many rural communities and a significant stress for providers, patients, and communities alike.

To date, resources for the project have relied upon grant funding plus a small component of professional billing. Unfortunately, up to this point, many of the services that are core to primary care integration are not reimbursable in traditional fee-for-service models. This situation may change with the introduction of new Medicare codes and funding allocations, specifically to support BHI, which leads to both quality and cost-effective care. <sup>12</sup> Likewise, accountable care organizations have already begun to recognize, via incentive reimbursements, the value of primary care-based behavioral health screening and intervention.

Overall, the authors hope that this paper will stimulate further dissemination and discussion of local experiences and ideas around this important model in healthcare's future. We further hope that this description of programmatic components felt by the team to be beneficial can help the specialty to define what may be promising or best practices for primary care/behavioral health integration.

As more models are implemented in larger organizations and in larger populations, we recommend that quantitative studies be done to measure improvements in behavioral healthcare quality, accessibility, and cost-effectiveness (eg, earlier age of first diagnosis of certain conditions, higher percentage of patients receiving indicated behavioral healthcare, decreased wait times between initial diagnosis and initiation of treatment, reduced rates of suicide and violence in communities served, reduced rates of psychiatric and other medical hospitalizations, and emergency visits, etc). Furthermore, we recommend that longitudinal studies be done to answer the important question of whether primary care/behavioral health integration can improve long-term workforce recruitment and retention in rural communities that are isolated by being on relatively small islands or by some other geographic barrier.

#### **Conflict of Interest**

None of the authors identity any conflicts of iterest.

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# Headaches More Common among Epilepsy Sufferers with Neurocysticercosis than Other Structural Brain Lesions

Erin K. Saito PhD; Bijal Mehta MD; Frances Wang; Beau Nakamoto MD, PhD; and Aaron M. McMurtray MD, PhD

#### **Abstract**

Neurocysticercosis is a leading cause of seizures and epilepsy in the developing world. Cysticercosis is endemic in many regions of Central and South America, sub-Saharan Africa, India, and Asia. Neurocysticercosis is of emerging importance because globalization has increased travel between Hawai'i and disease-endemic areas. Headache and epilepsy are two of the most common complications of neurocysticercosis infection. Currently, it is not known if epilepsy patients with neurocysticercosis are more likely to have headaches than those with other structural brain lesions or those with no structural brain abnormalities. This study was designed to investigate whether epilepsy patients with neurocysticercosis report co-morbid headaches more frequently than those with other or with no structural brain lesions. A retrospective cross-sectional study of all patients treated at a community based neurology clinic for epilepsy during a three-month period was performed. One-hundred sixty patients were included in the analytical study. Co-morbid headaches were more commonly present among those with neurocysticercosis (40%) than those with other structural lesions and those with no structural brain abnormalities (19% and 22%, respectively; P = .031). Headache frequency among those reporting co-morbid headaches did not differ significantly between the groups. Prevalence of co-morbid headaches is greater among epilepsy patients with neurocysticercosis than those with other structural brain lesions or no structural brain abnormality. Epilepsy patients with neurocysticercosis may be especially vulnerable to development of headaches and a thorough headache history should be obtained to help screen for affected individuals.

#### Keywords

Neurocysticercosis, headaches, epilepsy, seizure

#### Introduction

Neurocysticercosis is a parasitic worm infection acquired by humans through the ingestion of Taenia solium eggs that are shed in the feces of humans carrying the intestinal parasite.<sup>1</sup> Neurocysticercosis is especially common in Latin America, India, Africa, and China.1 Poor hygiene practices are the main factor contributing to transmission of the disease through the fecal-oral route.<sup>2,3</sup> Over the last several decades cysticercosis infections have become more common in the United States, with 221 deaths due to cysticercosis occurring between 1990 and 2002, including 33 among individuals born in the United States. 4 The economic costs of neurocysticercosis in the United States are significant, with treatment and hospitalization costs, lost working days, and losses of jobs estimated to approach \$8.8 million in the year 2000 alone.<sup>5</sup> One economic study completed in Los Angeles County showed that the economic costs associated with neurocysticercosis infection are especially great, with the average hospitalization charge for patients with neurocysticercosis approaching \$66,000, compared to \$29,000 for those without the infection. Neurocysticercosis is of emerging importance in Hawai'i because of immigration and tourism

from disease-endemic areas. According to the Hawai'i Tourism Authority, visitors from Asia to Hawai'i increased from approximately 225,000 visitors in 2006 to 778,000 in 2015. Visitors from Latin America to Hawai'i increased from approximately 19,000 visitors in 2006 to 27,000 visitors in 2015. The John A. Burns School of Medicine (JABSOM) at the University of Hawai'i at Manoa is also committed to training competent healthcare professionals with the skills to address critical global health problems. To that end, JABSOM has pursued alliances with medical schools and programs unique to the Asia-Pacific region, including Asia and Philippines. Neurocysticercosis is a leading cause of seizures and epilepsy in the developing world, is a growing health concern throughout the United States, and is relevant to healthcare providers in Hawai'i.

The most common presenting symptoms for patients with neurocysticercosis are seizures (78.8%), headaches (37.9%), focal neurologic deficits (16.0%), and signs of intracranial hypertension (11.7%). Additionally, common long-term complications associated with parenchymal calcified neurocysticercosis lesions include seizures (38.0%) and headaches (34.0%). The cause of headaches linked to neurocysticercosis is theorized to be due to inactive calcified parenchymal brain cysticerci which undergo structural changes and cause exposure of parasitic antigenic material to the host. The exposure of foreign material in the brain leads to transient inflammatory changes in the parenchyma producing painful sensations. The exposure of foreign material in the brain leads to transient inflammatory changes in the parenchyma producing painful sensations.

Others have reported an increased prevalence of primary headache disorders among those with calcified parenchymal brain cysticercosis, similar in magnitude to what is observed among patients with primary brain tumors. <sup>12</sup> The hypothesis for this study was that the presence of calcified parenchymal neurocysticercosis was associated with an increased prevalence of co-morbid headaches in epilepsy patients, compared to those with no structural brain abnormalities, and similar to those with other types of structural brain lesions such as primary brain tumors. An increased risk for headaches among epilepsy patients with calcified parenchymal neurocysticercosis would suggest that these patients may be more vulnerable to development of headaches, possibly related to factors specific to the parasitic infection, such as inflammation and ongoing immune system activation.

#### **Methods**

#### **Participants**

Participants were adults over the age of 18 years, who presented sequentially to a community-based neurology clinic located in

Los Angeles, CA, USA during a three-month period from October 1,2013 to December 30,2013 for evaluation or treatment of epilepsy. De-identified data were obtained and analyzed in a retrospective fashion for all participants. Institutional Review Board approval from the Los Angeles BioMedical Research Institute was obtained for retrospective analysis of already acquired and de-identified clinical data. All work was conducted in accordance with the Declaration of Helsinki (1964). Demographic information and clinical factors were determined by review of chart notes and ICD-9 codes.

#### **Diagnosis of Neurocysticercosis**

Diagnosis of brain parenchymal neurocysticercosis infection was made according to published guidelines. In summary, all of the patients included in this study met clinical diagnostic criteria for probable neurocysticercosis, based on the combination of neuroimaging findings of one or more punctate calcifications located in the brain parenchyma without alternative etiologic explanation, presence of neurologic complications such as headache or epilepsy, and membership in a population in which neurocysticercosis is endemic.

#### **Headache Frequency Determination**

Headache frequency was determined by self-report or caregiver report from chart notes. Headache frequency was calculated by dividing the number of headaches reported by the patient or caregiver during a three to six-month time interval (depending on the duration of time between scheduled clinic visits) by the number of months comprising the time interval to produce a rate consisting of number of headaches per month.

#### **Statistical Analysis**

Participants were divided into three groups: those with structural neuroimaging findings consistent with parenchymal calcified neurocysticercosis; those with other structural brain lesions such as brain tumors, old ischemic strokes, vascular malformations, structural lesions due to prior traumatic brain injury, and developmental abnormalities; and those with no structural abnormalities identified on neuroimaging studies. Presence or absence of headaches and other non-parametric data was then compared between groups using the chi-square test. Mean values for continuous demographic factors and other continuous variables, including headache frequencies, were compared between groups using an analysis of variance (ANOVA). A P-value of .05 or less indicated statistical significance and no correction for multiple comparisons was made. All statistical calculations were performed using SPSS version 22 (IBM corporation, New York, NY, USA).

#### Results

One-hundred sixty patients with epilepsy and neuroimaging results were evaluated in the clinic during the study period. These patients were approximately evenly distributed between the three groups, with 63 (39%) having neuroimaging findings consistent with parenchymal neurocysticercosis, 42 (26%) with

other structural lesions (8 with brain tumors, 8 with old ischemic strokes, 4 with vascular malformations, 14 with structural lesions due to prior traumatic brain injury, and 8 with developmental abnormalities), and 55 (34%) with no structural brain abnormalities identified on neuroimaging studies.

No significant difference in mean age was detected between the groups. The groups also did not differ significantly in use of tobacco, alcohol, or illicit substances, which could potentially trigger headaches. However, the groups did differ significantly in gender distribution, with more females present in the group with neurocysticercosis compared to the other two groups (Table 1).

For the main clinical outcome being evaluated, co-morbid headache disorders were reported more frequently among epilepsy patients with neurocysticercosis than those with either other structural brain lesions or no structural abnormalities (40%, 19%, 22%, respectively; P = .031). However, mean headache frequency did not differ significantly between the groups (Table 1).

#### **Discussion**

This retrospective cross-sectional study found increased prevalence of headaches among epilepsy patients with co-morbid calcified parenchymal neurocysticercosis compared to those with other types of structural brain lesions or those without structural brain abnormalities. The results of this study suggest that the presence of calcified parenchymal neurocysticercosis may be associated with increased likelihood for headaches among epilepsy sufferers. However, because this was a retrospective study, further research is needed to determine if a causal relationship exists between the calcified parenchymal lesions and the headaches.

Previous reports indicate that around 37% of patients with neurocysticercosis will report experiencing headaches. The percentage of epileptic patients with calcified parenchymal neurocysticercosis who reported headaches in this study was 40%, which is similar to the value reported in the literature.

Table 1. Demographic and Clinical Outcomes for Epilepsy Patients with Parenchymal Neurocysticercosis, Other Structural Brain Lesions, and no Structural Brain Abnormality.

	Neurocysti- cercosis (n = 63)	Other Lesions (n = 42)	Structurally Normal (n = 55)	<i>P</i> -Value
Mean Age in Years (SD*)	42 (13)	42 (13)	40 (13)	.588
Female (%)	42 (67%)	15 (36%)	28 (51%)	.017
Tobacco, alcohol, or substance use (%)	7 (11%)	3 (7%)	5 (9%)	.735
Headaches present (%)	25 (40%)	8 (19%)	12 (22%)	.031
Headache frequency per month (SD*)	17 (16)	12 (12)	19 (14)	.683

\*SD = Standard Deviation

Additionally, the percentage of patients in our study with non-cysticercosis related brain lesions and those with no structural abnormalities both reported comorbid headaches at rates that are essentially equivalent to what has been reported previously in the literature. <sup>13</sup> The increased frequency of headaches among those with neurocysticercosis compared to epileptic patients with other types of structural brain lesions may suggest that there is a mechanism specific to neurocysticercosis that is triggering headache generation in these patients.

Possibly, the headaches generated by calcified parenchymal neurocysticercosis may be triggered by a different mechanism than headaches caused by other types of structural brain lesions. Secondary headaches are often described as being similar to specific primary headache disorders based on the constellation of symptoms experienced by the patient, such as "migrainelike" or "tension-like" headaches. This terminology suggests that the secondary headache is occurring through a mechanism or pathway that is in some way similar to the mechanism or pathway that is implicated in generation of the primary headache disorder. One theory on how calcified parenchymal brain cysticerci may cause headaches is that an inflammatory response to the foreign parasitic material in the brain tissue is generated episodically due to remodeling of the calcified lesion.<sup>14</sup> The inflammation then leads to an increase in intracranial pressure and disruption of the blood brain barrier.<sup>14</sup> As a result, rates of synaptic transmission are affected and the primary manifestation is one of increased excitatory synaptic signaling. 15 This may then facilitate triggering of the trigemino-vascular pathway which is implicated in the generation of migraine headaches.<sup>15</sup> The increased synaptic transmission may also aid the spread of epileptic activity and contribute to seizure generation.

This study supports the proposed mechanism that focal areas of brain inflammation occurring episodically as a response to calcified cyst remodeling may be an important mechanism for headache generation in patients with neurocysticercosis. <sup>14</sup> Consequently, presence of calcified parenchymal neurocysticercosis may episodically trigger hyperexcitability of the neocortex and thereby contribute to development of both headaches and epilepsy. <sup>14</sup>

There are limitations to the study. First, there was a greater proportion of women among the group with calcified parenchymal neurocysticercosis than in the other two groups. Because female gender is known to be associated with a greater lifetime risk for developing headaches, this is a potential confounding factor that could not be excluded and, because of the relatively small sample size of this study, we were not able to control for this factor in the statistical analysis. A larger prospective study with equal gender representations would be useful in separating out the effects of gender on headache development in patients with calcified parenchymal neurocysticercosis. Second, because this was a retrospective cross-sectional study we

were not able to obtain comprehensive information related to the temporal relationship between development of headaches and calcified parenchymal neurocysticercosis lesions, which would be necessary to determine causation. Third, patients with multiple types of intracranial pathology were combined due to a limited sample size. Fourth, the cross-sectional nature of this study prevented collection of data regarding MRI findings such as the severity of cerebral edema and contrast-enhancement in the acute and chronic setting and the associated headache characteristics, severity, and responsiveness to therapies. Future studies could take into account headache specific factors such as headache type, family history of headaches, localization of headache pain, responsiveness to medications, adding a homogeneous comparison group with other structural lesions, and prospective collection of MRI characteristics such as the severity of cerebral edema and contrast-enhancement. This type of information would be interesting to know since it would help to clarify additional patient specific risk factors related to headache development and treatment efficacy. Another potential research direction could be to obtain pain scale information for all patients to include pain severity ratings of headaches of those with different types of structural lesions. It would be interesting to learn if characteristics such as the total number and/or location of calcified parenchymal neurocysticercosis lesions affect variables such as pain severity or other characteristics such as headache frequency or type.

#### **Conclusions**

The results of this study support the hypothesis that parenchymal calcified neurocysticercosis lesions may contribute to the development of headaches in epilepsy patients through episodic increases in inflammation related to ongoing cyst remodeling. Further research is needed to better understand the mechanisms by which calcified parenchymal neurocysticercosis lesions contribute to headache development. In particular, if episodic antigen release with resulting focal areas of inflammation is a causative mechanism, it would suggest the possibility of directed therapy targeting this mechanism through treatment with anti-inflammatory medications. As the frequency of neurocysticercosis cases in the United States continues to increase, the number of individuals suffering from chronic problems related to calcified parenchymal neurocysticercosis lesions such as epilepsy and headaches will likely increase as well.4 Consequently, more research on this disorder and treatment of common problems associated with these lesions could lead to better diagnostic methods and treatment options for future patients.

#### **Conflict of Interest**

None of the authors identify any conflict of interest.

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### MEDICAL SCHOOL HOTLINE

# From Laboratory Bench to Community: Tropical Medicine Students Promote Vaccination in Hawaiii

Yukie Lloyd-Sato MS; Eleanore Chuang BS; Priscilla Seabourn MS; Han Ha Youn BS; Bradley Thomas; Michael Fernandez; and Tiana Elisara

The Medical School Hotline is a monthly column from the University of Hawai'i John A. Burns School of Medicine and is edited by Satoru Izutsu PhD and Kathleen Kihmm Connolly PhD; HJMPH Contributing Editors. Dr. Izutsu is the vice-dean of the University of Hawai'i John A. Burns School of Medicine and has been the Medical School Hotline editor since 1993.

#### Introduction

On October 22, 2015, graduate students from the Department of Tropical Medicine, Medical Microbiology & Pharmacology (TRMD), and the Department of Microbiology at the University of Hawai'i (UH) at Manoa volunteered to assist a public screening of "Someone You Love: The HPV Epidemic" held by the Hawai'i Immunization Coalition (HIC). What began as a single volunteer opportunity sparked the Student Immunization Initiative (SII), with an objective to continue educating the public about vaccine-preventable diseases, and later expanded to prevention of all infectious diseases. SII is led by graduate students in TRMD, a department that provides future leaders in infectious disease research with a world-class transdisciplinary education encompassing basic, clinical, and translational aspects at the bench and in the field. Carrying on this mission, SII became a Registered Independent Organization at UH Manoa in Fall 2016, with the goal of providing validated medical knowledge to the general public in order to make informed decisions about healthcare.

This initiative was conceived during an immunology class taught by Dr. Sandra Chang, faculty adviser of the organization, when graduate students learned about the decline in vaccine uptake in the United States. With backgrounds in microbiology and infectious disease research, these students understood that vaccines have saved millions of lives and led to eradication and elimination of devastating diseases such as smallpox and polio. In this digital age, it has become easy for people to access information on the internet but increasingly difficult to distinguish scientific fact from fiction on which to base sound healthcare decisions. Since its founding, SII members have been actively involved in a number of education and outreach efforts promoting vaccination and disease prevention.

#### **Quest for a Cure**

Since its inception, SII has focused particular attention on efforts to reduce human papillomavirus (HPV)-related morbidity and mortality. As a member organization of the "Vaccine-preventable cancer workgroup," SII presented an exhibit at the 6th annual "Quest for a Cure: Progress in Cancer Research" community



event at the John A. Burns School of Medicine (JABSOM). The exhibit featured educational brochures and posters, a movie trailer on HPV and cancer, and an interactive jeopardy game to educate attendees on HPV vaccines, cervical cancer, and other HPV-associated cancers. Event participants who visited the exhibit expressed interest in learning more about preventing HPV-associated cancers and sharing the information with their children and grandchildren.

#### 2016 Hawai'i Public Health Conference

In addition to community outreach events, SII has actively participated in professional meetings. On October 14, 2016, SII officers presented a poster at the 2016 Hawai'i Public Health Conference, organized by the Hawai'i Public Health Association. Describing the organization's origin, projects, and goals, the poster attracted many participants, leading to new partnerships and collaborations. SII was engaged in planning meetings for National Public Health Week in April 2017 and is listed as a volunteer organization for the 2018 Global Public Health Conference (tentatively titled).

# Centers for Disease Control and Prevention (CDC) Pink Book Course

To inform vaccine providers about the HPV vaccine and share tips on how to discuss vaccination with patients, members hosted an informational booth at the CDC Pink Book Course on January 10-11, 2017. Organized by HIC and aimed primar-

ily at healthcare providers, the course covered updated vaccine dose schedules, administration best practices, along with the most recent recommendations from Advisory Committee on Immunization Practices (ACIP). It was the first CDC Pink Book Course held in Hawai'i in over twenty years! SII members attended the full course and received certificates of completion.

#### **Teen Health Camp**

SII works closely with medical students and their interest groups. In November 2016, SII had a booth at the 2016 Teen Health Camp at JABSOM. At the booth, SII members talked to students grade 6-12 about graduate school, career paths, and research at TRMD. Officers of SII were featured on KITV4 news coverage of the event on November 19, 2016. Link: https://www.instagram.com/p/BNBnIBvDPnw/?taken-by=siihawaii

#### **JABSOM Community Health Fair**

An informational booth was displayed by SII at this year's "Lamalama Ke Ola Kino" ("Glow with Health"), on January 15, 2017. Organized by medical students, the event exhibited health-related booths from food to fitness. SII members discussed the importance of HPV vaccination as cancer prevention with a broad spectrum of attendees. After participating in the CDC Pink Book Course just a few days earlier, members of SII were able to share valuable information about the most updated ACIP recommendations.

#### **Medical Mycology Workshop**

After a year of planning, SII hosted Hawai'i's first ever Medical Mycology Workshop at UH Cancer Center Sullivan Conference Center on January 20, 2017. American Society for Microbiology (ASM) Distinguished Lecturer Dr. Nancy S. Miller, Medical Director of Clinical Microbiology and Molecular Diagnostics from the Boston Medical Center and Associate Professor of Pathology and Laboratory Medicine at Boston University School of Medicine, covered a broad range of medically important fungi and presented real cases that illustrated diagnostic challenges. The event was funded by a grant from the ASM and supported by ASM Hawai'i Branch and student chapter. Attendees included healthcare providers, government and industry scientists, and faculty and students from UH Manoa. With overwhelmingly positive feedback, SII plans to make the workshop an annual event. A short article about the event is expected to be published in the newly launched ASM Microcosm magazine!

# **Distributing Information through Social Media**

Social media is effectively used by SII to connect with members of the community. Through the organization's website, Twitter, and Instagram, SII provides information on vaccine and health-related news as well as updates on ongoing and future projects. Currently there are 135 followers on Instagram and 80 followers on Twitter.

#### **Partnerships and Collaborations**

Through community activities and events, SII has received recognition and established partnerships with organizations such as HIC, Hep Free Hawai'i, Vaccine Preventable Cancer Workgroup, Hawaii Public Health Association, and Vaccine for the World's Children Japan Committee. The only official campus club for UNICEF USA in Hawai'i is SII. Furthermore, current and future SII presidents serve on the board for HIC, gaining valuable experience working on legislative issues and learning organization and management within a coalition.

#### **Future Directions**

SII has demonstrated its effectiveness in advocating for vaccination and disease prevention. Compared to larger not-for-profit and non-governmental organizations, student organizations like SII are flexible, mobile, and community-friendly. Students are able to incorporate new techniques, digital apps, and social media that enhance outreach to younger demographics. With outstanding support from JABSOM, TRMD, and its partner organizations, SII is able to access and distribute scientifically based educational materials at numerous health fairs and community events. In the future, SII will continue to participate in community health events and public health conferences and to expand current educational programs to reach local schools and hard-to-reach communities. Visit the SII website at siihawaii. org and follow Instagram and Twitter accounts @siihawaii.

#### **Acknowledgments**

Dr. Sandra Chang and members of faculty advisory committee are credited for their leadership and guidance. The Department of Tropical Medicine, Medical Microbiology and Pharmacology, partner organizations and collaborators are recognized for their unwavering support of SII. This experience has provided valuable insight into public health efforts to increase vaccination coverage for the people of Hawai'i.

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### INSIGHTS IN PUBLIC HEALTH

### Making Health Hawai'i's Shared Value

Matthew Turnure MPH and Virginia Pressler MD, MBA

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 Lance K. Ching PhD, MPH and Ranjani R. Starr MPH from the Hawai'i Department of Health.

#### Introduction

The mission of the Hawai'i State Department of Health (DOH) is to protect and improve the health and environment for all people in Hawai'i. To accomplish this mission, the DOH is involved in activities as wide ranging and diverse as disease outbreak control, chronic disease prevention and management, and environmental protection among many others. In late 2015, the DOH began a strategic planning process to address the current health needs of Hawai'i residents in the context of today's public health and health care landscapes. Programs throughout the department were engaged to establish priorities and objectives informed by a unifying conceptual framework.

The theme of the Strategic Plan is "Make Health Hawai'i's Shared Value." Underlying this theme are two concepts that are central to the DOH's approach to public health: the social determinants of health (SDOH) and the life course health development (LCHD) framework. The SDOH are the fundamental social and economic drivers of the conditions in which we live, such as our educational attainment, income level, race and ethnicity, and neighborhood and environmental safety.<sup>1,2</sup> A large and still growing body of research shows that while access to affordable and effective medical care is critically important, it is responsible for only 10%-20% of our health outcomes. The SDOH, however, account for 20%-45% of differences in health outcomes.<sup>3</sup> Related to the SDOH is the LCHD framework, which shows that individual health trajectories are determined by a multitude of determinants that interact and constantly change across the life span.4 In this framework, early life stages are the most crucial periods to encourage healthy growth and development, but each stage of life has its own unique challenges and opportunities to promote health. Prioritizing investments in the systems that create healthy environments where people of all ages live, learn, work, and play can lead to better health and quality of life for everyone who calls Hawai'i home.

The framework for the plan organizes objectives around three broad strategies for making health Hawai'i's shared value: Invest in Healthy Babies and Families (Table 1); Take Health to Where People Live, Work, Learn, and Play (Table 2); and Create a Culture of Health Throughout Hawai'i (Table 3). This article will introduce a top priority for each of these strategies

— reducing substance use and exposure for pregnant mothers, fostering the uptake of telehealth technologies in the state, and investing in better mental health — to explain the DOH vision in each area.

#### Table 1. Invest in Healthy Babies and Families

- 1. Reduce substance use and exposure for pregnant mothers
- 2. Decrease unplanned pregnancies
- 3. Support parents and extended ohana after childbirth
- 4. Promote optimal developmental screenings and services in early childhood
- 5. Enhance maternal bonding and obesity prevention through breastfeeding
- 6. Address conditions contributing to child and maternal mortality
- Plan for a system of care for adolescents that addresses physical and emotional health

#### **Healthy Babies and Families**

Even before conception, a mother can increase the chances of a healthy pregnancy and delivery by adopting a healthy lifestyle and working with her doctor and other health care providers to manage any medications or concerns as they arise. The DOH is working with the Hawai'i Department of Human Services (DHS) and community partners to implement the One Key Question Initiative® (OKQ), a model developed by the Oregon Foundation for Reproductive Health, to assure that pregnancies are wanted, planned, and as healthy as possible.

The OKQ model starts with health care workers asking women of reproductive age a simple question: "Would you like to become pregnant in the next year?" For women who wish to become pregnant, preconception counseling and care should be provided. Cessation of alcohol, tobacco, and other drug use, screening for and managing chronic conditions, monitoring any current medications, and optimizing weight status improve the chances of a healthy pregnancy and delivery. For women who do not desire pregnancy, the full range of contraceptive services should be discussed and offered, including long-acting reversible contraceptives. Women who are unsure or ambivalent should be made aware of all options and services that are available.

It is also important to support mothers during the prenatal period, a critical time for both the expecting mother and her child. Prenatal care visits that begin early in a pregnancy and continue regularly are associated with positive birth outcomes. One important aspect of a healthy pregnancy that may be addressed during a prenatal visit is the cessation of alcohol, tobacco, or other drug use. The DOH is promoting the practice of prenatal Screening, Brief Intervention, and Referral to Treatment (SBIRT), an evidence-based approach to identify, reduce, and prevent problematic substance use. 8

In the prenatal SBIRT model, every pregnant woman may be screened for substance use. If a patient screens positive for moderate risk substance use but not dependence, the provider may briefly counsel the patient, raising awareness of the substance use and its consequences, then motivating them towards positive behavior change. If the screening indicates high risk, the provider may refer the patient to further treatment. The SBIRT model provides the opportunity to intervene with both moderate and high risk users. The DOH will lead community efforts to create economic incentives, increase provider awareness, and better connect community resources to encourage adoption of SBIRT for expecting mothers.

#### Table 2. Take Health to Where People Live, Work, Learn, and Play

- 1. Invest in telehealth to improve health access
- 2. Prevent and contain epidemics and disease outbreaks
- 3. Improve connections between primary care and behavioral health
- 4. Improve life trajectories for vulnerable persons
- 5. Partner with communities to identify and meet their needs
- 6. Create communities where the healthy choice is the easy choice
- 7. Improve home, school, and workplace safety and wellness

#### **Telehealth**

Where we live can have profound effects on our health. Many communities in our island state face challenges accessing the medical care they need. Telehealth technologies such as live videoconferencing, secure forwarding of images to physicians, and remote monitoring can remove the barrier of geographic isolation in many situations, reduce travel time and expenses, and improve patient outcomes. Whether the originating site be a provider office, patient home, school, or other location, telehealth technologies truly offer an opportunity to take health into where people live, work, learn, and play.

Telehealth is not yet a major component of Hawai'i's health care system. According to the John A. Burns School of Medicine Physician Workforce Annual Report, submitted to the 29th Legislature in 2016, 15% of physicians responding to the survey report participating in telehealth. However, several existing examples of successful telehealth initiatives around the state demonstrate the feasibility and potential impact of the technologies. The Genetics Program of the Children with Special Health Needs Section in the DOH provides education, counseling, and

coordination services to children with genetic disorders and their families. The program uses telehealth technology to connect families across the state to geneticists and genetic counselors based on O'ahu, resulting in better access, reduced costs-pervisit, and high consumer satisfaction. The DOH's Child and Adolescent Mental Health Division (CAMHD) provides mental health prevention, assessment, and treatment services to children and adolescents with emotional and behavioral challenges. CAMHD has established a statewide video teleconferencing system that allows providers to conduct telehealth visits remotely with clients in a variety of locations, including school and home settings, cutting down intake and assessment times dramatically. In the private sector, the Hawaiian Islands Regional Stroke Network, funded in part by the Department of Health Neurotrauma Special Fund, connects stroke neurologists at The Queen's Medical Center "hub" in Honolulu with eight "spoke" hospitals around the state that do not have consistent access to a stroke specialist on-site, including hospitals in The Queen's Health Systems, The Hawai'i Health Systems Corporation, and Wahiawa General Hospital. The O'ahu-based neurologist assesses patients via high-definition videoconferencing and, if appropriate, authorizes administration of clot-busting treatments, greatly reducing time-to-treatment, lowering the risk of permanent disability, and saving lives.

The landmark enactments of Act 159 in 2014 and Act 226 in 2016 by the Hawai'i State Legislature set the stage for accelerated uptake of telehealth. 12,13 Act 159 required equivalent private insurance reimbursement for telehealth services compared to traditional face-to-face services. Act 226 followed two years later with a number of requirements and clarifications, including: requiring that Medicaid programs cover telehealth services; clarifying that telehealth encompasses store-andforward technologies, remote monitoring, live consultation, and use of mobile devices; ensuring that telehealth services are covered when originating in non-medical environments such as a patient's home; and specifying medical professional liability insurance policy requirements for telehealth. The DOH is committed to building on this foundation to assure that telehealth is a viable and sustainable way of delivering health care across the state. The DOH will convene a statewide telehealth council, comprised of the highest levels of government, healthcare, and technology to plan for a future of increased access to care for residents across the state.

#### Table 3. Create a Culture of Health Throughout Hawai'i

- 1. Invest in better mental health
- 2. Enforce public health and environmental regulations
- 3. Make public health and environmental data more accessible
- 4. Improve and protect Hawai'i's water, air, and land
- 5. Adapt to and mitigate effects of climate change
- 6. Enhance public health communications to influence, educate, and motivate
- 7. Enhance laboratory and scientific services



#### **Mental Health**

Mental health, which includes our emotional, psychological, and social wellness, is crucial throughout the life span, from infancy and early childhood through adulthood. Investing in better mental health is one way the DOH is creating a culture of health throughout Hawai'i.

The DOH is taking steps to address mental health concerns in the community with two efforts to integrate mental health services with primary care. The Alcohol and Drug Abuse Division (ADAD) recently received a grant from the Substance Abuse and Mental Health Services Administration (SAMHSA) that provides \$8.4 million over five years to support increased behavioral health screening for all adults in primary care settings. The grant will support development of a comprehensive statewide referral system and trainings for providers on how to integrate SBIRT into current practice. Another example of behavioral-primary care integration is the Living Well Hawai'i

project, a collaboration between the DOH Adult Mental Health Division and the Kalihi-Palama Health Center (KPHC), a federally qualified health center. The first of its kind in Hawai'i, this pilot project embeds primary care staff in behavioral health settings in order to create integrated care management teams, leading to more coordinated and patient-centered service-delivery for adults with serious mental illness.

The DOH also has services available 24 hours a day, 7 days a week to individuals experiencing a mental health crisis. The Crisis Line of Hawai'i provides supportive counseling and if needed will dispatch crisis workers to provide in-person crisis interventions in the community. Finally, to better care for the highest need individuals in our communities, a major milestone was achieved in 2016 when the Legislature approved \$160.5 million for the construction of a new state-of-the-art secure facility for the Hawai'i State Hospital in Kane'ohe.<sup>14</sup>

#### Conclusion

The projects and strategies discussed here are among the top priorities for the DOH moving forward. The department will invest in healthy babies and families by working to reduce substance use and exposure for pregnant mothers; take health into where people live, work, learn and play by fostering the uptake of telehealth technologies in Hawai'i; and create a culture of health in part by investing in better mental health. Of course, the department's work extends far beyond these examples. The Strategic Plan lays out objectives for every program across the DOH, and is available online at http://hawaii.gov/doh/strategicplan.

Making health Hawai'i's shared value means nurturing growth and development across the life span to establish positive health trajectories. It means understanding the unique health needs of communities across the state, and finding ways to share resources to meet those needs. It means looking for opportunities to improve health at every turn, whether those opportunities are in the doctor's office or in our schools, workplaces, or homes. Finally, it means that creating better health is an opportunity that we all share, both as individuals and as communities. The DOH will continue working with partners around the state to make this vision a reality.

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# THE DANIEL K. INOUYE COLLEGE OF PHARMACY SCRIPTS

### **Obesity: The Drug Dose Debate**

Cherie Chu PharmD; Louis Lteif PharmD; and Nicole Young PharmD

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The increasing prevalence of obesity has led to a global epidemic and a growing public health concern since obesity is a known risk factor for increased healthcare related morbidity and mortality. Hawai'i's obesity rate of 22.7% ranks as the 3rd lowest obesity rate in the United States, and its territories. However, Native Hawaiians or Pacific Islanders (NHOPIs) make up 26% of Hawai'i's population and prevalence of obesity in this population is approximately 55%. Although Hawai'i was rated as the healthiest state in the nation for 2016, local clinicians still face the issues of treating obese patients and their associated comorbidities of diabetes, cardiovascular disease, stroke, and cancer. And cancer.

One of the burning questions encountered for many clinicians when treating the obese population is, "Does this drug dose fit my patient?"

The World Health Organization (WHO) classifies obesity based on body mass index (BMI), a parameter calculated as a person's weight in kilograms divided by their height in meters squared. Generally, obesity is defined as having a BMI greater than 30 kg/m<sup>2</sup>. The WHO further breaks down obesity into the following classes; class I, II, and III defined as a BMI of 30 to 34.9 kg/m<sup>2</sup>, 35 to 39.9 kg/m<sup>2</sup>, and greater than or equal to 40 kg/m<sup>2</sup>, respectively.<sup>7</sup>

Drugs are commonly dosed using the FDA approved "one size fits all" dose, but some medications can be dosed by patient's weight, ie, mg/kg. Nevertheless, these dosing recommendations are largely based on studies that excluded obese patients, and do not take into account the pathophysiologic changes that may alter the effects of drugs in patients with obesity. The concept of a "one size fits all" dose remains a topic of debate with respect to safety and efficacy of pharmacologic treatments. Common drug classes that continue to have the "Obesity Drug Dose Debate" are anticoagulants and antimicrobials.

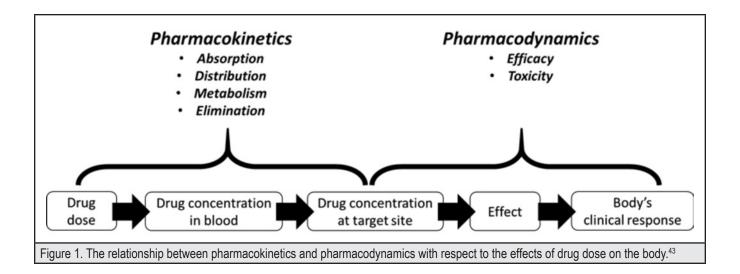
### **Pharmacokinetics and Pharmacodynamics**

Pharmacokinetics (PK) is described as the physiological effects of the body on a drug's absorption, distribution, metabolism, and elimination. Pharmacodynamics (PD) is described as the physiological effects of the drug on the body and may be thought of in terms of efficacy and toxicity. The relationship between PK and PD can be seen in Figure 1.

The highly varying physiology of patients with obesity may yield differing PK parameters such as volume of distribution (Vd) and drug clearance (Cl), than those seen in population clinical studies. Vd refers to the size of a body's compartment that needs to be "filled" in order to maintain the same concentration in the plasma. Changes in Vd would primarily alter the PK profile of lipophilic drugs, although hydrophilic drugs could also be affected due to an increase in the volume of lean muscle mass.11 Alterations in Vd and drug plasma concentrations may occur due to the increased ratio and distribution of fatty tissue to lean body mass. An increase in fatty tissue will increase the Vd for drugs with high lipophilicity, the ability of a chemical compound to dissolve in fats. This increase in drug sequestration in fatty tissue, then can theoretically decrease the drug plasma concentration, resulting in a failure of a given dosage of drug to achieve the desired response.

Drug clearance (Cl) is the ability of the body to remove drug from the blood or plasma. <sup>10</sup> Hydrophilic drugs are mainly eliminated through the kidney. <sup>12</sup> In obese patients, renal clearance may be increased, possibly through "obesity-related glomerulopathy," which is associated with increased renal plasma flow and increased filtration rate; however, this is not observed as a linear correlation with total body weight and calculation of Cl in obese is not well validated. <sup>11,13,14</sup> These changes in PK ultimately affect PD in obese patients, which leads to potentially enhanced, diminished, or delayed drug effects.

Furthermore, confounding variables occur during acute illness, such as decreased hepatic blood flow and acute kidney injury, may also alter Vd and Cl, further complicating drug dosing in obese patients. If higher doses are given in obese patients to accommodate for higher weight, there is concern for supratherapeutic responses and if doses are capped based on max doses for non-obese patients, there is concern for subtherapeutic responses to the administered drug. The conundrum of under versus over dosing in obese patients may lead to suboptimal treatment or increased adverse drug effects, respectively, both with potentially detrimental outcomes. Understanding the basic drug PK and PD variations that occur in obese patients allows for personalized care and may lead to improved clinical outcomes.



This paper addresses the issue of drug dosing in obese patients, specifically with anticoagulants and antibiotics. Proper dosing is necessary to assure optimal safety, efficacy, and additionally in the case of antibiotics, minimize the development of bacterial resistance.

#### **Anticoagulants**

Currently, there is a lack of standardized protocols and guidance on how to optimally dose both oral and injectable anticoagulants for therapeutic anticoagulation in obese patients. Controversy remains on whether these patients should be dosed by a fixed dose or dosed by weight for the most effective therapeutic interventions. Recommended fixed doses may be sub-therapeutic and thus raise the concern for an increased risk for clot formation. On the other hand, dosing by total body weight in obese patients raises concerns for over-anticoagulation and the increased risk of bleeding.

### Enoxaparin

Enoxaparin is an injectable anticoagulant commonly used for venous thromboembolism (VTE) treatment and prophylaxis. Obesity itself is considered a risk factor for VTE, and the dose for pharmacological treatment and prophylaxis in patients with obesity remains patient specific and varies between clinicians. <sup>15,16</sup> Enoxaparin doses of 40 mg daily for VTE chemoprophylaxis and enoxaparin 1 mg/kg twice daily for VTE treatment are recommended by different studies and are commonly used in practice. Although there is a lack of consensus regarding the optimal size descriptor (lean versus total body weight in varying BMI) for determining weight-based doses in patients with obesity, studies have shown that weight-based dosing has benefit for patients who fall into the category of Class 3 obesity (≥40kg/m²) and those who are above 190kg. <sup>11,17,18</sup>

A 2010 study by Freeman and colleagues compared the standard enoxaparin 40 mg daily fixed dose for VTE prophylaxis to high-dose (enoxaparin 0.5 mg/kg daily) and low-dose (enoxaparin 0.4 mg/kg daily) weight-based dosing in morbidly

obese patients. 15 The outcomes of the Freeman study showed that the high-dose, weight-based dosing group achieved target anti-Xa levels (0.2-0.5 IU/mL) more frequently, showing favor for the non-fixed, weight-based dosing. 15 In a 2011 case series by Deal and colleagues, enoxaparin doses for treatment of VTE correlated to anti-Xa levels in the morbidly obese. It was found that weight-based dosing of 1 mg/kg every 12 hours, with a maximum dose of 150 mg every 12 hours, resulted in enoxaparin doses ranging from 0.67 mg/kg to 1 mg/kg (median 0.8 mg/kg) with steady state anti-Xa levels falling within or above goal with no levels below goal.<sup>19</sup> While this case series favored capping the dose of enoxaparin for VTE treatment in morbidly obese patients in order to reduce risk of bleeding, other studies for VTE prophylaxis have determined that not capping doses for obese patients allows for appropriate achievement of therapeutic anti-Xa levels without increasing the risk of bleeding. 19-21 Thus, enoxaparin dosing in obesity remains highly controversial due to the lack of qualitative studies and the varying pharmacokinetic and pharmacodynamic alterations in the obese population altering Vd and Cl.22

Anti-Xa levels are commonly used in clinical practice to determine the degree of anticoagulation from enoxaparin. It is recommended to use these levels for monitoring enoxaparin dosing in obese patients to determine the safety and efficacy of the drug.<sup>23</sup> Established anti-Xa levels commonly used in practice are 0.5 to 2.0 IU/mL for full therapeutic dosing and 0.18 and 0.44 IU/ml for prophylactic dosing.<sup>24</sup> However, due to variations in individual institutional assays, it may be best for individual institutions to develop their own ranges.

#### **Oral Anticoagulants**

Direct oral anticoagulants (DOACs) target a specific factor in the clotting cascade, whereas warfarin, the hallmark anticoagulant, targets multiple clotting factors. DOACs such as dabigatran, rivaroxaban, apixaban, and edoxaban, are becoming more commonly used for treatment of venous thromboembolism (VTE) and for stroke prevention in atrial fibrillation due to their ease

of use and relatively favorable safety profiles compared to warfarin. Many of the landmark trials, which led to the Food and Drug Administration (FDA) approval of these drugs, did not include patients with morbid obesity (>120 kg or BMI >40kg/ m<sup>2</sup>). In the six years since the FDA approved these DOACs, sparse post-marketing PK and PD data has not helped prescribers to appropriately dose these agents in obese patients. Early PK studies of rivaroxaban and apixaban in healthy subjects, showed little difference in the peak or trough levels after one dose of each drug in subjects with normal weight versus those with weight >120kg.<sup>25,26</sup> Yet, in a recent review of DOACs by Buckley and colleagues, apixaban and rivaroxaban were reported to have reduced levels in obese patients, although the effect of this was not demonstrated in the clinical outcomes. Because of a lack of PK, PD, and clinical outcomes data for dabigatran and edoxaban, these drugs are typically not included in the ongoing debate on dosing in obese patients.<sup>27</sup>

Unlike enoxaparin, laboratory tests that can determine the degree of anticoagulation with DOAC's are not currently available for use in clinical settings. With little post-hoc analysis and clinical laboratory tests available to better inform clinicians on the degree of anticoagulation, caution should be exercised in dosage adjustments when using DOACs in obese patients.<sup>27,28</sup>

#### **Antibiotics**

Obesity has been regarded as a risk factor for infectious disease, and has been associated with poorer outcomes for many infectious disease states including bacteremia, nosocomial infections, surgical site infections, and skin infections.<sup>29,30</sup> The PK changes in obese patients affect antibiotic therapy, and should be taken into consideration for optimal antibiotic treatment in this population at risk for infectious complications. Three important antibiotic PD concepts include: (1) time of exposure of bacteria to an antibiotic, T>MIC; (2) the maximum achieved concentration of antibiotic in the body (Cmax/MIC); and (3) the combination of time and concentration (AUC/MIC).<sup>31</sup> The concept of time of exposure describes the time that a certain drug concentration is over the minimum inhibitory concentration (MIC), which is commonly referred to as T>MIC. A minimum inhibitory concentration (MIC) is the minimum concentration of antibiotic needed to inhibit visible growth of bacteria in a test tube. The more time (T) the concentration of the antibiotic in the body is above the MIC, the higher the bacterial kill. The second concept focuses on concentration of antibiotic in the body. Cmax is the highest concentration of the antibiotic achieved in the body after a dose is administered. The higher the ratio of Cmax/MIC (high Cmax/low MIC) the more effectively the antibiotic is able to kill the bacteria. The last concept is a combination of time dependent and concentration dependent killing that looks at the total exposure of the drug in the body or area under the curve (AUC). A larger AUC over a low MIC in a 24-hour period of time is another indication of antibiotic effectiveness in killing bacteria. The optimal ratio of AUC/ MIC depends on the type of bacteria and specific antibiotic

used, where the largest effect is seen when antibiotic exposure is maximized with respect to the MIC. <sup>31</sup>

Alterations in PK and PD parameters in patients with obesity, affect drug concentrations in the body and may directly affect the three concepts just reviewed. With the exception of a few antibiotics (aminoglycosides, vancomycin, daptomycin), there remains a paucity of data in regards to dosing antibiotics in the obese population. <sup>32</sup>Based upon dosing guidelines, the following recommendations outline the dosing of aminoglycosides, beta-lactams and vancomycin in obese patients.

#### Aminoglycosides

Aminoglycosides, such as gentamicin, amikacin and tobramycin, are hydrophilic molecules that rely on concentration dependent killing for efficacy. For non-obese patients, ideal body weight is typically utilized for dosing.<sup>33</sup> For the obese population, this approach might result in subtherapeutic serum concentrations, and thus, several studies suggest using dosing based on an adjusted body weight (ABW), with a correction factor of 0.4 for the additional weight in kilograms over the IBW. Prior studies, using ABW have demonstrated an improved prediction of aminoglycosides' Vd and is considered the best approach to tackle the increased total body clearance.<sup>31</sup> Therapeutic drug monitoring of aminoglycosides is recommended with drawing of appropriately timed peak and trough levels.

#### **Beta-lactams**

Beta-lactams are widely utilized and are comprised of penicillins, cephalosporins, carbapenems, and aztreonam. These hydrophilic molecules rely on time dependent properties of antibiotics for efficacy. Very few studies have evaluated dosing of penicillins in patients with obesity but some suggest using the upper end of the dosage ranges.<sup>32</sup> A study evaluating standard doses of piperacillin-tazobactam in patients with complicated intra-abdominal infections, found lower cure rates in patients with a BMI of 30 kg/m<sup>2</sup> or more. <sup>34</sup> PK/PD studies suggest using an extended infusion time of 4 hours (rather than the standard 30 mins) for piperacillin-tazobactam to achieve optimal levels for good outcomes. The extended infusion model was further validated in a case-study of a morbidly obese patient in whom piperacillin-tazobactam infused at a higher dose and extended time more consistently achieved desired levels and cure rates than the standard dose and infusion time. 35 Cefazolin is widely utilized for prevention of surgical site infections. Obese patients receiving a higher dose of 2 g versus the standard 1 g dose had lower rates of perioperative wound infections.<sup>36</sup> Similarly, a higher dose of cefepime (2 g every 8 hours) was needed in morbidly obese patients to achieve appropriate T>MIC of at least 60%.37 There are conflicting studies for the dosing of ertapenem. One study showed that lower concentrations of the antibiotic are achieved in obese patients who received the usual 1 g dose, resulting in inadequate treatment for patients with bacteria that exhibited higher MICs.38 Another study demonstrated identical cure rates in both patients with BMI of less than 30 kg/m² and more than 30 kg/m² when ertapenem was used for complicated intraabdominal infections.³4 Lastly, a study that examined aztreonam in obese patients had a much lower AUC, potentially due to higher Vd and Cl, and did not achieve therapeutic levels of aztreonam in obese compared to non-obese patients.³9

#### Vancomycin

Vancomycin is another hydrophilic molecule that depends on AUC/MIC ratio for efficacy. In the treatment of Methicillin-Resistant Staphylococcus Aureus (MRSA), a resistant bacteria for which vancomycin is the drug of choice, an AUC/MIC ratio of at least 400 is needed to achieve optimal outcomes. Several studies concluded that actual body weight should be used for dosing vancomycin in obese patients, rather than using a standardized defined dose, in order to achieve therapeutic vancomycin levels and optimal AUC/MIC ratios of >400.40 This is because vancomycin clearance in obese patients is higher than other patients, likely due to obesity related glomerulopathy, thus necessitating higher doses. Total body weight seems to be adopted by many institutions for determining loading doses of vancomycin with a cap of 2 or 3 grams.<sup>41</sup> However, the higher dosing may cause adverse effects: one study found a higher instance of nephrotoxicity in patients above 100 kg.<sup>41</sup> Maintenance dosing, however, seems to be more related to the measure of renal function rather than weight.<sup>42</sup>

#### Conclusion

This review discusses the variations in PK and PD parameters in patients with obesity and reviews some of the different dosing strategies for commonly used anticoagulants and antibiotics. The movement towards "patient specific" care should be taken into consideration for drug dosing in obese patients. PK and PD alterations as well as physiological changes during acute illness require close monitoring to determine the safety and efficacy of these commonly used drugs in obese patients. More studies are needed that incorporate larger population samples with BMI  $>40 \, kg/m^2$  to better understand and personalize pharmacotherapy for obese patients.

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### THE WEATHERVANE

RUSSELL T. STODD MD; CONTRIBUTING EDITOR

#### ATTENTION DISEASE; THERE'S FUNGUS AMONG US.

In November 2012, the Centers for Disease Control and Prevention (CDC) reported an outbreak of confirmed fungal meningitis caused by contaminated medication. The New England Compounding Center (NECC) made three contaminated lots of an injectable steroid that caused 750 cases of fungal meningitis in 20 states with 64 deaths. The CDC found Exserohilum rostratum and Aspergillus fumigatus in one case and a Cladosporium species was found in one case. The Food and Drug Administration (FDA) inspectors found contaminated drug batches and unsanitary conditions on equipment at NECC. Pharmacist Barry J. Cadden co-owner of the now closed NECC was charged with second-degree murder. Recently a federal jury in Boston acquitted Cadden on the murder charge, but convicted him of racketeering, mail fraud, and other crimes in the sale of contaminated medication. Prosecutors failed to show he had "specific intent to kill" to prove the murder charge, so he is spared a possible life prison sentence. The families of the 64 fatalities as well as many of the 750 other non-fatal victims might find fault with the decision. Sentencing on the convictions is scheduled for June 21.

#### GOT ON AS A DOCTOR; GOT OFF AS A PATIENT.

It is safe to say that everyone who flies on commercial trips in this decade is angry and disgusted with passenger treatment. Not only are air travelers deprived of elbow-room and knee space, they must pay to check baggage, use certain aisle seats, and use of a blanket, to mention a few previous givens. Moreover, air carriers admit that they frequently overbook busy flights and remove paid passengers to make space for more 'deserving' clients. United Airlines violated all normal courtesies when they directed Chicago airport security to physically remove a physician, dragging him down the aisle, and ejecting him from the flight. He refused to accept the financial offer because of his medical obligations the following day in Louisville. This Asian American doctor was injured when he resisted removal. Dr. Dao's attorney, Thomas Demetrio, said "You don't treat the people who help make the corporate entity you are like, Dr. Dao was treated." In the following days, the attorney was bombarded with calls from passengers and current and former United employees with tales of woe and abuse by United. Subsequently, Demetrio obtained a sealed settlement for his client. In fairness to United it should be noted that the airline was a regional carrier. Strangely, it took three days before United CEO Oscar Munoz apologized and said he was ashamed of United's action. But the bottom line is money, and since the petroleum glut, all the airlines are rolling in profits, and they just don't care.

#### PILING ON: HOW MOSQUITOS BUILD ON THEIR SUCCESS.

Many medical scientists have suspected that mosquitos are preferentially drawn to people infected with malaria, but no one has shown what piques the insects' interest. Recently the mechanism for how the Plasmodium apparently evolved to enhance the attraction was demonstrated in Sweden. Ingrid Faye, a biologist in Stockholm, found when watching mosquitos feed they ate more blood when HMBPP was present. The HMBPP molecule (4-hydroxy-3-methyl-but-2-enyl pyrophosphate) was studied for its effect on the immune system of the Anopheles mosquito. When the molecule was mixed with serum only, the insects ignored it, but when mixed with red blood cells they dined. The HMBPP hemoglobin produced greater amounts of airborne chemicals, aldehydes and monoterpenes, an aroma that attracted the Anopheles. So, it follows that people who have HMBPP percolating in their hemoglobin are more vulnerable than the general population.

## STILL SOME BUGS IN THE SYSTEM: ITS DEFINITELY NOT VIRTUAL PUKE.

The high tech evangelists predicted that 2016 would be a big year for virtual reality. Several VR headsets quickly hit the commercial market. People went to Sony and other tech designers for Christmas gifts others went on line to purchase headsets, ranging from \$300 and up. The headset blocks out all visual stimuli except the device, creating great avenues for games and whatever. All too soon, a new illness called VR sickness appeared. About 25 to 40 percent of people suffer from motion sickness, according to estimates. Women are more susceptible than men. Whatever the VR is focused on car, boat, plane, stairways, the game may cause nausea, dizziness, and headache. The technology is moving into other fields, real estate, autos, even school labs for field trips. Mark Zuckerberg, Facebook CEO, sees virtual reality as the next big social platform. So, like it or not, we have another bit of electronic wizardry we must learn to live with.

# \$66 MILLION TAX DOLLARS LATER THEY ARE STILL MAN'S BEST FRIEND.

The Defense Advanced Research Projects Agency spent \$66 million between 1997 and 2010 challenging 35 different research institutions to develop sensors that could detect explosives as capably as a dog. Canines have been found to detect butyric acid (smells like vomit or body odor) at the astonishingly low rate of 0.0004 parts per trillion. Moreover, when they come into contact with an odor, they can track it to its source. Working for the U.S. Army, the Southwest Research Institute tested a variety of animals compared to dogs. Cats were uncooperative, sheep and goats were deemed too stupid, but dogs, pigs, ferrets, coyotes, wolves, foxes, skunks, opossums, deer, and raccoons all made the cut. Overall, dogs won out. They have strong noses, they are compatible with people, they respond to training, and they beat technology paws down.

#### WHAT EVERY COLLEGE STUDENT NEEDS TO KNOW.

In March at Harvard Medical School technicians announced a smartphone app to give fertility-conscious men an accurate semen analysis, including sperm concentration, motility, and total count at a cost less than \$10. Included is a magnification attachment and a "microfluidic" chip. The download app magnifies and photographs the "loaded" chip, instantly reporting the results. No, no semen ever touches your phone. No smartphone data were reported regarding ova.

#### ADDENDA

- There are eight time zones in North America.
- Claxton, Georgia, claims to be the fruitcake capital of the world, closely followed by Harry and David, Oregon.
- Ihad no luck with dating. My biggest thrill was self-inflicted hickeys.
- Cowhand is an arthritic disability of dairy farmers.
- Beer nuts is the official disease of Milwaukie.
- If you want to try cross-country skiing, start with a small country.
- I wasn't any good in French or Italian, but I excelled in thousand island.
- Sex is natural, but not if it's done right.

#### ALOHA AND KEEP THE FAITH rts

(Editorial comment is strictly that of the writer.)

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