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BASIC SCIENCE, CLINICAL & TRANSLATIONAL RESEARCH

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Influences on Parental Feeding Practices in Low-Income African American Families at Three Parish Churches in New Orleans, Louisiana

Introduction

Childhood obesity is a growing epidemic in the United States. What's even more alarming is that the percentage of children between the ages of 6-11 years who meet the guidelines for obesity has drastically increased from 7% in 1980 to nearly 18% in 2010 (Adolescent and School Health, 2013). Moreover, the U.S. Department of Health and Human Services reports that the percentages of overweight children and adolescents between the ages of 6-11 years of age in the years 2007-2010, were 1.8 times higher among Non-Hispanic Blacks (African-American) than Non-Hispanic White girls within the same age range (Obesity and African Americans, 2014). With such disproportionately high percentages in the rates of obesity one may question what are the underlying causes that have led to the various health abnormalities in the African American diet in particular? While there may be genetic predispositions to obesity as well as many other health abnormalities that are prevalent within African-American culture, studies have suggested that "obesity-related" genes can be combatted by eating a healthy diet and getting enough exercise (Obesity and Prevention Source, 2014). Possible explanations of this growing obesity epidemic, and related chronic diseases affecting individuals of the low-income African-American population in the U.S. may be attributed to the lack of resources, such as access to stores with healthy food selections. Although one's food environment may serve as a strong proponent in the various health conditions that affect the low-income African-American community, there is a strong nurture component of the poor nutrition within African-American families that may also contribute to poor diets and associated health complications. Feeding is a central aspect of parenting that involves intense interactions between the parent and his/her child and such interactions may shape the child's eating behavior during a sensitive period of brain development, which may have a lifelong impact on one's diet and appetite regulation (Baughcum, 2001). Perhaps, there are underlying factors impacting parental feeding practices which have been perpetuated throughout time and contributes to the current state of many African-American's diet and health. Such factors include knowledge, culture, accessibility, affordability, and lifestyle, which may all play an integral role in determining what meal options a caregiver will provide for his or her family.

Objective:

The purpose of this project was to learn more about how parental feeding practices influence the nutrition choices of their children.

Methods and Approach:

Between July 1, 2014 and July 20, 2014, 45 individuals were recruited from the following three predominantly African- American church communities in New Orleans, Louisiana: The City of Love Church, St. Joseph Baptist Church, and Greater Morning Star Missionary Baptist Church. An anticipated total of 60 participants were expected to complete a paper copy survey amongst the three locations. However, only 45 participants turned in a completed survey. Two of the three churches, Greater Morning Star Baptist Church and St. Joseph Baptist Church, are located within the community of Algiers in New Orleans in a predominately African- American neighborhood. The City of Love Church is located within the predominately African-American New Orleans's uptown community. Based on the completed surveys, 17 individuals were recruited from the Greater Morning Star Baptist Church and St. Joseph Baptist Church. 13 individuals were recruited from The City of Love church. The following requirements had to be met in order for an individual to participate in the study: 1) Caregivers had to be 18 years or older; 2) Participants had to self-identify as African American; 3) Participants had to speak English; and they had to care for at least one child between the ages of 6-11 years old, with the child also self-identifying as African- American. A 14 question survey using a Lickert scale was administered and each question represented one of the five hypothesized categories for the influences on parental feeding practices: culture, knowledge, lifestyle, affordability and accessibility. The survey was self-crafted. The first four questions focused on the culture of the participants. Questions 5-8 focused on the knowledge that one has concerning healthy food choices. Questions 9-12 focused on the effects lifestyle may have on his/her food selections and meal preparations. Question 13 was targeted to the concerns of individuals enrolled in the Supplemental Nutrition Assistance Program (SNAP) and if they received enough benefits to feed their families on a monthly basis. Lastly, question fourteen addressed the concerns of having reliable transportation to a local supermarket. An information table was set up in each church's atrium, and members voluntarily inquired and completed a survey after church services. Each participant was handed a de-identified hard copy of the survey to complete on-site. As compensation, the participants were asked to provide a contact number and mailing address as an entry to a \$50 raffle ticket drawing. All identifying information was properly disposed upon the drawing of the winner. Each caregiver participant was also given handouts regarding USDA recommendations on daily exercise and child nutrition.

Results

Participants were asked to complete a 14 question survey, of which 45 surveys were completed. Through direct observation, primarily women participants identified as the primary caregivers compared to men. Participants were not asked to identify their gender within the survey.

Table 1.

QUESTION	RESPONSE (n= responder percentage)
CULTURE	
1. Food is the main part of my family gatherings.	Never : n= 0 Rarely: n=2.3% Sometimes: n= 4.5% Often: n= 15% Always: n= 77%
2. Healthy diets are for people trying to lose weight.	Never: n= 15.6% Rarely: n=8.9% Sometimes: n= 23% Often: n= 23% Always: n= 20% No answer: n= 8.9%
3. My child is healthy as long as they are not too thin or fat.	Never: n=20 % Rarely: n= 13.3% Sometimes: n= 38% Often: n= 15.6% Always: n= 13.3%
4. I like to try new ways to cook for my family.	Never: n=2.2% Rarely: n= 6.7% Sometimes: n= 22.2% Often: n= 24.4% Always: n=41% No answer: n= 2.2%
KNOWLEDGE	
5. You are able to choose healthy foods at the grocery store.	Very confident : n= 60% Somewhat confident: n= 31.1% Not confident at all: n= 6.6% Not sure: n=0%
6. Do you believe that making healthy food choices will help keep you and your family healthy?	Yes it will: n= 82% It will help a little: n= 16.6% No it will not : n=0% Not sure if it will help: n= 0% No answer: 2.2%

7. Growing up, I was taught that it was important to have a healthy diet.	Never: n= 11.1% Rarely: n= 40% Sometimes: n 4.4% Often: n= 17.8% Always: n= 24.4%
8. I read the nutrition labels before I buy food for my family.	Never: n= 13.3% Rarely: n= 13.3% Sometimes: n= 37.8% Often: n= 17.8% Always: n= 17.8%
LIFESTYLE	
9. Do you think it is difficult to eat a healthy meal?	Yes: n= 17.8% No: n= 68.8% Not sure: n= 11.1%
10. For question 9, if answered yes, please tell me why it is difficult for you to eat a healthy meal.	a) It takes too much time to prepare: n= 2.2% b) Healthy foods cost too much: n= 40% c) My family does not eat healthy foods d) It is difficult to find healthy foods that my family likes. (n = 2.2%) e) I do not know how to buy healthy foods. (no response) f) I do not know how to use food labels. (no response) h) I do not know what foods are healthy. i) Other. * (see below)
11. During mealtime my family eats together.	Never: n= 0% Rarely: n= 4.4% Sometimes: n= 13.3% Often: n= 13.3% Always: n= 62.2% No Response: 4.4%

12. Within my household, there are other individuals who can help me take care of my children.	Never: n= 17.8% Rarely: n= 17.8% Sometimes: n= 26.7% Often: n= 8.9% Always: n= 24.4% No response: n=4.4%
AFFORDABILITY	
13. I receive enough assistance from the SNAP benefits to feed my family.	Yes: n= 20% No: n= 60% I'm not sure: n= 13.3% No answer: n= 6.7%
Accessibility	
14. I have reliable transportation to buy my groceries from a supermarket.	Yes: n=78% No: n= 6.7% I'm not sure: n= 8.9% No answer: n= 4.4%

* Question 10 “other” response: Four individuals responded in total. Three individuals provided a written answer. The responses focused on not having healthy restaurants nearby, healthy foods tasted nasty, and few healthy choices available. One individual stated that they did but healthy foods.

*** Participants were asked to match their thoughts on each question with the provided answers.

Discussion:

Understanding the demographics and cultural background of one's patients can provide insight into delivering optimal care. Obesity and its associated medical problems has become a part of many individual's lives within American culture, particularly the low-income African-American culture. In order to understand the reasoning behind the prevalence of childhood obesity within minority African- American children, it is important to assess the environment of the child, including his/her parental guardianship. It is not enough for one to merely suggest monitoring one's dietary intake to maintain a healthier lifestyle. Looking at social factors and how it influences his/ her decision to eat certain foods plays a major role in one's dietary intake. Upon surveying low-income African- American caregivers, it was concluded that social factors do in fact play a role in one's decision-making; furthermore, such decisions may have a direct influence on the children of these caregivers. Food and culture are closely tied, and the value one places on food has a correlation to the cultural environment that he or she was immersed in. Food did prove to be a focal point of family gatherings, which may lead one to state that food is valued for the emotional bonding it brings rather than mere subsistence. Thus the type of food one consumes may not be monitored for health purposes, but, rather, selected for the emotional stimulus it brings. Cultural attitudes of healthy eating being seen as a means to diet and to lose weight, as well as health being judged by physique can also shape one's attitude towards certain food selections. Interestingly,

there was a spectrum of individuals who viewed healthy diets as a means for trying to lose weight. Such a belief may dissuade individuals from choosing healthier options because he/she is comfortable with his/her body type. Another point to mention is that one's definition of health can vary greatly. Perhaps, the participants, and many others within the African American community, view health as being at an ideal weight size, and thus, may not find a need to actively choose healthier food options. Having the proper knowledge concerning one's health is also reflective of the choices one will make regarding his/ her family nutrition. If one is never properly taught the standards of health, including one's diet, then it cannot be expected that the values conveyed to their children would differ. Factors such as lacking the time and proper financial resources also helps to shape the meals that a caregiver provides for his/ her family. Thus, social factors such as socioeconomic status can play a role in individuals planning meals based upon affordability as opposed to the effects that it has on one's health. Interestingly, 60% of the participants stated that SNAP benefits were not enough to feed their families. Having financial access to food may not seem as a barrier to purchasing nutritional food items; however, if the food stipend is not enough, perhaps individuals are still restricted to buying foods based on cost rather than the health benefits. Considering other aspects of the caregiver's life such as assistance in caring for his/her children or reliable transportation to the supermarket were also important in assessing the influences of his/her family's food selections. While proper transportation to a grocery store that provided healthy food selections did not appear as an issue, the availability of help within the household could have potentially been a concern for the primary caregivers. Having the burden of caring for children in all aspects of their lives, including meal preparations, can be stressful. Thus, one may tend to serve meals that are convenient rather than nutritious. Having additional help within the household can lessen such burden and perhaps give the caregiver more time to prepare meals that are more beneficial to their family. Possible limitations/ biases to this study could include not having an equal representation of male and female participants. The results could have possibly differed with a greater representation of male participants who may or may not have identified with the specific barriers outlined within the survey.

Overall, this project showed the importance of seeing the various factors that can influence one's decision making process as it relates to food and health. Various social factors did influence one's ability to properly provide a healthy lifestyle for his/her family. Moreover, the example that one set's for proper food nutrition can shape the attitudes of the children whom they care for, which may perpetuate cycles of healthy or non-healthy eating habits. These results suggests that the issues of obesity and poor dieting among African-Americans extend beyond poor judgment and lack of will-power. Rather, one's social/cultural makeup appear to play an integral role in one's decision making process. The prevalence of obesity within the African- American community, especially within children, can thus be related to one's culture and environment. As future leaders of the healthcare field, one can realize the various factors that may influence the lifestyle of his/her patients. One can use this knowledge to understand the patient's perspective and tailor healthcare in a way to maximize the patient's health.

Resources

Baughcum, Amy. "Maternal Feeding Practices and Beliefs and Their Relationships to Overweight in Early Childhood." *Development and Behavioral Pediatrics* . 22.6 (2001): n. page. Print.

Centers for Disease Control and Prevention . *Adolescent and School Health*. Atlanta : 2013. Print. <<http://www.cdc.gov/healthyyouth/obesity/facts.htm>>.

Obesity and Prevention Source. *Harvard School of Public Health* . N.p.. Web. <<http://www.hsph.harvard.edu/obesity-prevention-source/obesity-causes/genes-and-obesity/>>.

Office of Minority Health . *Obesity and African Americans* , 2013. Print. <<http://minorityhealth.hhs.gov/>>.

Bevan, Graham

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Heart Research Follow-up

Heart rate dependency of T-wave morphology in symptomatic and asymptomatic patients with type-1 Long QT Syndrome

Background:

The Congenital Long QT syndrome Type 1 (LQT1) is associated with syncope, life-threatening cardiac arrhythmias, and sudden cardiac death [1]. While heart-rate corrected QT interval (QTc) is predictive of cardiac events, not all symptomatic patients with LQT1 have a prolonged QTc [2]. The T-wave of the ECG may be valuable in risk-stratification of LQT1 patients. The T-wave represents ventricular repolarization and it can capture the repolarization heterogeneity that is arrhythmogenic in LQT1 [3, 4]. Patients with LQT1 have abnormal ventricular repolarization that is heart-rate dependent [5].

Objectives:

We examined heart rate dependent differences in T-wave morphology between symptomatic and asymptomatic LQT1 patients using Holter ECGs. We will determine the efficacy of these parameters in discriminating between symptomatic and asymptomatic patients to improve risk-stratification.

Methods:

We investigated the following descriptive parameters of T-wave morphology: QT interval, T-wave peak to T-wave end (TpTe), T-wave amplitude (Tamp), and complexity of repolarization (λ_2/λ_1) [6]. We examined 12-lead Holter ECGs (H12 recorder, Mortara, Milwaukee, WI) from 93 LQT1 patients: 42 asymptomatic (ASym) and 51 symptomatic (Sym) collected by Lane *et. al* [7]. We used the V2 lead because differences between types of Long QT may be greater here [8]. Using the University of Rochester-developed software, Comprehensive Analysis of Repolarization Signal (COMPAS). These measurements were based on both beat-to-beat ECG and representative median beats from 10 consecutive cardiac cycles. Through RR bin analysis, we categorized median measurements into 25 ms bins from RR intervals of 600ms to 1200ms [6, 9]. We compared the clinical characteristics and T-wave morphology parameters between the ASym and Sym groups using Wilcoxon Rank Sum. We used binary logistic regression to determine odds ratios for each t-wave morphology parameter at slow RR intervals (900-1200ms) and fast RR intervals (600-900ms).

Results:

Symptomatic patients had a greater QT in lead V2 at RR intervals > 925 ms, a greater TpTe at RR intervals > 875 ms, and a greater Tamp at RR intervals > 875 ms (p value <.05). There were no differences in λ_2/λ_1 between ASym and Sym at any bin intervals (p value >.05). Binary logistic regression of model showed goodness of fit wald chi-square p values <.05 for QT

and Tamp at slow heart rate and all T-wave morphology parameters at fast heart rates. At fast heart rates odds ratios for QT, Tamp, TpTe, and λ_2/λ_1 (95% Wald confidence intervals) were 1.006 (1.003, 1.009), 9.627 (5.658, 16.379), .975 (.965, .984), and 7.152 (1.972, 25.938), respectively. At slow heart rates odds ratios for QT, Tamp, TpTe, and λ_2/λ_1 (95% Wald confidence intervals) were 1.017 (1.013, 1.020), 33.441 (17.182, 65.084), 1.006 (.997, 1.015), and .713 (.208, 2.439), respectively. The percent concordant and percent discordant are 76.9% and 22.9% respectively.

Discussion:

Each of these T-wave morphology patterns fits the binary logistic regression model at fast heart rates but only Tamp and QT fit at slow heart rates. At fast heart rates, decreased TpTe and increased λ_2/λ_1 are associated with increased odds of being symptomatic. At slow heart rates Tamp and QT are directly associated with increased odds of being symptomatic. Further analysis may demonstrate how well these parameters can risk-stratify.

References

1. Moss, A.J., *Long QT Syndrome*. JAMA, 2003. **289**(16): p. 2041-4.
2. Priori, S.G., et al., *Risk stratification in the long-QT syndrome*. N Engl J Med, 2003. **348**(19): p. 1866-74.
3. Kuo, C.S., et al., *Characteristics and possible mechanism of ventricular arrhythmia dependent on the dispersion of action potential durations*. Circulation, 1983. **67**(6): p. 1356-67.
4. Extramiana, F. and C. Antzelevitch, *Amplified transmural dispersion of repolarization as the basis for arrhythmogenesis in a canine ventricular-wedge model of short-QT syndrome*. Circulation, 2004. **110**(24): p. 3661-6.
5. Couderc, J.P., et al., *Genotype- and Sex-Specific QT-RR Relationship in the Type-1 Long-QT Syndrome*. J Am Heart Assoc, 2012. **1**(2): p. e000570.
6. Vaglio, M., et al., *A quantitative assessment of T-wave morphology in LQT1, LQT2, and healthy individuals based on Holter recording technology*. Heart Rhythm, 2008. **5**(1): p. 11-8.
7. Lane, R.D., et al., *Changes in ventricular repolarization duration during typical daily emotion in patients with Long QT syndrome*. Psychosom Med, 2011. **73**(1): p. 98-105.
8. Struijk, J.J., et al., *Classification of the long-QT syndrome based on discriminant analysis of T-wave morphology*. Med Biol Eng Comput, 2006. **44**(7): p. 543-9.
9. Badilini, F., et al., *QT interval analysis on ambulatory electrocardiogram recordings: a selective beat averaging approach*. Med Biol Eng Comput, 1999. **37**(1): p. 71-9.

Bragg, Andrew

Preceptor:

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Use of Proton Pump Inhibitors for the Prevention of Septic Acute Kidney Injury

Abstract:

Sepsis is a syndrome of infection-related systemic inflammation that is responsible for over 200,000 annual deaths and \$16.7 billion in direct medical costs in the United States alone.¹ Among individuals in septic shock (the most severe degree of sepsis) as many as 60% will develop acute kidney injury (AKI), an abrupt loss of renal function that can lead to electrolyte imbalance, metabolic acidosis, and death.²⁻⁴ Not surprisingly, AKI is associated with significantly higher mortality for septic patients.⁵⁻⁸ Despite the prevalence and severity of this condition, the etiology of septic AKI remains poorly understood, and treatment is limited to supportive care.^{9,10}

Recent research has shown that suppression of the ATP4A proton pump by genetic deletion and by use of proton pump inhibitors (PPIs) strongly preserves kidney function in murine models of ischemic and septic AKI (publication pending). Because PPIs are commonly used for stress ulcer prophylaxis in critically ill patients, it is relatively simple to compare changes in kidney function across septic patients with and without PPI treatment.¹¹⁻¹⁵ In addition to kidney function, we will also compare mortality, length of hospital stay, and other outcomes across the exposure and control groups. Furthermore, PPI treatment in critically ill patients has been shown to slightly increase the risk of acquiring *Clostridium difficile* colitis, which is associated with significantly worse outcomes for patients.^{18,19} As a result, we will also be comparing incidence of *C. difficile* infection across both groups, in order to better quantify the risks associated with PPI treatment. We are in the process of reviewing medical records for patients admitted to University of Colorado Hospital with septic shock, and we expect to begin data analysis within the next 6 months.

Objectives:

We hope to demonstrate that early PPI treatment is associated with decreased incidence and severity of AKI among patients in septic shock. We will also evaluate potential adverse effects, especially *Clostridium difficile* infection. Although the design of this study does not allow us to demonstrate any causal relationships, we hope that it will provide the basis for a more robust trial to evaluate the efficacy of PPIs in preventing septic AKI.

Methods:

This is a retrospective cohort study of adult patients at the University of Colorado Hospital Emergency Department, admitted between October 1, 2011 and December 31, 2013. We screened all patients with an admitting or discharge diagnosis of septic shock (ICD-9 code 785.52). In addition, patients who received antibiotics in the Emergency Department and were admitted to the intensive care unit will be screened to determine if inclusion criteria were met (to capture cases who did not receive the ICD-9 diagnosis). During chart review, septic shock was defined as the presence of all of the following criteria in the Emergency Department, based on standard guidelines for diagnosis of septic shock.^{16,17}

- a. Suspected or confirmed infection, and receiving antimicrobial therapy

- b. Systemic inflammatory response syndrome (SIRS) defined by two or more of the following:
 - White blood cell count <4000 or >12000 cells/ml
 - Heart rate >90 beats/minute
 - Respiratory rate >20 breaths/minute or PaCO₂ < 32 mmHg
 - Temperature <36°C or >38°C
- c. Shock, deemed new or due to infection, as defined by at least one of the following after administration of at least 40 cc/kg of intravenous fluid:
 - Systolic blood pressure <90 mmHg
 - Mean arterial pressure <60 mmHg
 - Vasopressor therapy required for >1 hour

Patients meeting these criteria are grouped based on PPI treatment early in the hospital course. The primary exposure group consists of patients who received PPIs within 12 hours of Emergency Department presentation. Secondary exposure groups consist of 1) patients who received PPIs 12-36 hours after ED presentation and 2) patients who received PPIs 36-72 hours after presentation. The primary comparison group consists of patients meeting septic shock criteria who did not receive PPIs within 72 hours of ED presentation. Based on preliminary results, we anticipate that the final sample will include 300-350 patients.

The primary outcome we are interested in is the change in serum creatinine from baseline (first measurement in ED) to 72 hours (+/- 6 hours). Secondary outcomes will include change in serum creatinine from baseline to 7 days, need for hemodialysis, GI bleeding events, new diagnosis of *Clostridium difficile* colitis, ICU and hospital length of stay, and mortality.

Results:

Due to the tedious nature of chart abstraction, we do not have enough data to begin analysis yet.

Conclusions:

We have not collected enough data to draw any meaningful conclusions at this time. Data collection is ongoing, and we hope to begin analysis within the next 6 months. While the study design prevents us from inferring any causal relationships from this study, a positive result would provide the basis for a more robust trial in the future. However, if we find that PPI treatment increases the risk of *Clostridium difficile* colitis within this cohort, we will need to carefully consider the potential risks and benefits before any further trials begin.

References

1. Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. *Crit Care Med*. 2001;29(7):1303-10. PMID: 11445675
2. Bagshaw SM, Uchino S, Bellomo R, Morimatsu H, Morgera S, Schetz M, Tan I, Bouman C, Macedo E, Gibney N, Tolwani A, Oudemans-van Straaten HM, Ronco C, Kellum JA. Septic acute kidney injury in critically ill patients: clinical characteristics and outcomes. *Clin J Am Soc Nephrol*. 2007;2(3):431-9. PMID: 17699448
3. Uchino S, Kellum JA, Bellomo R, Doig GS, Morimatsu H, Morgera S, Schetz M, Tan I, Bouman C, Macedo E, Gibney N, Tolwani A, Ronco C. Acute renal failure in critically ill patients: a multinational, multicenter study. *JAMA*. 2005;294(7):813-8. PMID: 16106006

4. Plataki M, Kashani K, Cabello-Garza J, Maldonado F, Kashyap R, Kor DJ, Gajic O, Cartin-Ceba R. Predictors of acute kidney injury in septic shock patients: an observational cohort study. *Clin J Am Soc Nephrol*. 2011;6(7):1744-51. PMID: 21734090
5. Chertow GM, Burdick E, Honour M, Bonventre JV, Bates DW. Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. *J Am Soc Nephrol*. 2005;16(11):3365-70. PMID: 16177006
6. Bagshaw SM, Lapinsky S, Dial S, Arabi Y, Dodek P, Wood G, Ellis P, Guzman J, Marshall J, Parrillo JE, Skrobik Y, Kumar A. Acute kidney injury in septic shock: clinical outcomes and impact of duration of hypotension prior to initiation of antimicrobial therapy. *Intensive Care Med*. 2009;35(5):871-81. PMID: 19066848
7. Oppert M, Engel C, Brunkhorst FM, Bogatsch H, Reinhart K, Frei U, Eckardt KU, Loeffler M, John S. Acute renal failure in patients with severe sepsis and septic shock--a significant independent risk factor for mortality: results from the German Prevalence Study. *Nephrol Dial Transplant*. 2008;23(3):904-9. PMID: 18065435
8. Silvester W, Bellomo R, Cole L. Epidemiology, management, and outcome of severe acute renal failure of critical illness in Australia. *Crit Care Med*. 2001;29(10):1910-5. PMID: 11588450
9. Wan L, Bagshaw SM, Langenberg C, Saotome T, May C, Bellomo R. Pathophysiology of septic acute kidney injury: what do we really know? *Crit Care Med*. 2008;36(4 Suppl):S198-203. PMID: 18382194
10. Benes J, Chvojka J, Sykora R, Radej J, Krouzecky A, Novak I, Matejovic M. Searching for mechanisms that matter in early septic acute kidney injury: an experimental study. *Crit Care*. 2011;15(5):R256. PMID: 22030145
11. Cook DJ, Fuller HD, Guyatt GH, Marshall JC, Leasa D, Hall R, Winton TL, Rutledge F, Todd TJ, Roy P, et al. Risk factors for gastrointestinal bleeding in critically ill patients. Canadian Critical Care Trials Group. *N Engl J Med*. 1994;330(6):377-81. PMID: 8284001
12. Faisy C, Guerot E, Diehl JL, Iftimovici E, Fagon JY. Clinically significant gastrointestinal bleeding in critically ill patients with and without stress-ulcer prophylaxis. *Intensive Care Med*. 2003;29(8):1306-13. PMID: 12830375
13. Cook DJ, Griffith LE, Walter SD, Guyatt GH, Meade MO, Heyland DK, Kirby A, Tryba M. The attributable mortality and length of intensive care unit stay of clinically important gastrointestinal bleeding in critically ill patients. *Crit Care*. 2001;5(6):368-75. PMID: 11737927
14. Alhazzani W, Alenezi F, Jaeschke RZ, Moayyedi P, Cook DJ. Proton pump inhibitors versus histamine 2 receptor antagonists for stress ulcer prophylaxis in critically ill patients: a systematic review and meta-analysis. *Crit Care Med*. 2013;41(3):693-705. PMID: 23318494
15. Barkun AN, Bardou M, Pham CQ, Martel M. Proton pump inhibitors vs. histamine 2 receptor antagonists for stress-related mucosal bleeding prophylaxis in critically ill patients: a meta-analysis. *Am J Gastroenterol*. 2012;107(4):507-20; quiz 21. PMID: 22290403
16. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, Sevransky JE, Sprung CL, Douglas IS, Jaeschke R, Osborn TM, Nunnally ME, Townsend SR, Reinhart K, Kleinpell RM, Angus DC, Deutschman CS, Machado FR, Rubenfeld GD, Webb SA, Beale RJ, Vincent JL, Moreno R. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. *Crit Care Med*. 2013;41(2):580-637. PMID: 23353941
17. Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, Cohen J, Opal SM, Vincent JL, Ramsay G, Sccm/Esicm/Accp/Ats/Sis. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. *Crit Care Med*. 2003;31(4):1250-6. PMID: 12682500
18. Janarthanan S, Ditah I, Adler DG, Ehrinpreis MN. Clostridium difficile-associated diarrhea and proton pump inhibitor therapy: a meta-analysis. *Am J Gastroenterol*. 2012;107(7):1001-10. PMID: 22710578
19. Lagu, et al. The impact of hospital-onset *Clostridium difficile* infection on outcomes of hospitalized patients with sepsis. *J Hosp Med*. 2014;9(7). PMID: 24715578

BASIC SCIENCE, CLINICAL & TRANSLATIONAL RESEARCH

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Characterizing end stage renal disease patients starting hemodialysis with a catheter

Introduction

Hemodialysis (HD) is a treatment option for patients with end stage renal disease (ESRD)¹. Optimal dialysis can prevent a variety of uremic complications and can also extend the lifespan of patients with ESRD^{1,2}. Access to circulation is essential for HD and may be achieved in three ways: via arteriovenous fistulas (AVFs), arteriovenous grafts (AVGs) and catheters³. All three methods are usable for dialysis, but AVFs are preferred^{4,5,6}. When compared to catheter use, AVFs have been shown to have half the rate of septicemia⁷, 43% lower risk for cardiovascular-related mortality⁶, reduced rates of infection⁸ and reduced rates of all-cause mortality⁵. AVGs are considered suboptimal when compared to AVFs but are still safer than catheters⁴.

Despite AVFs being the preferred vascular access, approximately 30% of patients undergoing HD at URMC use a catheter as their permanent dialysis access. In addition, there are also patients using a catheter as they transition to an AVG or AVF (which typically takes two to three months to mature). Investigating why incident HD patients started with a catheter may reveal the obstacles to AVF/AVG placement and use. If identified, strategies to address these barriers would allow us to further optimize ESRD care at URMC.

Objective:

Our goal is to identify the reasons for why patients start HD with a catheter.

Methods:

Patients who began HD with a catheter in a URMC-network hospital/outpatient setting during 1/1/2012 to 4/15/2014 were identified through the Department of Nephrology's records. Patients dialyzing for fewer than 90 days, were under 18 years of age, or were being managed by Pediatric Nephrology but initiated HD after age 18 were excluded.

Charts of qualifying patients were accessed from Epic Systems eRecord and demographic information and lab values were collected. Physician notes were used to identify the cause(s) of CKD and ESRD and to recreate the history between the first nephrology consult and HD initiation. When possible, collected data were corroborated with patients' dialysis registration forms (Form 2728).

All data points were recorded and percentages, means, medians and standard deviations calculated in Microsoft Excel.

Additional analysis was done specifically for patient groups that constituted the top two reasons for catheter starts.

Results:

A total of 136 patients began HD with a catheter in this study. 58 (42.65%) of all HD catheter-starts suffered an acute kidney injury (AKI) on chronic kidney disease (CKD), while 19 patients (13.97% of all HD catheter-starts) refused to have an AVF/G put in place. When combined, these patients accounted for over half (56.62%) of all the 136 HD catheter-start patients.

28 of the 58 AKI on CKD patients were regularly seen by a nephrologist in an outpatient setting and were not considering a kidney transplant/on a transplant list. The cause of their CKD, last office visit GFR before initiating HD, and stage of CKD before initiating HD are summarized in Table 1.

Table 1. Patients with AKI on CKD being seen by a nephrologist and not considering/on kidney transplant list

		Number	% of Total (n=28)
Cause of CKD	Diabetes	14	50.00%
	Hypertension	10	35.71%
	Cardiorenal syndrome	5	17.86%
		Median	SD
Last office visit GFR before HD start		20.00	8.93
CKD Stage before HD start		4.00	0.66

Conclusions:

Our data show that AKI on CKD and patient refusal of AVF/G placement are major reasons for why ESRD patients at URMH start HD with a catheter. These results highlight the difficulty of managing CKD patients who are prone to AKI; patients with stable CKD could have similar laboratory values to the AKI on CKD patients in our study (GFR in the 20's) and not need referral to a vascular surgeon. However, superimposing an AKI on their CKD would potentially preclude fistula/graft planning altogether by necessitating an emergency HD start. Which CKD patients are susceptible to AKI and could benefit from an earlier referral is unclear and could be the focus of further study. Additionally, exploring why patients refused AVF/G placement could yield new insights that would aid clinicians in counseling and supporting similar patients in the future.

References:

1. Himmelfarb J, Ikizler TA. Hemodialysis. N Engl J Med. 2010 Nov 4; 363: 1833-1845.
2. Hemodialysis Adequacy 2006 Work Group. Clinical practice guidelines for hemodialysis adequacy: update 2006. Am J Kidney Dis 2006; 48 (Suppl 1): S2-90.
3. NIDDK, Web. 31 Jan 2014. <http://kidney.niddk.nih.gov/kudiseases/pubs/hemodialysis/>.
4. Dhingra RK, Young EW, Hulbert-Shearon TE et al. Type of vascular access predicts mortality in US hemodialysis patients. Kidney Int 2001; 60: 1443-1451.
5. Pastan S, Soucie JM, McClellan WM. Vascular access and increased risk of death among hemodialysis patients. Kidney Int 2002; 62: 620-626.
6. Wasse H, Speckman B, McClellan WM. Arteriovenous fistula use is associated with lower cardiovascular mortality compared with catheter use among ESRD patients. Semin Dial 2008; 21: 483-488.
7. Powe NR, Jaar B, Furth SL et al. Septicemia in dialysis patients: incidence, risk factors, and prognosis. Kidney Int 1999; 55: 1081-90.
8. Nassar GM, Ayus JC. Infectious complications of the hemodialysis access. Kidney Int 2001; 60: 1-13.

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CANCER ANXIETY AND PATIENT SELECTION OF MASTECTOMY OVER BREAST CONSERVATION THERAPY

Objectives: Breast conservation therapy (BCT) provides equivalent survival outcomes to mastectomy for women with early-stage breast cancer. Despite this, recent studies have reported increases in the rate of mastectomy and contralateral prophylactic mastectomy. We investigated the indications for mastectomy in a cohort of women. We sought to determine specific patient and clinical characteristics impacting this decision-making process.

Methods: A questionnaire was administered to 349 patients who had undergone previous unilateral or bilateral mastectomy for breast cancer during the years 2006 to 2010. The survey queried on demographics, surgical treatment received, and the rationale for those decisions. A retrospective chart review collected clinical characteristics and details surrounding the treatment decision-making process. Descriptive statistics were utilized for data summary.

Results: Of 349 patients surveyed, 326 had complete clinical data. Of those, 206 (63%) were not offered BCT and mastectomy was recommended by their physician. Of 206 not offered BCT, clinical data demonstrated BCT contraindications for 171 (83%) with multicentric disease or extent of disease prohibitive of BCT, 25 (12%) who failed BCT secondary to positive margins, and 10 (5%) with recurrence following BCT. The remaining 120 (37%) patients were offered BCT but chose mastectomy. Reasons provided for this decision (patients were allowed to choose more than one reason) included “felt mastectomy would reduce recurrence risk” in 85 (71%), “felt mastectomy would improve survival” in 44 (37%), “avoidance of radiation therapy” in 22 (18%), “felt mastectomy was a better option cosmetically” in 6 (5%), “avoidance of future surveillance imaging” in 3 (3%), and “encouragement by friends/family” in 2 (2%).

Conclusions: Nearly two-thirds of the patients undergoing mastectomy for breast cancer in our study were not offered BCT secondary to absolute and/or relative contraindications. For those patients electing mastectomy despite BCT eligibility, the predominant reason for their choice was anxiety over future cancer risk. Prospective studies are needed to determine whether patient education regarding perceived versus actual recurrence risk would alter this decision-making process.

References

NIH Consensus conference. Treatment of early-stage breast cancer. JAMA 1991;265(3):391.

Poggi MM, Danforth DN, Sciuto LC, et al. Eighteen-year results in the treatment of early breast carcinoma with mastectomy versus breast conservation therapy. Cancer 2003;98(4):697.

McGuire KP, Santillan AA, et al. Are mastectomies on the rise? A 13-year trend analysis of the selection of mastectomy versus breast conservation therapy in 5865 patients. Ann Surg Oncol 2009;16(10):2682.

Fisher CS, Martin-Dunlap T, et al. Fear of recurrence and perceived survival benefit are primary motivators for choosing mastectomy over breast-conservation therapy regardless of age. Ann Surg Oncol 2012;19:3246.

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Characterization of Peripheral Nerve Crush Injury

Background and Introduction:

Peripheral nerve injury is a key feature of trauma to the extremities and the recovery of the nerve takes longer than other types of injury. The severity and location of a peripheral nerve injury determine the optimal clinical intervention and prognosis. A mild peripheral nerve injury has the ability to regenerate without invasive treatment, whereas a severe nerve injury requires surgical intervention. It is critical to assess the severity of the injury to determine the optimal course of treatment, however current methods of distinguishing type and severity of injury are delayed for weeks post-injury.^{1,2}

The staging of peripheral nerve injury according to the currently accepted classification is suboptimal. This classification system was developed by Seddon and Sunderland and applies characteristics of individual neurons to entire nerves, defining injuries in binary terms such as neuropraxia, axonotmesis, or neurotmesis^{3,4}. However, the reality of peripheral nerve injuries is much more complex. In a large, injured peripheral nerve severed axons exist alongside intact axons and demyelinated axons, creating a lot of variability in structural integrity and functional outcome⁵. The difficulty in effectively classifying peripheral nerve injuries creates a diagnostic dilemma.

Different degrees of injury result in different time courses of recovery and improvement in function⁶. Our lab has previously found that 4-aminopyridine (4-AP) can be used to prolong the action potential of demyelinated axons and transiently improve the function of crushed peripheral nerves⁷. We hypothesize that this transient improvement represents the portion of the nerve that retains its architecture and thus want to determine what percent of the nerve must be intact to support the level of functional improvement that is seen with the administration of 4-AP.

Objectives:

To describe the architecture of the nerve that underlies the transient functional improvement seen in systemic administration of 4-AP to a mouse with a peripheral nerve crush injury. Furthermore, to characterize the changes in the amount myelin and neurofilament at the site of the crush injury, and proximal and distal to the injury.

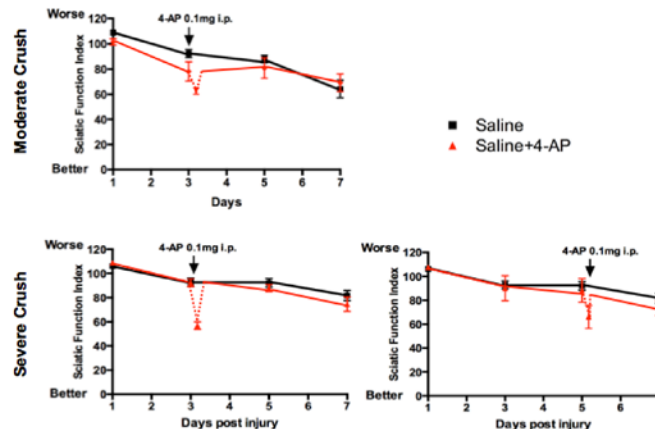
Methods:

We performed a standard moderate and severe crush injury to the sciatic nerves of mice. 4-AP was administered to a portion of the mice and Sciatic Functional index completed using standardized procedures. In another subset of mice the crushed nerves were harvested at day 3

and day 5 for immunohistochemical analysis. Cross sections of the nerve at sites proximal, at the site of the crush, and distal to the injury were stained for P0 (a marker of myelination) and neurofilament (NF). Quantitative analysis of stained cross-sections of the nerve was completed using FIJI software.

Results:

A transient, but significant improvement in SFI is seen when 4-AP is administered systemically. The functional improvement was more significant for the severe crush injuries than the moderate crush injuries (30% vs. 17%) at day 3. The improvement is less profound at day 5. This suggests that a critical window of available, but dysfunctional nerves exist following a crush injury.



The quantitative analysis of nerves with immunofluorescent staining for myelin and NF reveal that the injury propagates both proximally and distally. At 3 days post injury, all three positions (proximal, crush, and distal) show significantly decreased levels of myelin and NF compared to control nerves. Furthermore, this injury progresses so at day 5 there is even further demyelination and NF loss. Interestingly the demyelination that occurs is much more significant than the NF loss. This progressive demyelination at all positions around a crush injury has not been previously described in the context of the functional improvement seen with 4-AP.

Conclusions:

The overlay of the functional data with the quantitative analysis of the nerve architecture suggests that there is a critical window of available, but dysfunctional nerves following a crush injury. 4-AP is able to “awaken” these dysfunctional nerves and allow for a transient improvement in function. Analysis of the nerve architecture underlying this improvement suggests that the progressive demyelination is responsible for the decreased effect of 4-AP at day 5 post injury. This highlights the possible role of progressive demyelination in the early pathophysiology of peripheral nerve crush injury.

References:

1. Campbell WW. Evaluation and management of peripheral nerve injury. *Clinical Neurophysiology*. Sep 2008;119(9):1951-1965.
2. Grant GA, Goodkin, R, Kliot M. Evaluation and surgical management of peripheral nerve problems. *Neurosurgery*. Apr 1999;44(4):825-839.
3. Sunderland S. A classification of peripheral nerve injuries producing loss of function. *Brain*. 1951; 74(4):491-516.
4. Sunderland S. The anatomy and physiology of nerve injury. *Muscle & nerve*. Sep 1990;13(9):771-784.

5. Elfar JC, Jacobson JA, Puzas JE, Rosier RN, Zuscik MJ. Erythropoietin accelerates functional recovery after peripheral nerve injury. *Journal of Bone and Joint Surgery*. 2008;90:1644-1653.
6. Zingman A, Elfar JC. Erythropoietin mediated neuroprotection in relation to nerve crush injury. In press.
7. Tseng KC, Elfar JC. The potential diagnostic approach to characterize peripheral nerve injury using 4-AP. *Neurology*. April 2014; 82(10): Supplement P3.057.

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Potential Role of Novel MyolncRNA-11 in Cardiac and Skeletal Muscle Growth and Differentiation

Introduction:

Non-coding RNA, once considered “junk genomic material”, have been shown to be important in several developmental processes^{1,2}. This discovery has shifted our paradigm on genomic material outside the exome and has created excitement to explore regions of human genome that contain 98% of the genomic single nucleotide polymorphisms (SNPs). Consequently, many labs have collectively discovered and documented tens of thousands of non-coding RNA sequences³. With so many documented non-coding RNAs (ncRNAs), two broad classes have been created to classify them: short ncRNA (processed transcript length of <200 nucleotides) and long ncRNA (processed transcript length of >200 nucleotides)^{4,5,6}. However, the vast majority of the documented non-coding RNAs remain poorly characterized. As more non-coding RNAs are discovered and their functions uncovered, our perspective of genome content and the way we think of genes will change. Furthermore, we will gain new insight into disease-causing mutations associated with non-coding RNA function.

Objectives:

This study aims to further expand our understanding of long ncRNAs (lncRNAs) in the context of vascular smooth muscle cell (VSMC) and endothelial cell (EC) biology. More specifically, this study aims to further characterize some of the lncRNA discovered by the Miano lab, many of which are not annotated in any public database. By acquiring a better understanding of how lncRNAs fine tune gene expression in VSMC and EC, this study helps to aid in gaining insight into how non-coding RNA mutations might cause disease.

Methods:

This study used a systematic approach to studying lncRNAs, which was developed by the Miano lab (revised manuscript submitted). First, 3 lncRNAs of a subset of novel lncRNAs from novel RNA-seq screens were chosen for RNA expression validation using conventional (gel) and quantitative RT-PCR on panels of 15 human cell lines and 12 human tissues, including dated plasma from the URM Medical Center Blood Bank. The latter tissue panel is of importance from a clinical standpoint as circulating lncRNAs are increasingly being reported as biomarkers of disease and the Miano lab has already discovered 4 novel lncRNAs abundantly present in plasma. No protein experiments were done for these genes since they are, by definition, of low protein-coding potential. Then, RNA fractionation studies were performed to begin elucidating the localization (nucleus versus cytoplasmic). Dicer substrate RNAs (dsRNA) from Integrated DNA Technologies were ordered and tested for knockdown efficacy in *in vitro* studies using RT-PCR. After testing knockdown of lncRNA, effects of lncRNA knockdown on neighboring gene expression examined to determine whether the lncRNAs under investigation have any *cis*-acting effects on local gene expression.

Results:

Of the three lncRNAs examined, two (myolnc-11 and myolnc-14) were validated using conventional (gel) and quantitative RT-PCR on panels of 15 human cell lines and 12 human tissues.

Myolnc-14 was expressed in 14 of 15 human cell lines and 2 of 12 human tissues (heart and skeletal muscle). Myolnc-11 was expressed in 8 of 15 human cell lines and 2 of 15 human tissues (heart and skeletal muscle).

Myolnc-11 was further investigated as it has been shown to play a role in hypertrophic cardiomyopathy. Cell fractionation studies showed myolnc-11 is expressed equally in nucleus and cytoplasm. Knockdown of myolnc-11 with dsRNA showed a 2-fold decrease in nuclear myolnc-11 expression in RD cells. Conversely, stimulation of myolnc-11 with myocardin showed a 2-3 fold increase in nuclear myolnc-11 expression in HCASM cells. Cytoplasmic myolnc11 remained constant in dsRNA and myocardin stimulation studies.

Investigating the effects of knockdown and stimulation showed no change in expression of one of the neighboring genes (myoz-2).

Conclusions:

This study shows that myolnc14 may be a poor candidate to be a house keeping lncRNA, which was its hypothesized function, as it lacks ubiquitous expression across human cell lines and human tissues. However, it may serve a role in heart and skeletal muscle tissues since both tissue samples highly expressed myolnc-14.

This study also showed that myolnc-11 may serve a role in heart and skeletal tissues as it was highly expressed in both tissues. Furthermore, this study showed that myolnc-11 is localized in both the cytoplasm and nucleus. Additionally, this study showed that myolnc-11 is inducible by myocardin and that myocardin specifically induces nuclear myolnc-11. However, the effect of myolnc-11 on neighboring genes is unknown since knockdown and stimulation did not affect myoz-2 expression.

References:

1. Geisler S, Collier J. RNA in unexpected places: long non-coding RNA functions in diverse cellular contexts. *Nature Reviews Molecular Cell Biology* 14, 699-712 (2013)
2. Lee JT. Epigenetic regulation by long noncoding RNAs. *Science* 338:1435-1439 (2012)
3. The ENCODE Project Consortium. An integrated encyclopedia of DNA elements in the human genome. *Nature* 489, 57-74 (2012)
4. Okazaki Y, Furuno M, Kasukawa T, et al. Analysis of the mouse transcriptome based on functional annotation of 60,770 full-length cDNAs. *Nature* 420:563-573 (2002)
5. Kapranov P, Cawley SE, Drenkow J, Bekiranov S, Strausberg RL, Fodor SPA, Gingeras TR. Large-scale transcriptional activity in chromosomes 21 and 22. *Science* 296:916-919 (2002)
6. Lagos-Quintana M, Rauhut R, Lendeckel W, Tuschl T. Identification of novel genes coding for small expressed RNAs. *Science* 294:853-858 (2001)

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Increased TLR4 Expression in MLL-Rearranged Infant Acute Lymphoblastic Leukemia

Introduction: Relapse of acute lymphoblastic leukemia (ALL) is the leading cause of cancer death in children¹⁻³. Mixed lineage leukemia (MLL)-rearranged infant ALL (diagnosed <12 months) represents a high-risk subset of disease, in part because it is more resistant to chemotherapy than standard-risk childhood ALL⁴⁻⁶. The role that the immune system plays in chemotherapy resistance, specifically in modulating local responses to dying leukemia cells in the bone marrow, is poorly understood. We propose that chemotherapy treatment of ALL cells may alter the immune environment, by releasing damage associated molecular proteins (DAMPs) that activate the innate immune system^{7,8}. Toll-like receptors, particularly Toll-like receptor 4, may play an important role in recognition of DAMPs by generating downstream signals that affect local cytokine production by innate immune cells in the bone marrow^{7,8}.

Objective: To assess whether TLR4 is upregulated in ALL cells following doxorubicin treatment, and to assess whether there is a difference in TLR4 expression between high-risk MLL-rearranged ALL (MLL-ALL) and standard-risk (SR-ALL) ALL after treatment with doxorubicin, an anthracycline chemotherapy used in high-risk ALL therapy and recognized to induce immunogenic cell death

Methods: Primary human leukemia cells were isolated from either diagnostic bone marrow or pheresed peripheral blood (n=5; 1 MLL-ALL, 4 SR-ALL) of pediatric patients with ALL (RSRB #0024477) and placed in culture. Next, they received either no treatment, or 2 nM doxorubicin for 3 hours. Cells were then washed, cultured for an additional 24 hours and analyzed for mRNA expression by qPCR and TLR4 cell surface expression by flow cytometry. Fold-increase in TLR4 mRNA was calculated using the ddCt method using beta-glucuronidase as an endogenous reference gene. TLR4 expression, measured by mean fluorescence intensity (MFI) of a phycoerythrin-conjugated anti-TLR4 antibody, was measured using the gating strategy: 1) gating for lymphoblast populations using forward and side scatter, 2) isolating live cell populations by gating on 7AAD 3) isolating pre-B leukemia cells by gating on CD19+. Compensation was performed using beads and IgG isotype controls were used as a negative control for nonspecific antibody binding while Thp1+LPS (human macrophage cell line) and SupB15 (pre-B ALL cell line) were used as positive staining controls for TLR4 and CD19 respectively.

Results: Both qPCR and flow cytometry showed some basal level of TLR4 expression in all ALLs tested. (qPCR: MLL-ALL, 0.050, SD±0.015; SR-ALLs, 0.013-0.150, SD±0.060). Of the 5

ALL cells tested, the high-risk MLL-rearranged infant ALL was the only ALL to consistently show an increase in TLR4 mRNA level by qPCR after doxorubicin treatment (4.22 fold increase, $p < 0.05$). The other, standard-risk ALLs showed no significant changes in TLR4 message level after treatment. Although initial flow cytometry experiments showed an increase in TLR4 expression ($\Delta\text{MFI} = 1555$) in MLL-ALL cells after doxorubicin treatment, live/dead analysis showed that chemotherapy treatment produced an autofluorescence artifact, confirmed by the use of an IgG PE isotype control against live MLL-ALL ($\Delta\text{MFI} = 1359$, IgG PE isotype; 1328, MLL-ALL).

Conclusions and Future Directions: The increase in TLR4 mRNA expression in MLL-ALL may provide a receptor mechanism in the pathogenesis of high-risk ALL. Downstream effects of TLR4 activation may result in increased cell survival or promote inflammation through either a MyD88-dependent or independent mechanism and activation of NF- κ B pathways^{9, 10}. Studies are underway to address whether chemotherapy treatment produces differences in NF κ B expression in our primary leukemia cells. If so, this has future implications as a prognostic marker and/or potential therapeutic target. MyD88 signaling is now being recognized as potential component of immune escape and prognostic marker in human cancers¹¹, specifically chronic lymphocytic leukemia¹². Future studies required measurement of TLR4 and its downstream receptors in at least 5 MLL-ALL's to address the limited sample size. In addition, time course experiments to determine TLR4 surface expression between 0-72 hours after doxorubicin therapy are planned.

References:

1. SEER Cancer Statistics Review, 1975-2010. Bethesda: National Cancer Institute; 2013.
2. Hunger SP, Lu X, Devidas M, et al. Improved survival for children and adolescents with acute lymphoblastic leukemia between 1990 and 2005: a report from the children's oncology group. *J Clin Oncol*. 2012;30(14):1663-1669.
3. Pui CH, Campana D, Pei D, et al. Treating childhood acute lymphoblastic leukemia without cranial irradiation. *N Engl J Med*. 2009;360(26):2730-2741.
4. Hilden JM, Dinndorf PA, Meerbaum SO, et al. Analysis of prognostic factors of acute lymphoblastic leukemia in infants: report on CCG 1953 from the Children's Oncology Group. *Blood*. 2006;108(2):441-451.
5. Pieters R, Schrappe M, De Lorenzo P, et al. A treatment protocol for infants younger than 1 year with acute lymphoblastic leukaemia (Interfant-99): an observational study and a multicentre randomised trial. *Lancet*. 2007;370(9583):240- 250.
6. Behm FG, Raimondi SC, Frestedt JL, et al. Rearrangement of the MLL gene confers a poor prognosis in childhood acute lymphoblastic leukemia, regardless of presenting age. *Blood*. 1996;87(7):2870-2877.

7. Fang H, Ang B, Xu X, et al. TLR4 is essential for dendritic cell activation and anti-tumor T-cell response enhancement by DAMPs released from chemically stressed cancer cells. *Cell Mol Immunol*. 2013 Dec 23.
8. Ehrchen JM, Sunderkötter C et al. The endogenous Toll-like receptor 4 agonist S100A8/S100A9 (calprotectin) as innate amplifier of infection, autoimmunity, and cancer. *J Leukoc Biol*. 2009 Sep;86(3):557-66. doi: 10.1189/jlb.1008647.
9. Akira S. Toll-like receptor signaling. *J Biol Chem* 2003; 278: 38105–8.
10. Akira S, Takeda K. Toll-like receptor signalling. *Nat Rev Immunol* 2004; 4: 499–511.
11. Kelly M, Alvero A, Chen R, et al. TLR-4 Signaling Promotes Tumor Growth and Paclitaxel Chemoresistance in Ovarian Cancer. *Cancer Research*. April 1, 2006 66; 3859
12. Barcellini W, Imperiali FG, Zaninoni A, et al. Toll-like receptor 4 and 9 expression in B-chronic lymphocytic leukemia: relationship with infections, autoimmunity and disease progression. *Leuk Lymphoma*. 2013 Oct 21.
13. Children's Oncology Group protocol AALL1131 (Current Protocol for High- and Very-High Risk Pre-B cell ALL, 2014).

BASIC SCIENCE, CLINICAL & TRANSLATIONAL RESEARCH

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Phase I of National Library of Medicine Research Study on Patient Use of Internet Resources

Abstract:

Access to reliable and easy-to-understand health information continues to be a problem in poor and minority communities. This creates obstacles in informed decision making and may be problematic for managing medical conditions appropriately. One possible avenue in addressing this deficit in information is through technology and the internet. For example, MedlinePlus (a website full of tools to educate patients on health conditions) was created specifically in the hope of increasing access to medical information. Patient portals are another means of using technology to empower and educate patients. However, in underserved communities, it is unknown how best to increase awareness of these important resources. This research project attempts to address the concern over a lack of health information in underserved communities by studying attitudes and practices related to internet usage among the patient population at three federally qualified health centers in Rochester. The ultimate goal of this project is to discover if resources like MedlinePlus or patient portals can have a positive impact on patient care in these settings. In order to intervene meaningfully, baseline knowledge of how this population uses the internet is necessary. Based on this information, it can be elucidated how best these technological resources may be able to serve patient needs. In this phase of the project, 304 surveys were collected from patients attending appointments at the three health centers on their practices and attitudes related to the internet. Preliminary analysis of the collected data suggests that while awareness of these resources is lacking, interest in them is substantial. Furthermore, it seems training programs to assist those who are not technologically competent are justified as many in the population lack the technical skills necessary to avail themselves of these invaluable resources.

Objectives:

1) To better understand how patients at three federally qualified health centers use the internet and their attitudes about internet usage. 2) To apply this information to increasing awareness of MedlinePlus and usage of the patient portal. 3) To address the fundamental lack of medical information in underserved communities.

Methods:

A survey instrument was constructed to collect baseline information on this patient population's attitudes and practices related to internet resources and patient portals. The survey was given on site at three separate federally qualified health centers in the Rochester area. Data were collected by research assistants using RedCap by interviewing patients in waiting rooms.

Data were secured using password protections and was completely anonymous. 304 surveys were collected during the period of study.

Results:

Surveys were collected and analyzed on RedCap. Internet usage in this population was mixed. Among the sample 29.1% never used the internet while 44.8% used the internet every day. Among all participants, 54.2% had never used the internet to look up information about their health (27.1% report having no access to a computer) while 33% report using the internet at least monthly to look up information. Among those who had used the internet to look up information about their health 59.4% were either “interested” or “very interested” in using the internet as a tool in understanding information about their health and 81.9% reported the internet to be “useful” or “very useful” in this regard. However, among those who had used the internet to look up information about their health, 80.3% had never heard of MedlinePlus and only 6 participants reported using it. 76.2% of those surveyed had never heard of the patient portal. However, 64% of those interviewed were “interested” or “very interested” in using the portal, and 57.7% were “interested” or “very interested” in accessing the portal on a smart phone.

Conclusions:

1) Increased awareness of the resources of MedlinePlus and patient portals may be a key area in helping to provide health information to underserved groups. 2) For a large segment of this patient population, implementation of training programs may assist in the increased usage of these resources as many patients in this population lack experience with computers and the internet.

References

Calman N, Kitson K, & Hauser D. Using information technology to improve health quality and safety in community health centers. *Progress in Community Health Partnerships*. 1: 83-88 (2007).

Gibbons CM. Use of health information technology among racial and ethnic underserved communities. *Perspect Health Inf Manag*. 8: 1-13 (2011).

Ketcham JD, Lutfey KE, Gerstenberger E, Link CL, & McKinlay JB. Physician clinical information technology and health care disparities. *Medical Care Research and Review*. 66: 658–81 (2009).

Sheets L, Gavino A, Callaghan F, & Fontelo P. Do language fluency and other socioeconomic factors influence the use of PubMed and MedlinePlus? *Appl Clin Inform*. 4: 170-184 (2013).

Szczepura A. Access to healthcare for ethnic minority populations. *Postgrad Med J*. 81: 141-147 (2005).

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Clinical Efficacy, Safety, and Feasibility of Using Video Glasses During Interventional Radiologic Procedures

Introduction: Many patients have anxiety regarding medical procedures (1,2). This increase in anxiety can have detrimental effects on the health of a patient, since anxiety can lead to physiologic stress, which can then cause a decreased immune response (3,4). Furthermore, patients who experience anxiety regarding surgical procedures tend to have more complications after the procedure, tend to need more pain medication after the procedure, and tend to need more anesthesia during the procedure (5,6). Patients undergoing interventional procedures who have high anxiety levels often also require more medication and longer procedure times (7).

Because of these negative effects that anxiety can have for patients undergoing various procedures, different strategies to reduce patient anxiety have been investigated. Examples of such strategies include listening to music before surgery or using audiovisual technology with pediatric patients undergoing magnetic resonance imaging (MRI). Studies investigating interventions such as these have found various benefits, such as decreased patient anxiety and reduced needs for sedation (8,9,10). Video glasses enable patients to watch movies or other programming in order to serve as a distraction from the procedure, and may also serve as a way to reduce patient anxiety.

Objectives: The purpose of this project is to evaluate the safety, feasibility, and clinical efficacy of using video glasses in a variety of interventional radiologic procedures.

Methods: From August 2012 to August 2014, 86 patients undergoing various outpatient interventional radiologic procedures successfully completed the study at the University of Rochester Medical Center Department of Imaging Sciences at Strong Memorial Hospital, University Imaging at Highland Hospital, or University Imaging at Science Park. The patients were randomized to either a control (no video glasses, n=43) or intervention (video glasses, n=43) group. A State-Trait Anxiety Inventory (STAI) was given to the patient before and after the procedure. Doses of sedation (midazolam) and analgesia (fentanyl), as well as length of procedure, were also recorded. Average mean arterial pressure (MAP), heart rate (HR), respiratory rate (RR), and pain score, were recorded before, during, and after the procedure.

Post-procedure complications and any adverse events related to using video glasses were recorded. Attending physicians, residents, and nurses completed post-procedure surveys evaluating the safety and feasibility of using video glasses. Post-procedure satisfaction surveys were filled out by a subsection of the patients in the intervention group.

Results: A total of 86 patients successfully completed the study. Overall, women had higher pre-procedure STAI scores compared to men ($p=0.0104$). Patients with high state pre-procedure anxiety (STAI scores ≥ 43 , $n = 22$) required slightly higher amount of sedation and significantly higher analgesia during the procedure compared to patients with low state pre-procedure anxiety (STAI scores < 43 , $n = 64$). Patients using video glasses had significantly reduced levels of anxiety compared to the control group (17.1% vs. 8.3%; $p=0.0424$). Patients using the video glasses also had significantly reduced mean arterial pressures compared to the control group ($p=0.0128$). There was not a significant difference in amount of sedation and analgesia, nor a significant change in heart rate, respiratory rate, pain score or procedure time, between the intervention group and the control group. None of the patients experienced any adverse events related to use of video glasses. Post-procedure surveys filled out by the patients in the majority of cases showed that the video glasses were not distracting and did not interfere or pose a safety issue during the procedure. Overall, most patients stated they enjoyed the video content and use of video glasses, and would use the video glasses again for a future procedure.

Conclusion: Video glasses can be safely used during many interventional radiologic procedures without disturbing the work of physicians and nurses. These glasses can be used to reduce patient anxiety and improve the overall experience that patients have while undergoing these procedures.

References:

1. Horne DJ, Vatmanidis P, Careri A. Preparing patients for invasive medical and surgical procedures 1: adding behavioral and cognitive interventions. *Behav Med* 1994; 20:5–13.
2. Mueller PR, Biswal S, Halpern EF, Kaufman JA, Lee MJ. Interventional radiologic procedures: patient anxiety, perception of pain, understanding of procedure, and satisfaction with medication-a prospective study. *Radiology* 2000; 215:684-688.
3. Grieve RJ. Day surgery preoperative anxiety reduction and coping strategies. *Br J Nurs* 2002; 11(10):670–678.
4. Starkweather AR, Witek-Janusek L, Nockels RP, Peterson J, Mathews HL. Immune function, pain, and psychological stress in patients undergoing spinal surgery. *Spine* 2006; 31(18):E641-E647.
5. Stirling L, Raab G, Alder EM, Robertson F. Randomized trial of essential oils to reduce perioperative patient anxiety: feasibility study. *J Adv Nurs* 2007; 60(5):494–501.
6. Spaulding NJ. Reducing anxiety by pre-operative education: make the future familiar. *Occup Ther Int* 2003; 10(4):278–293.
7. Schupp JS, Berbaum K, Berbaum M, Lang EV. Pain and anxiety during interventional radiologic procedures: effect of patient's state anxiety at baseline and modulation by nonpharmacologic analgesia adjuncts. *J Vas Interv Radiol* 2005; 16:1585-1592.
8. Cooke M, Chaboyer W, Schluter P, Hiratos M. The effect of music on preoperative anxiety in day surgery. *J Adv Nurs* 2005; 52(1):47–55.
9. Arsian S, Ozer N, Ozyurt F. Effect of music on preoperative anxiety in men undergoing urogenital surgery. *Aust J Adv Nurs* 2008; 26(2): 46–54.
10. Harned RK 2nd, Strain JD. MRI-compatible audio/visual system: impact on pediatric sedation. *Pediatr Radiol* 2001; 31(4):247-50.

BASIC SCIENCE, CLINICAL & TRANSLATIONAL RESEARCH

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Knowledge and Awareness of Long-Acting Reversible Contraception (LARC) Among City of Rochester Young Women

Introduction:

Teen pregnancy leads to a number of critical health and social issues including school dropout, poverty, child illness, etc. Substantial public costs are associated with adolescent pregnancy. Despite efforts to reduce teen pregnancy in the United States, adolescent birth rates remain among the highest of the developing world at 34.3/1000. The problem is even more prominent in Rochester, NY, as shown by a rate of 56/1000.

Inconsistent or incorrect contraceptive use is an important contributor to teen pregnancy. LARC includes the intrauterine device (ParaGard or Mirena), which lasts 5-10 years, and the implant (Nexplanon or Implanon), which lasts up to three years. These passive prevention methods eliminate the adherence issues associated with common methods like the oral contraceptive pill, which requires active daily administration. LARC is currently recommended as first-line contraception for teens by WHO, CDC, ACOG, AAP, etc.

Despite its benefits, LARC usage remains very low. Factual knowledge about LARC is low, as is awareness of where to obtain it free and confidentially. Promotion of LARC usage among Rochester teens is an appropriate strategy to reduce unintended or adolescent pregnancy. The Hoekelman Center at the URMH Pediatrics Department is beginning a three-year community-level health education project to raise LARC awareness amongst community leaders, health care providers, and young women.

Objectives: The goal for this project was to collect information about the current knowledge and attitudes that young women in Rochester have towards LARC. This project took place before the Hoekelman Center's health education project began, to get a sense for the current level of LARC knowledge in Rochester. In the coming months and years, other researchers will conduct similar projects, to evaluate the impact that the Hoekelman Center's health education project is having on LARC awareness in Rochester.

Methods: This study involved four focus groups that took place in the summer of 2014. With the help of local health educators, young women between the ages of 15 and 19 were recruited to participate in an hour-long focus group, in which they were shown simple images of some of the most popular contraception methods (intrauterine device, birth control shot, birth control pills, birth control implant, condoms, emergency contraception, birth control ring, and birth control

patch), and asked to discuss what they knew and thought about these different options. They were also asked to quantitatively rate how likely they would be to recommend the different options to a friend.

Results: Based on the quantitative data from eleven participants in their answer to the question "How likely would you be to recommend this birth control method to a friend, on a scale of one to ten?", it was found that the birth control implant was the most highly recommended option, followed by condoms, the intrauterine device, and then the birth control shot. The birth control patch and ring were the two least popular methods. The qualitative data showed that many myths remain about LARC methods in this population, some of the most common being that the birth control implant requires a surgery for placement, and that the intrauterine device can perforate the uterus and travel to other areas of the body.

Conclusions: The young women that were recruited for our study were all involved in pro-social youth groups, which had given them some previous exposure to LARC methods. Therefore, the data reflects a subset of the population of young women in Rochester who are well educated and excited about LARC. Even though the results did not match the original expectation of evaluating baseline awareness, it is a positive sign for the future of the longitudinal health education project to see that young women are welcoming of LARC methods. Future directions of research may involve focus groups with a subset of young women not involved in pro-social groups to get baseline data for the health education initiative, as well as focus groups with the young women who have expressed excitement and early adoption of LARC methods, to gain insight on how to best disseminate this information to the rest of their peer group.

References:

1. ACTRochester. (2013). Youth risk behavior. Retrieved, 2013, from <http://www.actrochester.org/children-youth/youth-risk-behavior/rate-teen-pregnancy>
2. Centers for Disease Control and Prevention. (April 2, 2013). Teen pregnancy prevention. Retrieved February/15, 2013, from <http://www.cdc.gov/teenpregnancy/>
3. Committee on Adolescent Health Care, Long-Acting Reversible Contraception Working Group. (2012). *Adolescents and long-acting reversible contraception: Implants and intrauterine devices*. (No. 539).American College of Obstetricians and Gynecologists.
4. Kost, Kathryn, et al. Estimates of contraceptive failure from the 2002 National Survey of Family Growth. *Contraception* 77.1 (2008): 10-21.
5. Mestad, R., Secura, G., Allsworth, J. E., Madden, T., Zhao, Q., & Peipert, J. F. (2011). Acceptance of long-acting reversible contraceptive methods by adolescent participants in the contraceptive CHOICE project. *Contraception*, 84(5), 493-498.
6. Metro Council for Teen Potential. (2010). *Teen birth and teen pregnancy statistics for Rochester, New York*. Unpublished manuscript.
7. Secura, G. M., Allsworth, J. E., Madden, T., Mullersman, J. L., & Peipert, J. F. (2010). The contraceptive CHOICE project: Reducing barriers to long-acting reversible contraception. *American Journal of Obstetrics and Gynecology*, 203(2), 115. e1.

8. Ventura, S. J., Curtin, S. C., & Abma, J. C. (2012). National vital statistics reports. *National Vital Statistics Reports*, 60(7)
9. Whitaker, A. K., Johnson, L. M., Harwood, B., Chiappetta, L., Creinin, M. D., & Gold, M. A. (2008). Adolescent and young adult women's knowledge of and attitudes toward the intrauterine device. *Contraception*, 78(3), 211-217.
10. Winner, Brooke, et al. Effectiveness of long-acting reversible contraception. *New England Journal of Medicine* 366.21 (2012): 1998-2007.

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An analysis of the estrogen receptor-alpha LXXLL motif in estrogen-mediated protein co-recruitment and downstream signaling pathways

Introduction: The mechanism behind Estrogen Receptor-alpha ($ER\alpha$) and its subsequent activation is important in understanding the basis behind estrogen-mediated signaling in breast cancer, as well as for developing new, safe therapies to treat cancer and symptoms of menopause. Upon binding to an agonist, $ER\alpha$ dimerizes and undergoes a conformational change that exposes a LXXLL amino acid motif on helix 12 of the protein. Exposure of this motif allows other coregulatory proteins, such as steroid receptor coactivator 1 (SRC-1), to bind and lead to downstream target gene expression and proliferation. This occurs primarily through a genomic pathway, in which the newly formed complex acts as a nuclear transcription factor.^{1,2,3}

Recently, the use of Tissue Selective Estrogen Complexes (TSECs) has been shown to provide the therapeutic benefits of an agonist without the dangerous side effects of aberrant $ER\alpha$ activation as encountered with previous therapies.⁴ TSECs consist of a mixture of estrogen, a true agonist, and a Selective Estrogen Receptor Modulator (SERM). As $ER\alpha$ functions in its dimerized state, the question of mixed occupancy - one monomer occupied by an agonist, the other by a SERM - is an important one. While past studies have looked at profiles of agonists and SERMs alone, the coactivator recruitment and functional consequences for these mixed occupancy dimers remain to be fully characterized. Understanding the mechanism behind these complexes is crucial to our comprehension of the differential regulation of $ER\alpha$ in therapies and treatment.⁵

Objectives: We aim to study the effect of a mixed $ER\alpha$ by using the presence or absence of a mutation to mediate inactivation or activation of the transcription complex, respectively. This project examines the effect of a mutated LXXLL motif on coregulatory protein binding and downstream signaling effects. We hypothesized that due to the mutation in the protein binding region of helix 12, an altered protein recruitment profile would lead to an altered downstream target gene expression and signaling profile.

Methods: Tandem $ER\alpha$ plasmid constructs were cloned to contain a mutation in one, both, or none of the monomers in the dimer (WT/mut, mut/mut, WT/WT) by site-directed mutagenesis and restriction enzyme digestion. Prior to assay, plasmids were transfected into the endogenously $ER\alpha$ -negative cell line C4-12 (established cell line) and treated with varying amounts of either an endogenous agonist (estradiol) or a SERM (bazedoxifene).

Co-immunoprecipitation: Cells were collected 48 hours post treatment with estradiol. Cells were lysed under non-denaturing conditions to keep protein-protein interactions intact. Protein lysates were incubated with an antibody directed against SRC-1, protein complexes pulled down by magnetic beads containing protein G, and analyzed via standard western blotting techniques.

Gene Expression: RNA was collected and purified from cells 24 hours post-treatment with estradiol. cDNA from purified RNA was assayed using quantitative PCR for known ER α target genes TFF1, GREB1, PTGS2, PDZK1.

Results: By co-immunoprecipitation, it is evident that the mutated ER α tandem plasmid does not bind SRC-1 – a well-established coregulatory protein. Transfection in C4-12 cells does not affect the absolute levels of SRC-1 available in the cells, validating our findings to be those of a difference in binding rather than absolute SRC-1 expression. Furthermore, the mutated tandem appears to give a different target gene profile, with a significant inhibitory effect on the expression of known target gene TFF1.

Conclusions: Altering the LXXLL motif in just one of the two monomers in the ER α dimer complex is sufficient to impact substantial differences in the protein-protein interactions and downstream target gene expression in the ER α signaling pathway. Future directions would include assaying a wider range of known coregulatory proteins and target genes. In addition, proliferation assays would elucidate the functional significance of these mutations with respect to estrogen-mediated growth.

References

1. Hall, Julie M., et al. The Multifaceted Mechanisms of Estradiol and Estrogen Receptor Signaling. *Journal of Biological Chemistry*. October 2001; 276: 36869-36872.
2. Bjornstrom, L. and Sjoberg, M. Mechanisms of Estrogen Receptor Signaling: Convergence of Genomic and Nongenomic Actions on Target Genes. *Molecular Endocrinology*. 2005 Apr;19(4):833-842.
3. Kong, E.H., et al. Structure and Mechanism of the Oestrogen Receptor. *Biochemical Society Transactions*. 2003; 31(1) 56-59.
4. Pickar, JH., and Mirkin, S. Tissue-selective agents: selective estrogen receptor modulators and the tissue-selective estrogen complex. *Menopause Int*. 2010 Sep;16(3):121-8.
5. Greene, G. and Laine, M. Unpublished data: personal correspondence.
6. Dong, D.D., et al. Functional Analysis of the LXXLL motifs of the human glucocorticoid receptor: association with altered ligand affinity. *J Steroid Biochem Mol Biol*. 2006 Oct;101(2-3):106-17.

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Gastrointestinal bleeding and risk of subsequent thrombosis with continuous-flow left ventricular assist device

Background: Left ventricular assist devices (LVADs) offer an innovative treatment option for patients with advanced heart failure. HeartMate II (HMII), has become the most widely used LVAD. It is a continuous-flow non-pulsatile device that requires chronic anticoagulation. Gastrointestinal (GI) bleeding and thrombosis are common complications of continuous-flow LVADs.

Objectives: We aimed to identify predictors of a thromboembolic (TE) event among HeartMate II (HMII) patients who have already had one or more GI bleed. We hypothesized that patients who have had multiple GI bleeds are at higher risk of subsequent TE events.

Methods: This was a retrospective review of 126 patients who had HMII implantation between January 2011 and February 2014 at the University of Rochester Medical Center, Rochester, NY. GI bleeding was defined as a GI bleed requiring admission, transfusion ≥ 2 units of blood products, or intervention via endoscopy or interventional radiology, occurring ≥ 7 days from LVAD implant. Clinical data were retrieved for each GI bleeding event, including etiology of bleed, GI procedures, INR, LDH, medication changes, administration of blood products, and subsequent GI bleeds and/or TE events. A TE event was defined as confirmed or suspected pump thrombosis leading to explant of LVAD and/or death, or ischemic stroke.

Results: We identified 42 patients with 71 GI bleeding events. There were 6 subsequent TE events among 5 patients, which included 4 patients with pump thrombosis and 2 with stroke. The TE events occurred an average of 105 ± 167 days post-implant. Patients with TE events had an average of 3.2 ± 1.8 total GI bleeding events versus 1.5 ± 1.2 total GI bleeding events in patients without TE events ($p=0.098$). A TE event occurred after an average of 1.7 ± 0.8 bleeds. In 1 (20%) case, a patient with a TE event had exactly one GI bleeding event whereas in 26 (70%) cases, patients without a TE event had exactly one GI bleeding event ($p=0.047$). There were 2 (40%) and 4 (11%) females in the TE event and GI bleeding-only groups, respectively ($p=0.14$). The mean ages at implant of the TE event group and GI bleeding-only group were 63 ± 6 and 61 ± 12 , respectively ($p=0.49$). There were 23 (55%) patients with ischemic cardiomyopathy and 29 (69%) with history of smoking. At least one GI procedure was performed in 67 (94%) cases. The etiology of GI bleed was an AVM in 27 (40%) cases, unknown in 22 (33%) cases, and non-AVM in 18 (27%) cases. At the time of bleeding, patients were taking aspirin in 61 (86%) cases, warfarin in 59 (83%) cases, heparin in 6 (9%) cases, dipyridamole in 5 (7%) cases, and enoxaparin in 2 (3%) cases. Risk factors for having a gastrointestinal bleed were African-American race (HR: 4.16; 95% CI: 2.02 to 8.57; $p=0.0001$) and age over 60 years at implant (HR: 2.70; 95% CI: 1.39 to 5.26; $p=0.0034$).

Conclusions: GI bleeding was common among patients supported with HMII. Many patients who had GI bleeds had subsequent GI bleeds and in some cases had subsequent TE events. Patients with TE events had more GI bleeding events overall, and were more likely to be female. Groups more likely to have a bleed included African-Americans and patients over age 60 at time of implant. While older age is a well-

known risk factor for having a GI bleed after LVAD implantation, race has never been shown to significantly impact risk. Further studies should be done to confirm this finding. This supports the hypothesis that the etiology of GI bleeding on LVAD support is multi-factorial and includes a genetic component.

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Development of a High-Throughput Assay for Identification of Bone Marrow Stromal-Derived Factors That Enhance Acute Lymphoblastic Leukemia Cell Survival

Introduction:

Childhood B-lineage acute lymphoblastic leukemia (ALL) is the most common form of malignancy in children. While cure rates for newly diagnosed ALL are high, 25% of these patients relapse, and ALL still accounts for a large proportion of cancer-associated deaths in children each year. ALL cell survival is poor in the absence of bone marrow stromal cells (BMSC), and thus it is thought that BMSC provide necessary trophic signals to leukemia cells. Our lab is developing a conceptually simple screening system to identify these factors that support ALL survival. We have observed that BMSC prevent apoptosis of primary ALL cells in serum-free conditions, and we reason that interfering with the production of key stroma-derived trophic factors will lead to increased ALL cell apoptosis *in vitro*. If anti-apoptotic signals from stromal cells to leukemia cells were identified, novel molecular targets for ALL therapy could be developed.

Objectives:

Acute lymphoblastic leukemia (ALL) cells die in the absence of bone marrow stromal cells (BMSC) *in vitro*. Our lab is focusing on identifying BMSC-derived factors that support ALL survival. By co-culturing ALL and BMSC, we have shown previously that manipulation of key anti-apoptotic factors from stroma results in decreased ALL cell viability when measured by flow cytometry. We hypothesize that a single-well ATP-luminescence assay could also be used to assess ALL viability, making our system more amenable to high-throughput screening.

Methods:

The assay has 3 components: (1) human bone marrow stromal cells (BMSC) and (2) primary ALL cells (not established cells lines); and (3) G418, a compound that interferes with global protein synthesis in stromal cells. We employ a mesenchymal stromal cell line immortalized with a human TERT gene, which has been shown to be representative of primary human stroma. 20,000 BMSC are placed into 96-well plates. After 48 hours, cells are treated with G418 and washed. 30,000 primary human ALL cells are then added to the wells in serum-free media. 5 days later, viable ALL cells are counted either by flow cytometry or an ATP-luminescence assay (CellTiter-Glo®, Promega).

Results:

(1) Interference of stromal cell protein synthesis significantly increases ALL cell apoptosis. BMSC were treated for 6 hours with 25µg of G418, an irreversible inhibitor of protein synthesis.

Wells were then washed with serum-free medium. ALL cell apoptosis was higher on G418-treated stroma (flow cytometry: 6178 ± 215 viable ALL cells on treated stroma vs. 10923 ± 1733 on un-manipulated stroma, $p\text{-value}=0.001$). The results were replicated in the ATP-luminescence assay (0.24 ± 0.46 RLU on treated stroma vs. 1.84 ± 0.47 RLU on un-manipulated stroma, $p<0.0005$).

(2) Flow cytometry and ATP-luminescence detect similar reductions in ALL cell viability on G418-treated stroma. We have previously used flow cytometry to quantitate viable ALL cells, and we hypothesize that measurement of intracellular ATP is a potential alternative. BMSC were again treated with $25\mu\text{g}$ G418 and washed with serum-free medium. ALL cell viability was assessed using flow cytometry and ATP-luminescence assay. Numbers of viable ALL cells were extrapolated from luminescence data using a standard curve. G418-treated stroma yielded a $42.20 \pm 9.77\%$ reduction in ALL cell viability when measured by flow cytometry, and a $50.01 \pm 15.65\%$ reduction when measured by ATP-luminescence assay ($p=\text{ns}$).

Conclusions:

The ATP-luminescence assay could be used to assess ALL cell viability in our BMSC-ALL co-culture system. Furthermore, its quick and simple procedure makes the assay a potential high-throughput alternative to flow cytometry. Additional experiments must be conducted to determine if the ATP-luminescence assay can detect changes in ALL viability after siRNA knockdown of single stromal genes.

References:

- 1) Manabe A, Coustan-Smith E, Behm FG, Raimondi SC, Campana D. Bone marrow-derived stromal cells prevent apoptotic cell death in B-lineage acute lymphoblastic leukemia. *Blood*. 1992;79:2370-2377.
- 2) Mihara K, Imai C, Coustan-Smith E, et al. Development and functional characterization of human bone marrow mesenchymal cells immortalized by enforced expression of telomerase. *Br J Haematol*. 2003;120:846-849.
- 3) Petty RD, Sutherland LA, Hunter EM, Cree IA. Comparison of MTT and ATP-based assays for the measurement of viable cell number. *J Biolumin Chemilumin*. 1995;10:29-34.
- 4) Siegel R, Ma J, Zou Z, Jemal A. Cancer statistics, 2014. *CA-Cancer J Clin*. 2014; 64:9-29.

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Time to Efficacy for Corticosteroid Injection for Subacromial Impingement

Introduction: Corticosteroid injections are commonly used by a variety of medical specialties for a range of musculoskeletal issues. Current reports of the procedure's 'use' and 'effectiveness' are largely driven on physician-to-physician anecdotal evidence². Various formulations and dosages regimes exist with little evidence on the duration of symptomatic relief or time to efficacy.

Objectives: Our aim is to collect clinical data from individuals receiving first time subacromial corticosteroid injections with the goal of evaluating the time to efficacy. This efficacy will be analyzed with regard to the patient's perception of the treatment, as well as through a standardized measure.

Background: Studies completed regarding such injections varied in their reported effectiveness and duration of relief anywhere from none at all to one week to a year^{2, 3, 4}. Further, reviews have been mixed in its analysis of the effectiveness of injection results⁴. One meta-analysis did demonstrate a significant difference in symptom relief between corticosteroid injections and placebo at the two-week mark¹. A review of nonsurgical care for subacromial impingement syndrome demonstrated a marked average reduction in pain following a corticosteroid injection for most patients for up to one year³. Patients for whom nonsurgical injection options for subacromial impingement syndrome are not successful, arthroscopic surgical options usually yield positive results that can last well over ten years, and can therefore be a viable further treatment option³.

Methods: Patients in the University Sports Medicine Clinical Center receiving a subacromial injection of mixed corticosteroid and anesthetic injection of celestone and lidocaine for relief of impingement symptoms were offered an opportunity to enroll in this study. Only individuals who had never before received a subacromial corticosteroid injection were included in enrollment. Twenty-nine patients were enrolled, five of which were unable to complete the data collection process. After receiving informed consent, patients were asked to rate their pre-injection pain levels on a scale of 1-10, to complete a questionnaire regarding their expectation of relief, and finally to complete a standardized QuickDASH survey. The higher the QuickDASH score, the lower the patient's functionality. Patients were contacted on a daily basis for two weeks following the injection, by email or phone, and were asked to respond to four questions, regarding their current level of pain, their remembered pre-injection level of pain, the

degree to which they felt relief from their injection and whether or not they felt their injection was a success. QuickDASH scores were also collected on a weekly basis for six weeks after initial enrollment.

Results: At the present stage of data collection, thirteen of the patient responses were ready for analysis, and it is on these that we are reporting. At the two-week mark, nine patients referred to the injection as a success and saw at least moderate relief of their impingement symptoms. Three patients were unsure at the two-week mark if their injection was a success and one believed the injection was not a success. Both groups, successful and not, saw a decrease in average QuickDASH score over the two-week period. The QuickDASH scores decreased with significance within the successful group ($P < 0.01$) but not in the unsuccessful group ($P > 0.5$) over the initial two-week period. There was a significant difference in QuickDASH scores for the thirteen individuals in aggregate between the initial reading and the two-week mark ($P < 0.05$) as well as a significant decrease in reported pain levels during the same interval ($P < 0.01$). There was no significant difference in QuickDASH levels between the two-week mark and the six-week mark ($P > 0.5$).

Conclusions: While the rest of our patient data must be analyzed and used in conjunction with a patient data sample collected in the same manner last year, a few general trends arose in this data sample regarding time to efficacy and expectation of relief for a subacromial injection. According to our preliminary results, there is no significant difference in functionality between the two-week and six-week mark and therefore physicians might have a good idea, soon after injection, how much longer term relief a patient will likely experience. Further, clinicians may be able to quickly delineate between patients for whom the injection will be a success relative to those who will experience little eventual symptomatic and functional relief. Those who did not feel that their injection was a success at the two-week point also did not have a significant difference in QuickDASH scores between the initial and two-week time period. Further analysis with the collective data will need to be done on the difference in functionality for those who experience relief versus those who do not, relative perceived pain scales, and precise timeframes for successful systematic relief.

References

1. Arroll B, Goodyear-Smith F. Corticosteroid Injections for Osteoarthritis of the Knee: a Meta-Analysis. *BMJ*. 2004 Apr 10;328(7444):869
2. Cole BJ, Schumacher R. Injectable Corticosteroids in Modern Practice. *J Am Acad Orthop Surg* 2005; 13:37-46
3. Harrison A, Flatow E. Subacromial Impingement Syndrome: a review article. *J Am Acad Orthop Surg* 2011; 19:701-708
4. Koester M, Dunn W, Kun J, Spindler K. The Efficacy of Subacromial Corticosteroid Injection in the Treatment of Rotator Cuff Disease: A Systematic Review. *J Am Acad Orthop Surg* 2007; 15:3-11
5. Thiem U, Lamsfub R, Gunther S, Schumacher J, Baker C, Endres H, Zacher J, Burmester G, Pientaka L. Prevalence of Self-Reported Pain, Joint Complaints and Knee or hip Complaints in adults Aged ≥ 40 Years: A Cross-Sectional Survey in Herne, Germany. 2013; DOI: 10.1371/journal.pone.0060753

BASIC SCIENCE, CLINICAL & TRANSLATIONAL RESEARCH

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Facilitating Diabetes Self-Management in Limited Health Literacy Populations: Barriers and Implementation

Background:

The Diabetes Literacy Project is a global, multi-center study funded by the European Commission's 7th Framework Programme, working to develop and implement best-practice paradigms for facilitating self-management of Type 2 diabetes mellitus in patients identified as low or limited health literacy. Effective management of chronic disease, unlike acute disease, requires continuous and extensive patient self-management and high levels of patient self-efficacy, and this is a particular challenge in low health literacy populations, defined as patients with lower ability to comprehend and accurately utilize health information. Within this large, multi-phase project examining multiple modalities for designing and implementing diabetes self-management interventions, the UCSF site has partnered with the University of Southampton in the United Kingdom on Work-Package 8, developing (UK site) and implementing (UCSF, UK, and Ireland sites) a web-based intervention educating diabetes patients on the benefits of physical activity for managing their condition.

Objectives:

- Implement the UK-designed physical activity intervention website in a setting with 1) a large proportion of diabetic patients and 2) a large proportion of low health literacy patients.
- Measure the efficacy of the website intervention in its two forms, a static version and an interactive version: is this an effective method for promoting physical activity as a self-management strategy for low health literacy patients with diabetes? Does emphasis of audiovisual and interactive components increase engagement for patients with low health literacy?
- Analyze recruitment and intervention efficacy for confounding factors: health literacy is highly multifactorial—are outcomes different for patients with limited English proficiency (LEP)? For patients of various race/ethnicity backgrounds? For patients of various computer literacy backgrounds?

Methods:

- *Setting for Recruitment:* San Francisco General Hospital, General Medicine Clinic. This is an outpatient internal medicine clinic that serves mostly uninsured and underinsured (MediCal), with a high proportion of low SES, low-income patients, with a large proportion of Latino/a and Asian-American patients, most from immigrant backgrounds. Approximately 1/3 of GMC patients have a standing diagnosis of Type 2 diabetes mellitus, and the vast majority of GMC patients have 2 or more concurrent chronic disease diagnoses.

- *Recruit eligible patients:* (a) must speak English to be able to successfully comprehend intervention content, (b) have a standing diagnosis of Type 2 diabetes mellitus
- *Recruitment Protocol:*
 1. Appointment List Generation: for each clinical shift, algorithm generated excluding patients with no English proficiency and did not have diabetes.
 2. Systematic communication with providers: approach providers on a shift-by-shift basis, discuss eligibility of each patient (secondary exclusion criteria: documented English proficiency incongruent with functional English proficiency, patient experiencing psychosocial distress or is too acutely ill to participate).
 3. Session with patients identified in both stages as eligible: patients given option to engage with website intervention.
- *Participation:* Participation option of accessing intervention website at home (via URL and instructions), or option of being escorted to SFGH Library with free computers available for use.
- *Analysis:* Analysis of recruitment, and barriers/facilitators to patient engagement with the website intervention.

Results:

Results are at this point preliminary, as my role in the project was to create a protocol for recruitment, and initiate the process of implementation. An n of ~360 patients for the first month of recruitment were selected by the appointment list generator as eligible, but an average of only 4-5 patients per clinic shift were identified by providers as eligible to be interviewed. Out of each cohort of 4-5 patients fulfilling all primary and secondary eligibility criteria, an average of 3-4 were able to be interviewed, with an average of 0-1 agreeing to participate in the study. For the four weeks I recruited for Work-Package 8 at SFGH, 18.8% of patients interviewed agreed to participate. However, it is notable that this represents only 16 patients approached, 14 interviewed, and 3 agreeing to participate.

Conclusions:

Given that the Diabetes Literacy Project, and its component Work-Package 8, are global studies, with the majority of development and implementation occurring in EU member states, it is clear from the preliminary evidence that crucial barriers exist to effective outreach to the target patient cohort. The vast majority of patients at the GMC are part of low-income, vulnerable communities in the City of San Francisco, and definitions of “low health literacy” are clearly different across national boundaries. The objective for Work-Package 8 is to perform an effectiveness study comparing intervention completion rate and physical activity knowledge between the static and interactive arms of the website trial; however, this is, as of now, infeasible given critical barriers that have surfaced within the first month of recruitment. Using Russ Glasgow’s RE-AIM Framework to analyze the preliminary results of study recruitment from an implementation science framework, specific barriers to recruitment have manifested in the “Reach” and “Adoption” realms of the framework. In analyzing the “reach” of the study, all but 4 interviewed patients reported their average weekly computer/Internet usage as “not at all”, and reported minimal to no computer literacy, with the rest of the patients declining to participate reporting being too acutely ill/recently hospitalized or a sense of distrust for research infrastructure. In analysis of patients listed under the initial cohort of 360 selected by the appointment list generation algorithm, the discrepancy between documented English proficiency and functional English proficiency was the single most important factor in ruling out candidates for the study—English proficiency as documented in their chart was based on very basic interactions with front desk staff, and actual English proficiency was found to be too low in the majority of patients upon review for secondary eligibility criteria. Given this preliminary evidence, the “adoption” component of intervention implementation seems to be playing a large role in recruitment outcomes between the UCSF site and study sites in the UK and Ireland, further

complicating the question of establishing best-practice paradigms for patient self-management of diabetes in low health literacy populations. Overall, though the results are preliminary and there has not yet been opportunity for statistical analysis, clear trends for significant barriers to recruitment have surfaced amongst SFGH GMC's population of very limited English proficiency, low to nonexistent computer literacy, and low SES patients, who are highly representative of the true "low health literacy" populations of California and the United States at large—the populations who continue to be the most vulnerable to detrimental diabetes mellitus outcomes.

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Flaum Eye Institute

Subbasal corneal nerve changes following exposure to desiccating environment

Introduction: Aqueous tear deficient dry eye syndrome is known to be associated with a number of subbasal corneal nerve changes, including increased tortuosity and branching. Exposure to desiccating environments is a risk factor for clinically reported dry eye syndrome and may also precipitate the development of such abnormal nerve fiber patterns.

Objective: To investigate the development of abnormal corneal nerve morphology consistent with aqueous tear deficient dry eye in mice exposed to a desiccating environment.

Methods: C57BL/6J and DBA/2J mice were placed in a low-humidity, increased air-flow environmental chamber for 14 days. Control mice were placed in a normal environment for the same duration. Corneal whole mounts were stained immunohistochemically to reveal nerve patterns using neuronal β -tubulin specific Tuj1 as a nerve marker. Fluorescent microscopy was used to assess the parameters of interest.

Results: Nerve branching and tortuosity consistent with that reported in aqueous tear deficient dry eye patients in previous literature (Zhang, et al) was observed in 4 out of 18 experimental mice. Morphologic assessment of the remaining experimental mice and all control mice was not possible due to failure to visualize nerve structures following the staining protocol.

Conclusions: Exposure to a desiccating environment may induce changes in the subbasal corneal nerves consistent with those seen previously in patients with aqueous tear deficient dry eye syndrome. Inconsistent staining results suggest that further refinement of immunohistochemistry protocols and/or consideration of alternate nerve visualization methods is necessary for future study in corneal whole mounts.

References:

1. American Academy of Ophthalmology Cornea/External Disease Panel. Preferred Practice Pattern® Guidelines. Dry Eye Syndrome, 2013, American Academy of Ophthalmology: San Francisco, CA.
2. The epidemiology of dry eye disease: report of the Epidemiology Subcommittee of the International Dry Eye WorkShop (2007). Ocul Surf, 2007. 5(2): p. 93-107.

3. Gayton, J.L., Etiology, prevalence, and treatment of dry eye disease. *Clin Ophthalmol*, 2009. (3): p. 405-412.
4. Barabino S, Shen LL, Chen L, Rashid S, Rolando M, Dana MR. The controlled-environment chamber: a new mouse model of dry eye. *Invest Ophthalmol Vis Sci*, 2005. 46(8): p. 2766-2771.
5. Barabino S, Dana MR. Animal models of dry eye: a critical assessment of opportunities and limitations. *Invest Ophthalmol Vis Sci*, 2004. (45):1641-1646.
6. Suzuki M, Massingale ML, Ye F, Godbold J, Elfassy T, Vallabhajosyula M, et al. Tear osmolarity as a biomarker for dry eye disease severity. *Invest Ophthalmol Vis Sci*, 2010. (51): p. 4557-4561.
7. Khanal S, Tomlinson A, Diaper CJ. Tear physiology of aqueous deficiency and evaporative dry eye. *Optom Vis Sci*, 2009. 86(11):1235-1240.
8. Sullivan BD, Crews LA, Sonmez B, et al. Clinical utility of objective tests for dry eye disease: variability over time and implications for clinical trials and disease management. *Cornea*, 2012. 31(9): p. 1000-1008.
9. Labbe A, Alalwani H, Van WC, Brasnu E, Georgescu D, et al. (2012) The Relationship between Subbasal Nerve Morphology and Corneal Sensation in Ocular Surface Disease. *Invest Ophthalmol Vis Sci* (53): p. 4926-4931.
10. Labbe, A., et al., Corneal nerve structure and function in patients with non-sjogren dry eye: clinical correlations. *Invest Ophthalmol Vis Sci*, 2013. 54(8): p. 5144-5150.
11. Mantelli, F., et al., The cellular mechanisms of dry eye: from pathogenesis to treatment. *J Cell Physiol*. 2013. 228(12): p. 2253-2256.
12. Dartt, D.A., Neural regulation of lacrimal gland secretory processes: relevance in dry eye diseases. *Prog Retin Eye Res*, 2009. 28(3): p. 155-177.
13. Esquenazi, S., et al., Comparative in vivo high-resolution confocal microscopy of corneal epithelium, sub-basal nerves and stromal cells in mice with and without dry eye after photorefractive keratectomy. *Clin Experiment Ophthalmol*, 2007. 35(6): p. 545-9.
15. Arany S, Catalan MA, Roztocil E, Ovitt CE. *Ascl3* knockout and cell ablation models reveal complexity of salivary gland maintenance and regeneration. *Dev Biol*, 2001. 353(2): p. 186-193.
16. Zhang M., et al., Altered corneal nerves in aqueous tear deficiency viewed by in vivo confocal microscopy. *Cornea*, 2005. 24(7): p. 818-824.

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The Relationship between the Society for Vascular Surgery Lower Extremity Threatened Limb Classification System and Patient Outcomes in Tibial Angioplasty

Introduction:

Critical limb ischemia (CLI) describes a subgroup of patients with a threatened lower extremity due to chronic ischemia. The numerous existing classification systems, like the Fontaine and Rutherford systems, characterize perfusion but do not adequately categorize extent of tissue loss and infection. A new framework, the Society of Vascular Surgery (SVS) Lower Extremity Threatened Limb Classification System, was developed by Mills et al in 2014 to include three major factors known to impact the threat to a limb: Wound, Ischemia and foot Infection (WIFI). Each domain is graded on a 0 to 3 scale, following which the scores can be aggregated to determine risk of amputation and likelihood of benefit from revascularization. Due to its recent conception, the SVS WIFI scale still requires rigorous validation. We sought to evaluate the relationship between WIFI grades and postoperative outcomes in patients who underwent tibial angioplasty.

Objectives:

We sought to evaluate the relationship between WIFI grades and postoperative outcomes in patients who underwent tibial angioplasty.

Methods:

We examined perioperative and long-term mortality and complications in 672 patients who had tibial angioplasty performed at Beth Israel Deaconess Medical Center from 2004 to 2013. Patients were retrospectively graded according to the WIFI system, and follow-up data were obtained via medical records. Chi-squared analysis, Fishers' Exact Test and multivariable logistic regression were performed for data analysis.

Results:

Preliminary results were only available for wound grade at time of abstract publication. Of 672 patients who underwent tibial angioplasty, 41% had a wound grade of 2 (Table 1). No significant difference was found in thirty-day mortality among the four wound grades, but three-year mortality was significantly higher in wound grade 3 than in wound grade 1 (44% vs. 27%, $P < 0.001$). History of diabetes mellitus (DM) was associated with higher wound grade (60%, 79%, 82% and 90% for wound 0, 1, 2 and 3 respectively, $P < 0.001$). Congestive heart failure (CHF) and chronic renal insufficiency (CRI) were also associated with a higher wound grade (CHF 12%, 27%, 27% and 44% for wound 0, 1, 2 and 3, respectively, $P < .001$; CRI 11%, 20%, 31% and 34% for wound 0, 1, 2 and 3, respectively, $P < .001$).

Conclusions:

Though preliminary results are only available for wound grade at this time, there is a clear correlation of wound grade with risk factors, mortality and complications. We anticipate that further analysis of ischemia and foot infection grades will reveal more such correlations. The WIfI system shows promise in its ability to accurately characterize CLI, although further research is needed before wide adoption of this system as a clinical decision-making tool.

References:

Mills, J. L., Conte, M. S., Armstrong, D. G., Pomposelli, F. B., Schanzer, A., Sidawy, A. N., & Andros, G. (2014). The Society for Vascular Surgery Lower Extremity Threatened Limb Classification System: risk stratification based on wound, ischemia, and foot infection (WIfI). *Journal of Vascular Surgery*, 1, 220-34.e1-2.

Wound Grade	#	%	Ischemia Grade	#	%	Foot Infection Grade	#	%
0	155	23	0	39	6	0	425	63
1	190	28	1	330	49	1	163	24
2	277	41	2	200	30	2	73	11
3	50	7	3	103	15	3	11	2

Table 1: WIfI grades on 672 patients who underwent tibial angioplasty from 2004 - 2013
(n=672)

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Studying PARP-13 localization and formation of cytoplasmic processing bodies and/or stress granules under stress conditions

Abstract:

Stress granules are non-membrane bound cytoplasmic structures that form in response to cellular stress, and their presence has been linked in neurodegenerative diseases, such as amyotrophic lateral sclerosis (ALS) and frontotemporal lobar degeneration¹. The current understanding of their composition, dynamics and role in cellular processes is incomplete, although studies have suggested that these and other similar cytoplasmic ribonucleoprotein complexes may play roles in a diverse set of developmental and cellular functions²⁻⁴. Previous studies have shown that stress granules contain many of the initiation factors classically associated with protein translation (eIF3, eIF4A and others), hence they are considered sites of translation stalling and mRNP degradation^{1, 5, 6}. Additionally, cytoplasmic processing bodies (P-bodies), which are constitutively present in human cells, are involved in the degradation of mRNA. There is a dynamic exchange between P-bodies and stress granules during translation stalling/degradation, and it is hypothesized that disruption of this relationship may contribute to disease pathology¹.

Significant evidence, including immunostaining studies and genetic analyses, have shown that poly(ADP-ribose) polymerase 13 (PARP-13) localizes to stress granules. There are two isoforms of the protein, PARP-13.1 and PARP-13.2, with the former containing a catalytically inactive PARP domain on its C-terminus that the latter lacks; otherwise, the two isoforms share the same conserved functional domains⁷. In fact, previous studies show that PARP-13 plays an integral role in the mediation of miRNA silencing under stress conditions⁸. The enclosed abstract and project therein is not a functional assay, but rather analyzes the degrees of PARP-13 localization and the formation of P-bodies and/or stress granules under a variety of conditions in human cell lines, including oxidative stress and transfection with a viral double-stranded RNA mimic. In addition, a HeLa cell line that contains a knockout of the PARP-13 gene was analyzed in plasmid-mediated restoration assays for the reconstitution of P-bodies and stress granules.

Objectives:

This study sought to contribute to understanding the localization of PARP-13 to stress granules and/or P-bodies in response to stress applied to HeLa cells. In addition, one of the objectives was to study the restoration of stress granule formation in PARP-13 knockout cells by transfecting the cells with PARP-13.1 and PARP-13.2 plasmids.

Methods:

HeLa cell lines were utilized for the in vivo studies of cellular responses. To study the effects of oxidative stress on P-body and stress granule formation in both wild-type and PARP-13 knockout HeLa cell lines, cells plated at 1×10^5 cells/mL were treated with sodium arsenite (250 μ M for 30 min). Following treatment, an immunostaining protocol was carried out that used different fluorescently-conjugated secondary antibodies to detect AT-rich regions of DNA (for nucleus localization), PARP-13 and a canonical stress granule or P-body marker; antibodies against eIF3 and 4ET were used in stress granule and P-body studies, respectively. Immunofluorescence images of fixed cells were attained, and the presence of stress granules or P-bodies and the localization patterns of PARP-13 were noted.

Similar experiments were conducted to study responses to viral infection by utilizing poly(I:C), a known mimic of viral double-stranded RNA. Cells plated at 1×10^5 cells/mL were treated with 1 μ g/mL poly(I:C) for 6 hours. Additionally, samples were treated with different dilutions of the poly(I:C) stress for 8 or 16 hours, and Western blotting analysis was carried out to observe any differences in PARP-13 expression due to varying dilutions and exposure times.

To assess the restoration of PARP-13 expression in PARP-13 knockout cells, 1×10^5 cells/mL were treated with an approximately 1.1 μ g/mL DNA plasmid cocktail that contained 12.5% PARP-13.1 plasmid, 37.5% PARP-13.2 plasmid and 50% control plasmids; these proportions were based off of previous unpublished data from Dr. Yoshinari Ando, a postdoctoral fellow in the lab. As with the oxidative stress and viral mimic experiments, immunostaining protocols were carried out and Western blotting was conducted to analyze protein levels.

Results:

Preliminary results affirm previous studies in showing arsenite treatment is sufficient to induce stress granule formation in both wild-type and PARP-13 knockout cells, and it is insufficient to induce significant P-body formation in either cell line. Additionally, data indicate that PARP-13 significantly localizes to stress granules following arsenite treatment. Treatment with poly(I:C) was able to upregulate stress granule formation in wild-type cells but not in PARP-13 knockout cells, supporting previous indications that different pathways promote stress granule formation dependent on the nature of the stress.

Additionally, during the analysis of PARP-13 knockout cells transfected with various restoration plasmids, it was noted that both PARP-13.1 and -13.2 localize to stress granules, but calculations using the Pearson's correlation coefficient suggest that PARP-13.2 localizes more strictly to stress granules. Transfection with the PARP-13.2-containing plasmid (alone or in conjunction with the PARP-13.1-containing plasmid) was able to induce stress granule formation, but transfection with the PARP-13.1-containing plasmid alone was unable to induce stress granules in knockout cells.

Conclusions:

Although the conclusions from these studies need to be verified by reproducing their data with continued experimentation, the preliminary results show that PARP-13.2 alone is sufficient to induce stress granule formation, and that the PARP-13 seems to be necessary to upregulate stress granule formation in cells treated with poly(I:C). Oxidative stress was sufficient to induce a pathway that increases stress granule formation even in the absence of PARP-13, further supporting studies that show that oxidative stress and viral double-stranded RNA constructs

induce stress granules by different mechanisms. Investigation into the functional and clinical significance of these conclusions is necessary. These studies alone contribute to a growing body of knowledge regarding the formation and composition of stress granules in human cells.

References:

1. Ramaswami, M., Taylor, J.P. & Parker, R. Altered ribostasis: RNA-protein granules in degenerative disorders. *Cell* **154**, 727-36 (2013).
2. Weil, T.T. et al. Drosophila patterning is established by differential association of mRNAs with P bodies. *Nat Cell Biol* **14**, 1305-13 (2012).
3. Thedieck, K. et al. Inhibition of mTORC1 by astrin and stress granules prevents apoptosis in cancer cells. *Cell* **154**, 859-74 (2013).
4. Dougherty, J.D., White, J.P. & Lloyd, R.E. Poliovirus-mediated disruption of cytoplasmic processing bodies. *J Virol* **85**, 64-75 (2011).
5. Anderson, P. & Kedersha, N. Stress granules: the Tao of RNA triage. *Trends Biochem Sci* **33**, 141-50 (2008).
6. Buchan, J.R. & Parker, R. Eukaryotic stress granules: the ins and outs of translation. *Mol Cell* **36**, 932-41 (2009).
7. Leung, A.K. et al. Poly(ADP-ribose) regulates stress responses and microRNA activity in the cytoplasm. *Mol Cell* **42**, 489-99 (2011).
8. Leung, A., Todorova, T., Ando, Y. & Chang, P. Poly(ADP-ribose) regulates post-transcriptional gene regulation in the cytoplasm. *RNA Biol* **9**, 542-8 (2012).

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Weighted Helmet Impact Measures Correlate with Brain White Matter Changes After One Football Season of Repetitive Head Hits.

Background:

Repetitive head hits (RHH) incurred during sports like football produce acute changes in brain white matter (WM) that may contribute to Chronic Traumatic Encephalopathy (CTE) many years later. More precisely defining the relationship between RHH and acute WM changes is a necessary first step in developing efforts to reduce the long-term risk of CTE. The WM changes are difficult to visualize and quantify with current clinical imaging studies. Diffusion tensor imaging (DTI) allows a quantitative measurement of changes in white matter based on diffusion of water along the axons in the brain (1). We specifically examined changes in fractional anisotropy (FA), which is a scalar measurement (0-1) describing water's diffusion, with zero being equal diffusion in all directions, and one being water diffusing along a single axon. Even with the ability to quantify these changes as indicators of injury severity, it is difficult to predict or estimate these changes with current metrics or other non-DTI measurements that would be useful in a clinical setting. Prior studies report an inconsistent relationship between acute WM changes and the cumulative number and magnitude of head impacts incurred over a sport season (2). These studies did not account for the interval of time between head impacts (TBH), nor for the period of time between head impacts and DTI scanning (TUD), both of which are likely to influence the appearance of WM at the end of the football season (3). In order to address these gaps, we developed several new head impact metrics weighted for TBH and TUD.

Objectives:

1. To determine if the weighted cumulative head impact metrics correlate with changes in brain WM after a single season of collegiate football
2. To determine if weighted cumulative metrics correlate better than an unweighted metrics with WM.

Methods:

In the 2011 football season, 10 University of Rochester football players wore helmets equipped with the head impact telemetry system (HITS) (2). The helmets recorded impacts at every practice and game during the season. The HITS measures linear acceleration, rotational acceleration, Gadd Severity Index (GSI), Head Impact Criterion 15 (HIC15), and HIT severity profile (HITsp) with each head impact. The WM changes were measured using DTI, which were performed at the beginning and end of the football season. DTI changes in each subject were defined as the percent of all WM voxels with a significant increase in FA as well as a significant decrease in FA from the beginning to end of the football season

One unweighted metric and three weighted metrics were analyzed. The unweighted metric simply summed all the values for a single HITS impact measure. The first weighted metric determined a value for each impact measure based on the current hit and the time since prior hits, and was known as the time between hits metric (TBH). The second metric known as the time until DTI (TUD) determines an impact value for each hit based on the number of days between the hit and the date of DTI scan. The final metric combined the TBH and TUD into a single mathematical equation, known as the TBH-TUD metric. The three above weighted metrics were summed in the same fashion as the unweighted metric.

Results:

Unweighted cumulative, TBH, and TUD values show a statistically significant direct relationship with fractional anisotropy (FA) decrease. The highest r^2 values for FA decrease are seen when the TUD metric was used to weight HIC15 and GSI. Both linear and logistic regressions for all time-weighted metrics show statistically significant relationships with FA increase. The significant relationships are seen most consistently with FA increase. However, the TBH-TUD metric shows the highest r^2 for FA increase for all impact measures. In summary, linear models correlate better with changes in FA decrease, while logistic models are better at predicting changes in FA increase.

Conclusions:

The use of time-weighted impact estimates correlate with the changes in white matter seen on DTI. Weighting the forces allows for better predictability of FA changes in DTI in comparison to a simple unweighted cumulative force.

References

1. Shenton, M. E., Hamoda, H. M., Schneiderman, J.S., Bouix, S., Pasternak, O, Rathi, Y., ...Zafonte, R. (2012) A review of magnetic resonance imaging and diffusion tensor imaging findings in mild traumatic brain injury. *Brain imaging and Behavior*, 6(2), 137-92. doi: 10.1007/s11682-012-9156-5
2. Funk, J. R., Rowson, S., Daniel, R. W., & Duma, S. M. (2012). Validation of concussion risk curves for collegiate football players derived from HITS data. *Annals of Biomedical Engineering*, 40(1) 79-89. doi: 10.1007/s10439-011-0400-8
3. Fujita, M., Weig, E. P., & Povlishock, J.T. (2012) Intensity- and interval specific repetitive traumatic brain injury can evoke both axonal and microvascular damage. *Journal of Neurotrauma*, 29(12), 2172-80. doi: 10.1089/neu.2012.2357

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Molecular Basis of Colon Cancer Metastasis: Effectors of E-Selectin Binding

Background

Colorectal cancer is the second leading cause of cancer-related death among both men and women in the United States, claiming more than fifty-thousand lives each year¹. The danger lies in its virulent capacity to metastasize². Tumor metastasis is a multi-step process nearly identical to that which mediates leukocyte trafficking to sites of tissue injury under shear blood flow conditions. The first step of this process is the engagement of E-selectin, a C-type lectin expressed on activated endothelium, to E-selectin ligands expressed on the cancer cells^{3,4}. E-selectin ligands are sialofucosylated structures presented on protein or lipid scaffolds. The prototypes of these structures are the glycoforms known as sialylated Lewis^x (sLe^x) and sialylated Lewis^a (sLe^a); these consist of a lactosamine backbone made up of alternating N-acetylglucosamine (GlcNAc) and galactose (Gal) units, which is decorated with a terminal sialic acid (NeuAc) and a fucose (Fuc) in an $\alpha(1,3)$ or $\alpha(1,4)$ linkage, respectively, to the GlcNAc residues⁴. Previous studies have suggested that O-sialofucosylated variant isoforms of the ubiquitous protein CD44, termed hematopoietic cell E-/L- selectin ligand (HCELLy), function as E-selectin ligands on the colon cancer cell line LS174T^{5,6}. Sialofucosylated carcinoembryonic antigen (CEA) has also been identified as an E-selectin ligand (CEA-EL) on CD44 knockdown LS174T cells⁷, although the degree to which its functions complement or oppose those of CD44 is yet to be elucidated. Both CD44 and CEA are extremely pleiotropic molecules, and often, the splice variant isoforms of CD44 and CEA that are expressed on cancer cells are different from those isoforms expressed physiologically. Thus, further insight into the structure and function of these glycoproteins is warranted as they could serve as targets of directed therapy against highly metastatic, circulating cancer cells.

Objective:

The objective of my research was to characterize the E-selectin ligands expressed on cancer cells, primarily in terms of the protein scaffolds, (CD44 or CEA), on which they are presented.

Methods:

Colorectal cancer cell lines *LS174T*, *HCT-8*, and *HT 29* were obtained from the American Type Culture Collection (ATCC) and maintained as described. Twenty-seven flash frozen tissue samples were obtained courtesy of Dr. Wells Messersmith and Dr. John Arcaroli of the University of Colorado at Denver, consisting of a mixture of human-in-mouse xenotransplanted colorectal cancer (CRC) specimens and human biopsy CRC specimens. Several of these specimens were paired; i.e., the biopsy specimen and the xenotransplant specimen were derived from the same patient. Still other paired specimens consisted of primary tumor samples and liver metastases

derived from the same patient, enabling this comparison as well. Lysates of all tissue samples and cell lines were prepared using an appropriate EDTA-free detergent buffer, along with sonication. The samples were then assessed for their relative CD44/HCELLv or CEA/CEA-EL expression using immunoprecipitation, SDS-PAGE/western transfer, and immunoblotting using various antibodies as probes.

Results:

At the present stage of data collection, it appears that HCELLv and CEA-EL have equal potential to contribute to the E-selectin ligand activity of colorectal cancer cells. HCELLv (i.e. the E-selectin binding glycoform of CD44) is predominantly observed as a 160 kDa band on SDS-PAGE gels. CEA-EL (the E-selectin binding glycoform of CEA) is predominantly observed as a 180-200 kDa band on SDS-PAGE gels. Lower molecular weight isoforms of CD44 and CEA, while observed in the tumor samples and cell lines, have no E-selectin ligand activity. On native colon tissue, defined as normal (non-cancerous) colon tissue adjacent to a tumor, E-selectin ligand activity was observed only on a 90 kDa isoform of CD44 and on a 250 kDa isoform of CEA, with no E-selectin ligand activity on the 160 kDa and 200 kDa isoforms as in the tumors. There was no native CEA activity in the liver, but HCELL was again expressed as the 90 kDa standard isoform in native hepatocytes adjacent to a *CRC* liver metastasis. Significant pleiotropism was observed in the xenotransplanted *CRC* specimens, with both CEA-EL and HCELLv being presented on higher and lower molecular weight than those observed in the primary biopsy samples. It is probable that the selective pressures exerted by the process of xenotransplantation caused these cells to alter their E-selectin ligand expression. No tangible differences were observed in the E-selectin ligand activity of primary colon tumors and their liver metastases.

Conclusions/Future Directions:

While more data is required to draw absolute conclusions, a few general trends were repeatedly observed in the data collected thus far:

1. A 160 kDa isoglycoform of HCELLv is an E-selectin ligand on colon cancer cells derived from biopsy tissue. This is a significant observation because all prior work characterizing HCELLv in colon cancer has been done on immortalized cell lines, which are far removed from primary tissue and often grown in very artificial conditions.
2. A 200 kDa isoglycoform of CEA-EL is an E-selectin ligand on colon cancer cells derived from biopsy tissue. Again, all prior work characterizing CEA-EL has been done on cell lines, and moreover, on CD44 knock down subclones of cell lines. Our results show that even just-isolated colon cancer cells have significant CEA-EL expressivity.
3. Xenotransplantation of human colon cancer specimens results in pleiotropism of E-selectin ligand expression compared to that in identical, non-xenotransplanted colon cancer specimens. As mentioned, it is possible that different selective pressures exerted on these cells as a byproduct of the xenotransplantation result in this pleiotropism. However, it is also possible that these selective pressures enable only the most virulent cancer cells in the biopsy sample to survive, thus leading to enrichment of the sample for E-selectin ligand expressing cells, and enabling even minor E-selectin ligands to be detected.

Overall, this research project was valuable because it explored colorectal cancer biology extremely proximal to the native conditions in which colorectal cancer develops, i.e., using direct biopsy samples. It also analyzed the credibility of pre-clinical studies using xenotransplanted mouse specimens. Further exploration of the emerging trends is likely to yield results with interesting translatable potential.

References:

1. *Colorectal Cancer Detailed Guide*. Atlanta, Ga: American Cancer Society;2012.
2. *Colorectal Cancer Facts and Figures 2011-2013*. Atlanta, Ga: American Cancer Society;2011.
3. Jacobs PP, Sackstein R. CD44 and HCELL: preventing hematogenous metastasis at step 1. *FEBS Lett*. Oct 20 2011;585(20):3148-3158.
4. Sackstein R. Glycosyltransferase-programmed stereosubstitution (GPS) to create HCELL: engineering a roadmap for cell migration. *Immunol Rev*. Jul 2009;230(1):51-74.
5. Burdick MM, Chu JT, Godar S, Sackstein R. HCELL is the major E- and L-selectin ligand expressed on LS174T colon carcinoma cells. *J Biol Chem*. May 19 2006;281(20):13899-13905.
6. Hanley WD, Burdick MM, Konstantopoulos K, Sackstein R. CD44 on LS174T colon carcinoma cells possesses E-selectin ligand activity. *Cancer Res*. Jul 1 2005;65(13):5812-5817.
7. Thomas SN, Zhu F, Schnaar RL, Alves CS, Konstantopoulos K. Carcinoembryonic antigen and CD44 variant isoforms cooperate to mediate colon carcinoma cell adhesion to E- and L-selectin in shear flow. *J Biol Chem*. Jun 6 2008;283(23):15647-15655.

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Donor Human Milk Availability Promotes Breast Milk Feeding Among VLBW Infants in California, Lowers Hospital Rates of NEC

Introduction: Breastfeeding is widely considered the optimal form of nutrition for all infants, but it is especially important for babies born prematurely. In preterm infants, human milk feeding is associated with a lower risk of necrotizing enterocolitis (NEC), retinopathy of prematurity, and sepsis.^{1,2,3} Human milk is one of the only known protective agents against NEC.⁴ Studies have shown that enteral feeding containing at least 50% human milk in the first 14 days of life is associated with a six-fold decrease in the odds of NEC.¹ Because of the challenges associated with breastfeeding infants in the NICU, donor human milk is often used as a substitute for a mother's own milk.⁵ However, the majority of currently available data on donor human milk and NEC rates in preterm infants comes from studies conducted over 20 years ago.⁶ There has also been some debate about whether access to donor human milk could actually lead to decreased breastfeeding—the idea being that availability of an alternate human milk source could lead to attenuated efforts to promote lactation among mothers of preterm infants.⁷ Data collected by the Italian Association of Human Milk Banks shows that donor human milk is actually associated with an increased rate of exclusive breastfeeding in very low birth weight (VLBW, birth weight < 1500 grams) infants⁷, but it is hard to analyze data about human milk banks in the United States. Data from human milk banks in the U.S. is not standardized and there is a lack of a central depository.⁵ The Human Milk Banking Association of North America (HMBANA) has stated that this could be hindering research, quality improvement initiatives, and implementation of donor milk programs in NICUs.⁵

Objectives: Our project had several aims. Our overarching purpose was to link data from the California Perinatal Quality Care Collaborative (CPQCC) with data from the Mothers' Milk Bank of San Jose. The CPQCC is an organization that collects data from 132 NICUs in California, gathering information on the care of over 90% of California's NICU admissions of VLBW infants. This provides a sizeable and meaningful database from which very real information about NICU infant care in California can be extracted. The Mothers' Milk Bank of San Jose is the largest human milk bank in the United States (in terms of distribution) and the only human milk bank that distributes donor human milk to NICUs in California. By combining these two datasets, we were hoping to get a pretty clear picture of donor human milk use and benefits in California. Our first aim was to see what has been happening to the availability of donor milk in California over the period of 2007-2013. In addition, we wanted to see if the availability of donor human milk in a hospital may have had an effect on the rates of NEC and breastfeeding at discharge for VLBW infants at that hospital.

Methods: We used data from the CPQCC and the Mother's Milk Bank of San Jose. In order to track donor human milk availability over time, we calculated and plotted the percentage of NICU births that occurred in a hospital with donor human milk available over the course of 2007-2013. This plot was stratified according to NICU level. In California, Regional NICUs take care of the sickest patients who may require subspecialty and/or surgical care, Community NICUs can care for VLBW infants who may require prolonged respiratory support, and Intermediate NICUs care for infants who have less need for intensive respiratory support.

22 hospitals were identified that underwent a clear transition from not having donor milk to having donor human milk available at some point during the course of 2007-2013. Paired t-test analyses were performed to compare rates of breastfeeding and rates of NEC among VLBW infants before and after these hospitals acquired donor human milk.

A multivariable logistic regression model was devised to examine which hospital, medical, and sociodemographic factors were associated with breast feeding among VLBW infants.

Results: (1) Donor human milk availability in California NICUs is increasing overall. Over the course of 2007-2013, the percentage of NICU infants that had donor human milk available to them increased, regardless of NICU level. There seems to be a greater push to have donor human milk available among Regional and Community NICUs. In 2007, 38.2% of premature infants in Regional NICUs had donor milk available to them and in 2013, 81.3% of premature infants in Regional NICUs had donor milk available to them.

(2) The availability of donor human milk in a hospital is correlated with an increase in the rate of breastfeeding at discharge among VLBW infants. The mean difference before/after donor human milk for the 22 hospitals that underwent a clear transition over the course of 2007-2013 was a +10.0% absolute increase in rate of breastfeeding at discharge.

(3) The availability of donor human milk in a hospital is correlated with a decrease in the rate of NEC among VLBW infants. The mean difference before/after donor human milk for the 22 hospitals that underwent a clear transition over the course of 2007-2013 was a -2.6% absolute decrease in rate of necrotizing enterocolitis. This translated to a change from an average hospital NEC rate of 6.6% before acquiring donor human milk to an average hospital NEC rate of 4.3% after donor human milk was available.

(4) The availability of donor human milk in the hospital where a VLBW infant was being treated is a strong positive predictor of breastfeeding at discharge. A multivariable logistic regression model for breastfeeding at discharge found that the presence of donor human milk yielded an odds ratio of 1.47 with a 95% confidence interval of [1.41, 1.54].

Conclusions: The availability of donor human milk in NICUs in California has increased since 2007. The potential consequences of this influx of donor human milk seem to be favorable. Paired t-test analyses found that introduction of donor milk led to a decrease in hospital rates of necrotizing enterocolitis and an increase in breastfeeding at discharge among VLBW infants. In a multivariable logistic regression for breastfeeding at discharge, availability of donor milk was a strong positive predictor.

References

1. Sisk PM, Lovelady CA, Dillard RG, Gruber KJ, O'Shea TM. Early human milk feeding is associated with a lower risk of necrotizing enterocolitis in very low birth weight infants. *J Perinatol* 2007, **27**: 428-433.
2. Hylander MA, Strobino DM, Pezzullo JC, Dhanireddy R. Association of human milk feedings with a reduction in retinopathy of prematurity among very low birthweight infants. *J Perinatol* 2001, **21**(6): 356-362.
3. Hanson LA, Korotkova M. The role of breastfeeding in prevention of neonatal infection. *Semin Neonatol* 2002, **7**(4): 275-281.
4. Stevenson DK, Blakely ML. Necrotizing enterocolitis: an inherited or acquired condition? *NeoReviews* 2006, **7**(3): e125-e134.
5. Brownell EA, Lussier MM, Herson VC, Hagadorn JI, Marinelli KA. Donor human milk bank data collection in North America: an assessment of current status and future needs. *J Hum Lactation* 2014, **30**(1): 47-53.
6. McGuire W, Anthony MY. Donor human milk versus formula for preventing necrotising enterocolitis in preterm infants: systematic review. *Arch Dis Child Fetal Neonatal Ed* 2003, **88**: F11-F14.
7. Arslanoglu S, Moro GE, Bellu R, Turoli D, De Nisi G, Tonetto P, Bertino E. Presence of human milk bank is associated with elevated rate of exclusive breastfeeding in VLBW infants. *J. Perinat. Med.* 2013, **41**(2): 129-131.

COMMUNITY HEALTH SUMMER RESEARCH

UR Well: a safety net for Rochester's underserved

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According to the U.S. Census Bureau, the medically uninsured rate for the six counties comprising the Rochester metropolitan area is 10.2%. UR Well's mission is to provide high-quality healthcare to those individuals who are uninsured and underinsured in the community of Rochester. The UR Well clinic at Asbury First United Methodist Church provides acute care and physical examinations, whereas St. Joseph's Neighborhood Center provides longitudinal primary care to its clients. Not only do these clinics provide access to those who otherwise lack care options, but they also exposes medical students at the University of Rochester to urban healthcare and issues of social justice. Additionally, this service is believed to reduce inappropriate use of emergency medical services within the University of Rochester Medical Center.

Every summer, three dedicated student administrators complete an internship at Asbury and St. Joseph's to ensure the successful operation of the two clinics while many students are away from Rochester. The students also develop research projects that further the goals outlined in the clinic mission statement. The projects this past summer (a) recruited additional patients to UR Well, (b) referred those patients without primary care physicians from UR Well at Asbury to UR Well at St. Joseph's, and (c) assessed satisfaction among preexisting clients.

The first project focused on recruiting additional patients to UR Well at St. Joseph's. St. Joseph's actively participated in facilitating patient's enrollment in both medicaid and marketplace plans of the Patient Protection and Affordable Care Act (PPACA), and helped newly insured patients transition to new providers. As a result of their concerted effort to capitalize on the new law, St. Joseph's found that its patient census decreased nearly 20% in a few months. Given that providers at St. Joseph's now had ample room on their schedules, an outreach project was developed that focused on establishing interpersonal connections with other institutions that service the indigent or underserved members of the community. A new brochure was designed and printed in both English and Spanish, and a member of the UR Well summer internship team personally contacted food pantries, soup kitchens, university student health offices, social service agencies, and religious centers around Monroe County. He then traveled to all of these locations to build a reciprocal relationship in which patients at St. Joseph's would be referred to other social services when appropriate, and each organization would refer potential patients to the clinic. In the second arm of the outreach project, a relationship was established between the University of Rochester Medical Center Emergency Department and St. Joseph's to further reduce inappropriate emergency care services by those lacking a primary care physician.

The second project focused on establishing a referral process from Asbury to St. Joseph's. Until this year Asbury and St. Joseph's existed as separate entities. To remedy this shortcoming, a referral system was established to offer better follow-up care to those seeking

care at Asbury. Those clients who lack insurance and are seeking a primary care physician are connected directly to the Healthcare Access Team at St. Joseph's. This team arranges a meeting with every potential patient to review their finances and can then direct them toward the best option for receiving healthcare services. This ensures that patients will be connected to an additional support system after they leave the acute care clinic and can help St. Joseph's build-up their patient population.

The third project focused on assessing patient experiences at UR Well at Asbury. Previously, there had been no studies assessing patient satisfaction within the UR Well network. The acquisition of patient feedback in this setting would enable UR Well to continue to offer high-quality care to those most in need by recognizing areas of strength and improving on areas of weakness. To this end, a unique post-visit survey was developed using pre-existing surveys developed by the Consumer Assessment of Healthcare Providers and Systems (CAHPS) surveys of the United States Department of Health and Human Services as a framework. Survey administration is ongoing and it is anticipated that the survey will be completed by 80 patients over the 4 month study period.

INTERNATIONAL MEDICINE RESEARCH

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To know or not to know: Disclosure of terminal illness status to cancer patients in South Korea

Introduction:

Most Western physicians and patients believe as ethical the idea that patients deserve to know their diagnosis. Disclosure of terminal illness is believed to be critical for patient input in their medical care and the decision-making process from that perspective.¹⁻³ Patient awareness of terminal illness has been shown to help maintain patient autonomy in medical decision-making. Failing to disclose terminal illness may inhibit open discussion of best care options and can lead to increased disagreements in care.⁴ Most patients in Korea indeed prefer to be involved in making medical decisions; however, there is still a significant minority – nearly 30% – that prefers not to be involved.⁵ This may reflect a cultural trait, in which Korean, and East Asian cultures in general, entrust their families or physicians with treatment decisions.⁶⁻⁷ We expect that most patients and caregivers will prefer patient involvement in decision-making.

Specifically within the field of oncology, 80% of Korean physicians preferred to disclose a patient's terminal cancer to the patient,⁸ and almost all patients and caregivers believed that patients should be informed of terminal illness.⁹ A basic reason cited was that the patient should have a right to know the truth about their medical condition. Other reasons mentioned included resolving unfinished business, taking appropriate care of themselves in cooperation with healthcare professionals, and relieving themselves and their families of the burden of useless treatments.⁹ Whether the patient paid for treatment costs also played a factor in preferences in disclosure. Patients and family caregivers are more likely to prefer disclosure of terminal illness if the patient is paying the treatment cost, highlighting the economic burden of disease.¹⁰ We hypothesize that the majority of families and physicians who disclose terminal illness do so on the grounds of the patient's right to know the truth.

However, there are some patients, families, and physicians who prefer not to disclose a patient's terminal status. Some families and physicians may protect patients from the bad news to give them hope for the future. Telling them the bad news might discourage the patient from fighting the disease. Patients who object to being told the truth reflect this idea, viewing the

disclosure as meaningless and conveying a sense of helplessness.^{9, 11} A cultural perspective on nondisclosure unique to Asian cultures is that the sense of filial responsibility may lead to family members keeping burdensome information from patients and making end-of-life decisions on behalf of the patient.¹² We hypothesize that caregiver families who choose not to disclose terminal illness will express desires to protect the patient, but will express anxiety that the patient will find out about their terminal status.

Despite the general recommendation of disclosure, the true rates of disclosure of terminal illness in Korea are not as unanimous. One study by Yun et al (2010) reported that only 58% of patients in an oncology ward and 83% of family caregivers were aware of the patient's terminal status. This study also reported that 30% of patients who were not told of their terminal illness eventually correctly guessed it from their worsening condition.¹⁰ Another study by Ahn et al (2013) reported that roughly two-thirds of terminal patients admitted to palliative care services in Korea were aware of their terminal illness.⁴ These rates were, however, actually higher than in some Western studies, where the percentages were 30-40% for patient awareness, and 80% for family caregivers.¹³⁻¹⁶

Patient emotional responses to learning of terminal illness are varied, ranging from sadness, depression, grief, denial, anger, stress, fear, worry, guilt, regret, and loneliness. Interestingly, the manner in which the bad news is learned has an effect on the emotional response. Patients who learned of their terminal status indirectly, whether by chance or by guessing from their own worsening condition, experienced more severe distress and lower quality of life.¹¹

Objectives:

This study aimed to investigate motives for disclosure or nondisclosure of a patient's terminal illness status in South Korea, and the emotional outcomes of disclosure or nondisclosure. The research questions specifically investigated were: 1) What are the primary driving factors for caregivers and physicians disclosing or not disclosing a patient's terminal status in South Korea? 2) What are the decision-making dynamics among terminal patients, caregivers, and physicians in South Korea? 3) How does disclosure or nondisclosure of terminal illness to patients impact the patient-family relationship within this setting?

Anticipated motives for disclosure of terminal illness include families' and/or physicians' belief in the patient's right to know of terminal illness, the desire for the patient to be a part of his/her own medical decision-making process, and a necessity for dialogue on end-of-life arrangements. Motives for nondisclosure may include protection of the patient against bad news or an unhappy death. For patients who know of their terminal status, decision-making was anticipated to be a mutual and equitable process among all three parties involved; conversely, it was predicted that the families of patients who are unaware of their terminal status would be the primary decision-makers. From the Western perspective, it'd be expected that the majority of patient-family relationships would not be negatively impacted by disclosure of terminal illness, but that nondisclosure may lead to anxiety for those caregivers who choose not to share that information with their patients.

Results:

Results were divided into four broadly themed categories – disclosure, decision-making, relationships, and patient age.

Disclosure

As expected, common reasons cited by physicians, caregivers and patients in favor of disclosure of a terminal cancer patient's terminal status were of the patient's basic right to know his/her own health situation, patient participation in treatment and medical care, and necessary preparations for the end of life.

All physicians who were interviewed believed that terminal patients should eventually receive the news that they are indeed terminal. Most physicians preferred to disclose a patient's terminal status to the caregiver first, citing an implicit duty of the caregiver to be the ultimate decision-maker on whether to disclose to the patient or not. The most difficult aspect of disclosure commonly noted was the idea that the physician was delivering emotionally damaging news; several physicians even felt a personal responsibility for the failure of cancer treatment. Physicians also mentioned examples of patients who, when not told of their terminal status, probably guessed it anyways from their declining health.

Caregiver opinions on whether to disclose or not varied. Reasons cited for non-disclosure included a potential loss of hope for a patient still receiving treatment, and unnecessary stress/burden. There were several instances of non-disclosure only initially – a unique reason cited was a lack of courage on the part of the caregiver. Several caregivers, whether or not they disclosed immediately or after a prolonged duration, requested the physician to disclose a patient's terminal status. Of note, a particular difficulty cited of non-disclosure was that caregivers emotionally suffered when the patient was in pain but was unaware of the cause.

All patients interviewed were fully aware of their own terminal status. Several patients mentioned that they found out by "accident" – they either guessed their condition or overheard a conversation revealing their terminal status. Most patients were in favor of knowing of one's own terminal status. One particularly revealing reason cited in favor of disclosure was that a patient wanted to mentally "control" the disease and more actively fight it in a psychological capacity. This seemingly contradicts a preference of caregivers not to disclose out of fear that the patient would lose hope or give up on any treatment they might still be receiving.

Decision-making

Physicians generally regarded their role in end-of-life (EOL) decision-making to be one of explaining all treatment and/or palliative options and recommending a best course of action. Caregivers and patients were in unison regarding their perceived roles in a patient's medical care. With respect to palliative options, such as whether to leave the hospital or enter hospice, patients were the decision-makers if they knew of their own terminal status; when patients were unaware of their terminal status, caregivers tended to take the dominant role in medical decision-making for the patient.

Regarding continued treatment, caregivers and patients tended to defer to the recommendation of the physician. A common theme was that caregivers and patients lacked the

medical knowledge to seek an alternative, with several patients even expressing dissatisfaction at the gulf of knowledge between physicians and caregivers/patients. As one interviewee noted, “doctors are the law. We do as they tell us.” Non-informed medical decision-making seemed to be the prevailing theme with regards to treatment.

Relationships

Physicians expressed regret at the tenuous physician-patient relationship in situations in which the patient was unaware of his/her terminal status. Physicians felt that they were not able to have an honest conversation with these patients, having to provide roundabout explanations to questions that patients might have.

Patients and caregivers expressed significant frustration at both the Korean medical system and at physicians for inaccessibility. As the time allowed for patient visits at many major hospitals is about five minutes, patients and caregivers alike felt that they received insufficient detail about the patient’s status throughout the disease process. In addition, they were unable to have questions about the patient’s medical care answered, compounding the paucity of medical information available to patients and caregivers.

Patient age

Physicians noted a greater tendency of caregivers to hide a patient’s terminal status with older patients – specifically when the caregiver was the child of the patient. Some possible reasons suggested by physicians were that the emotional trauma experience by older patients would be overwhelming, that patients would be unnecessarily burdened, older patients’ mental incapacity to understand diagnosis, and protection of parents from bad news as a manifestation of filial piety. A majority of caregivers indeed reflected these physician views. Several physicians also noted that both patients’ and caregivers’ emotional reactions to hearing news of terminal illness were more muted for older patients, possibly a reflection of death being less unexpected at an older age.

Conclusion:

While interviewed patients and physicians were near-universal in their opinions that the patient should know of his/her own terminal status, the ultimate decision of disclosure in South Korea is the responsibility of the caregiver. Caregiver responses suggest that this decision is a case-by-case one, with a multitude of relevant factors. Interviewees acknowledged that a patient’s age was a major consideration in the decision to disclose, and also influenced reactions thereafter. Interviewees revealed that the Korean healthcare system greatly impacts medical knowledge available to patients and caregivers, and thus end-of-life and treatment decision-making. These influences notwithstanding, patients’ experience of terminal cancer and role in their own medical care rests largely on caregivers’ decisions to disclose or not.

References:

1. Good MD, Good BJ, Schaffer C, et al. American Oncology and the Discourse on Hope. *Cult Med Psychiatry*. 1990. 14:59-79.
2. American Thoracic Society: Withholding and Withdrawing Life-Sustaining Therapy. *Ann Intern Med*. 1991.115:478-484.

3. Council on Ethical and Judicial Affairs, American Medical Association: Guidelines for the Appropriate Use of Do-Not-Resuscitation Orders. *JAMA*. 1991. 265:1868-1871.
4. Ahn E, Shin DW, Choi JY et al. The Impact of Awareness of Terminal Illness on Quality of Death and Care Decision Making: A Prospective Nationwide Survey of Bereaved Family Members of Advanced Cancer Patients. *Psychooncology*. 2013. 22(12):2771-8.
5. Mo HN, Shin DW, Woo JH et al. Is Patient Autonomy a Critical Determinant of Quality of Life in Korea? End-of-Life Decision Making From the Perspective of the Patient. *Palliat Med*. 2011. 26(3):222-31.
6. Ruhnke G, Wilson S, Akamatsu T et al. Ethical Decision Making and Patient Autonomy. *Chest*. 2000.118:1172–1182.
7. Seo M, Tamura K, Shijo H, Morioka E, Ikegame C & Hirasako K. Telling the Diagnosis to Cancer Patients in Japan: Attitude and Perception of Patients, Physicians and Nurses. *Palliat Med*. 2000. 14: 105–110.
8. Han SW, Chung HY, Han SH. A Study on the Attitudes Toward Dying Patients [in Korean] *J Korean Neuropsychiat Assoc*. 1990. 29:1408–1425.
9. Yun YH, Lee CG, Kim SY et al. The Attitudes of Cancer Patients and Their Families Toward the Disclosure of Terminal Illness. *J Clin Oncol*. 2004. 22:307–314.
10. Yun YH, Kwon YC, Lee MK et al. Experiences and Attitudes of Patients with Terminal Cancer and Their Family Caregivers Toward the Disclosure of Terminal Illness. *J Clin Oncol*. 2010. 28(11):1950-7.
11. Surbone A: Truth Telling to the Patient. *JAMA*. 1992. 268:1661-1662.
12. Cheng KY, Ming T, Lai A. Can Familism Be Justified? *Bioethics*. 2011. 26(8):431-9.
13. Aabom B, Kragstrup J, Vondeling H et al. Defining Cancer Patients as Being in the Terminal Phase: Who Receives a Formal Diagnosis, and What are the Effects? *J Clin Oncol*. 2005. 23:7411–7416.
14. Wright AA, Zhang B, Ray A et al. Associations Between End-of-Life Discussions, Patient Mental Health, Medical Care Near Death, and Caregiver Bereavement Adjustment. *JAMA*. 2008. 300:1665–1673.
15. Dahlstrand H, Hauksdottir A, Valdimarsdottir U et al. Disclosure of Incurable Illness to Spouses: Do They Want to Know? A Swedish Population-Based Follow-Up Study. *J Clin Oncol*. 2008. 26:3372–3379.
16. Cherlin E, Fried T, Prigerson HG et al. Communication Between Physicians and Family Caregivers About Care at the End of Life: When Do Discussions Occur and What is Said? *J Palliat Med*. 2005. 8:1176–1185

INTERNATIONAL MEDICINE RESEARCH

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ASSESSING CLINICAL IMPROVEMENTS OF RECONSTRUCTIVE SURGERY IN PATIENTS WITH ADVANCED SPINAL DISEASE IN ETHIOPIA

Abstract:

Spinal deformities due to congenital defects and / or TB or HIV infections pose a challenging public health issue for patients in developing nations such as Ethiopia. These abnormalities can lead to decreased lung function, inability to perform physical tasks, and social stigmatization for those afflicted. Surgical procedures have been shown to be effective in improving clinical outcomes for these patients; however, a systematic analysis of patient's perceptions on surgical outcomes is lacking. In this prospective cohort study, students from the University of Rochester administered a questionnaire to 77 post-operative spine patients seen by Dr. Rick Hodes in Addis Ababa Ethiopia (36 in the summer of 2013, and 41 in the summer of 2014). Preliminary data showed that patients (average age 16.3 years \pm 2.8 years) who had a surgical spinal procedure on an average of 15.6 months (\pm 7.3 months) before enrollment reported improvement in terms of self-perception of health, ability to perform daily activities, and decreased pain interference during the day and while sleeping. This study aimed to show how, and by how much, post-operative spinal patients' lives have changed since their surgery.

Background / Introduction:

Ethiopia, Africa's second most populous country, has a disproportionately high incidence of communicable diseases due to the public health challenges faced by its predominantly impoverished population. This includes poor access to safe drinking water and proper housing, as well as poor food sanitation¹⁰. As a result, incidence rates of malaria, HIV, and tuberculosis (TB) have continued to increase over the past decade. In particular, TB has become a growing public health concern in the country, with the World Health Organization (WHO) estimating a prevalence of 210,000 (170,000 – 250,000) affected individuals and a mortality rate of 18 per 100,000 individuals in 2012¹¹.

While TB typically affects the lungs, the bacteria can also invade and inflame the intervertebral joints of cervical and upper thoracic regions of the spine. This can result in a severely crippling spinal deformity called Pott's disease, manifesting as vertebral collapse and, if

left untreated, kyphosis. While this condition occurs in approximately 1% of patients with TB, the steady rise in prevalence of TB in developing nations makes this disease a growing global health issue^{5,9}. Moreover, as one meta-analysis suggests, other causes of non-traumatic spinal cord injuries (NTSCI) disproportionately affect Ethiopians including those caused by congenital defects, HIV infection (17% of the total NTSCI's studied), tumor-related / degenerative cases (22%) and myelitis (4%)⁸.

Suggested indications for surgical intervention for patients with Pott's disease and other non-traumatic spinal cord injuries include neurological deficits due to compression of the spinal cord (present in 10-43% of patients), spine instability due to a kyphosis exceeding 40 degrees, resistance to TB drugs, and paraplegia⁹. A retrospective study investigating data from 694 patients in Turkey with Pott's disease found that decompressive surgery plus anti-TB chemotherapy remains the best mode for treatment of the disease¹². In patients with less severe cases (i.e., without neurological disorders and a kyphosis less than 30 degrees), indications for surgery are not as clear. In one retrospective study, 70 cases of adult patients with spinal TB not associated with kyphosis or neurological deficits in India were reviewed, and 69 out of 70 patients were successfully treated with conservative medical therapy alone⁷. Moreover, the literature on surgical management of Pott's disease in children is mostly limited to retrospective case studies. One retrospective study reviewed 64 pediatric patients who were treated surgically for Pott's disease found that 72% of subjects improved in grade according to the Kumar and Kalra clinical scoring system, while 28% remained constant or worsened in grade following surgery⁴. The need for prospective, observational data assessing post-surgical outcomes in both pediatric and less severe adult cases of Pott's disease is evident.

Dr. Rick Hodes, a University of Rochester alumnus, has been working in Addis Ababa, Ethiopia for the past two decades and is currently the senior consultant at a Catholic mission dedicated to treating patients with a variety of diseases, including TB-induced kyphosis. Dr. Hodes utilizes surgical interventions to treat patients with advanced forms of this disease, and the patient testimonials, as well as before and after images (see Figure 1), clearly show how this treatment has positively impacted patients' quality of life and overall daily functioning³. However, a systematic, scientific analysis of the clinical outcomes experienced by these post-operative patients is lacking.

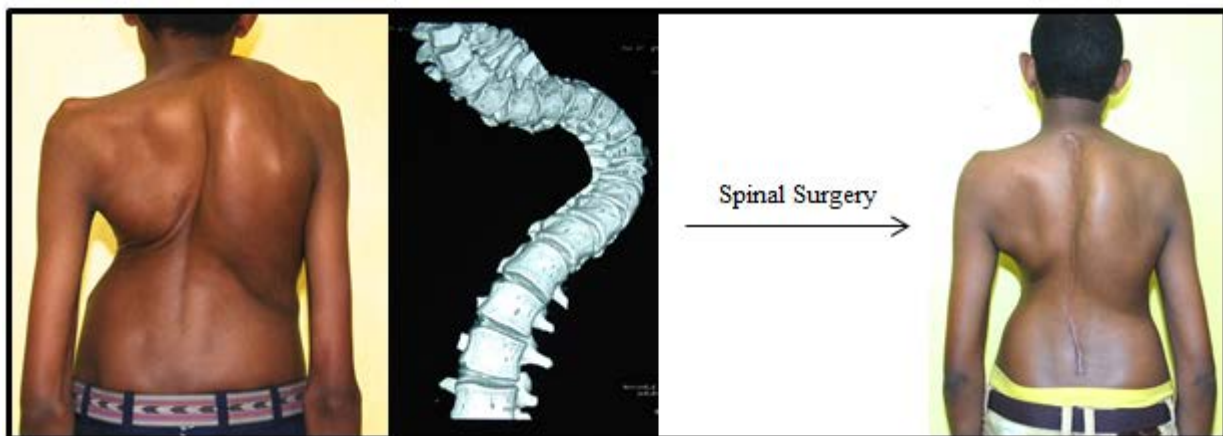


Figure 1: Typical spinal patient pre- (left two images) and post-surgery (right image)

Objectives:

The primary aim of this prospective cohort study was to quantitatively assess the clinical outcomes of reconstructive spinal surgery performed on Dr. Hodes' patients with severe spinal disease in Addis Ababa, Ethiopia, utilizing a self-administered questionnaire developed in the summer of 2012. We sought to examine how this clinical intervention affected a patient's quality of life, physical and psychosocial function, sleep hygiene, and neurological function.

Methods:

Eligible patients were identified using the clinic's database of all postoperative spine patients. Patients were ineligible if they were under 8 years old and / or had surgery less than six months ago. They were called and asked if they would be willing to return to clinic to learn about and potentially participate in the study. The study was explained and informed consent obtained before enrollment. Surveys were administered by the researchers, translated with the help of a volunteer at the clinic, and filled out individually by the subjects.

Our survey, the 'Preliminary Retrospective Questionnaire: Post-Kyphoscoliosis Corrective Surgery', was developed in 2012 and consisted of 29-items modified from the SF-36⁶ and SRS-22¹ surveys. This modified survey, which was translated into Amharic, aimed to quantitatively assess improvements in quality of life and general physical/psychological functioning of patients who have received corrective spinal surgery. The questionnaire was broken down into seven broad categories: 1) general improvements since the surgery, 2) limitations of activities, 3) effect on work or other activities, 4) pain, 5) feelings/emotions, 6) sleeping, 7) neurologic function, and a final open ended response asking the subject to 'list suggestions for improvement on your medical care.' Categories 1 through 7 utilized an ordinal scale.

Survey responses were entered into and analyzed in Microsoft Excel. Frequency distribution of subject age, gender, time since surgery, previous TB treatment, and response to questions was calculated. Scoring of modified responses to the SF-36 and SRS-22 items were performed following previously established guidelines^{1,6}.

Results:*Demographics*

During the summers of 2013 and 2014, 79 patients were enrolled into the study. Two were excluded from analysis since they were younger than 8 years old. Of the 77 eligible participants, 48% (n=37) were male with an average age of 16.9 years (SD = 3.3 years). 83% (n=64) had spinal surgical procedures performed in Ghana, Africa, 12% (n=9) had spinal surgical procedures in Ethiopia, Africa, and the remaining 1% (n=4) had surgeries in other locations (Dallas, TX or Vancouver). The average time since surgery upon study enrollment was 26 months (SD=24.7 months) and 10% (n=7) of patients had received TB treatment prior to study enrollment.

Demographic	
	<i>Mean (SD)</i>
Age	16.9 (3.3)
Time since surgery (months)	26.0 (24.7)
	<i>Percent (n)</i>
Male	48.1% (37)
Previous TB Treatment	9.9% (7)
Surgery in Ghana	83% (64)

Table 1: Participant demographics

Survey Responses

According to survey results, 77.6% of participants reported very good to excellent health, and 92% reported their health is somewhat to much better now than before surgery. Similarly, 71.4% reported a lot of change in the shape of their backbone and 100% reported somewhat to a lot of change in their backbone as compared to before surgery. The mean responses for selected questionnaire items are given in Table 1. Patients reported that their health, ability to bath and dress self, shortness of breath while performing tasks, and the amount of bullying or teasing they received due to their deformities all on average much better than before surgery and pain interference with daily activity and ability to sleep without back discomfort was somewhat better than before surgery.

Response	Mean (SD)
Self-perception of health as compared to before surgery	1.3 (0.7)
Ability to bath or dress self	1.2 (0.5)
Shortness of breath after surgery	1.4 (0.7)
Pain interference with daily activities	1.6 (0.9)
Amount of bullying/teasing experienced	1.4 (0.7)
Ability to sleep without back discomfort	1.6 (0.9)

Table 2: Mean participant response regarding change in overall health, pain, and social experiences since before surgery. Scale: 1 = Much better now than before surgery, 2 = Somewhat better now than before surgery, 3 = About the same, 4 = Somewhat worse now than before surgery

Interestingly, there was a significant decrease in shortness of breath while performing tasks ($p < .0001$) and a significant decrease in sleep interference due to back pain ($p = .0014$) compared to before surgery. While patients on average reported less bullying compared to before surgery, the change was not significant.

Conclusions:

This study provides insight into spinal patients' perceptions of their health and clinical outcomes following a spinal surgery procedure in a third-world setting. Overall, these patients have shown improvement in their health, a decrease in their physical pain, and improvements in their spinal shape. Ideally, this quantitative analysis can provide physicians and surgeons with a deeper understanding of expected clinical outcomes when treating spinal deformities with surgical therapies and shed light on patients' experiences before, during, and after their surgeries.

References

1. Asher, M., Lai, S. M., Burton, D., & Manna, B. (2003). The Reliability and Concurrent Validity of the Scoliosis Research Society-22 Patient Questionnaire for Idiopathic Scoliosis. *Spine*, 28(1), 63-69.
2. Braun, Melanie & Niebulski, Hannah (2013). *Clinical Improvement with Reconstructive Surgery in Patients with Advanced Spinal Disease in Ethiopia*. Poster presented at the University of Rochester Medical School Summer Research Poster Session, Rochester, NY.
3. Hodes, Rick. (2013). The Official Website of Dr. Rick Hodes. *rickhodes.org*. Retrieved January 5, 2013 from <http://rickhodes.org>.
4. Kumar, R., Srivastava, A. K., & Tiwari, R.K. (2011). Surgical management of Pott's disease of the spine in pediatric patients: A single surgeon's experience of 8 years in a tertiary care center. *Journal of Pediatric Neurosciences*, 6(Suppl1): S101-S108.
5. Lifeso, R. M., Weaver, P., & Harder, E. H. (1985). Tuberculous spondylitis in adults. *The Journal of bone and joint surgery. American volume*, 67(9), 1405-1413.
6. McHorney, C. A., Ware Jr, J. E., & Raczek, A. E. (1993). The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. *Medical care*, 247-263.
7. Nene, A., & Bhojraj, S. (2005). Results of nonsurgical treatment of thoracic spinal tuberculosis in adults. *The Spine Journal*, 5(1), 79-84
8. New, PW, Cripps RA, & Bonne Lee B (2014). Global maps of non-traumatic spinal cord injury epidemiology: towards a living data repository. *Spinal Cord*, 52, 97 – 109.
9. Rasouli, M. R., Mirkoochi, M., Vaccaro, A. R., Yarandi, K. K., & Rahimi-Movaghar, V. (2012). Spinal tuberculosis: diagnosis and management. *Asian spine journal*, 6(4), 294-308.
10. The U.S. Ethiopia GHI Team. (2010, December). The United States Global Health Initiative – Ethiopia Global Health Initiative Strategy. *ghi.gov*. Retrieved January 11, 2014, from <http://www.ghi.gov/whereWeWork/docs/EthiopiaStrategy.pdf>.
11. The World Health Organization. (2012, July). Key indicators for the world, WHO regions and individual countries – Annex 4. *who.int*. Retrieved January 11, 2013 from http://www.who.int/tb/publications/global_report/gtbr13_annex_4_key_indicators.pdf.
12. Turgut, M. (2001). Spinal tuberculosis (Pott's disease): its clinical presentation, surgical management, and outcome. A survey study on 694 patients. *Neurosurgical review*, 24(1), 8-13.

INTERNATIONAL MEDICINE RESEARCH

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Needs Assessment and Piloting of Adolescent Sexual Health Intervention in Yantaló, Peru

Background:

Yantaló is a small, jungle community in the San Martin region of Peru with limited access to health care and a corresponding lack of resources to address public health issues such as the high prevalence of STIs and adolescent pregnancies. Dr. Luis Vasquez founded the Yantaló Peru Foundation with the intention of increasing Yantaló's access to health care as well as catering specifically to the health needs of the community. As part of this goal, he hopes to provide sexual health education classes geared especially towards the young adult subset of the population. Research on sexual health educational interventions has shown that interventions can have behavioral impacts on participants when the interventions have clear messages that are reinforced and culturally informed. These behaviors can include delayed sexual intercourse initiation, decreased sexual risk behaviors, increased contraceptive use, and reduced incidence of STI transmission and unwanted pregnancies.

Objectives:

The objectives of our sexual health education study in Yantaló were to qualitatively assess the baseline sexual health knowledge of our adolescent target population, to establish a framework for teaching sexual health in the new clinic in Yantaló, and to pilot an easy-to-use and effective curriculum for sexual health education that would continue to be used after we left.

Methods:

We taught ten 90-minute sexual health workshops in the local secondary school, Colegio Dionisio Ocampo Chavez, to approximately 280 students. Seventy of these students between the ages of 12 and 17 were enrolled in our research study. In order to participate in the study, participants needed to have a completed permission form from their parents, to sign the assent form provided to them at the beginning of our workshop, and to complete both a pre-workshop survey and a post-workshop survey which provided us with information about the participant's demographics as well as their level of sexual health knowledge. All of the data were de-identified and each permission form,

assent form, and survey was linked with a unique participant number to allow for paired analysis and tracking of study forms. Data forms were stored in a locked room when not being used.

The sexual health workshop was composed of 10-15 minute block lessons covering topics including sexual anatomy and physiology, safe sex practices, STI information and prevention, contraceptive use, and a condom demonstration and practice activity. The first 15 minutes of each class were used to give information about the study, obtain consent, and administer the pre-survey, and the final 15 minutes were used for the post-survey and to answer anonymous questions about sexual health written on notecards distributed at the start of the class.

Results:

Quantitative results are still pending. Qualitatively, many adolescents enjoyed the use of visual diagrams and hands-on activities included in the class. They also responded with thoughtful and persistent questions during the final anonymous question-and-answer time at the end of class. In the lower grades, we were not allowed by the school to do a formal condom demonstration and we received several questions as to whether one could get diseases from using condoms, etc. Both students and teachers asked questions concerning STIs and expressed interest in further instruction on the subject.

Conclusions:

Initial analysis demonstrates the importance of teaching about sexual anatomy, sexually transmitted infections, and contraception to adolescents aged 12 to 17 in Yantalo, Peru. Older children generally demonstrated limited knowledge of these three areas despite a concrete sexual health curriculum in school. The largest deficits were seen in anatomy, while the greatest interest and the majority of anonymous questions concerned contraception and condom use. There were also significant deficits in knowledge about STIs which led to increased interest and frequency of questions both during this lesson and in the anonymous question-and-answer portion of the class.

Overall, after the workshop, students showed modest gains in knowledge based on test parameters. Barriers to the workshop's effectiveness included using a short answer test format, as well as limited time in a 1.5 hour class. In order to assess the effectiveness of this workshop, we would recommend changing the format of the surveys to be multiple choice (to achieve a higher response rate) and to change the content of the questions to see if the participants understand and have mastered the most critical learning objectives. If implemented, the alterations to protocol could ensure that comparing the pre-test and the post-test could be an evaluation method of the curriculum and format. We also recommend completing all forms of consent / assent and any IRB form tracking prior to class times.

The goal of our single class curriculum was to teach critical concepts, skills, and information about reproductive health including recognizing common signs and symptoms of STIs and how to access appropriate medical care, which types of contraceptives are effective and how to use them, and how to have consensual and safe communication in a relationship. If the course accomplished these goals, it can be used by volunteers to teach in rural schools or clinics to impart critical knowledge along with an anatomical and physiologic context while simultaneously allowing for greater access to the workshop by limiting it to a single instructional period.

References

Ilene S Speizer, Robert J Magnani, Charlotte E Colvin, The effectiveness of adolescent reproductive health interventions in developing countries: a review of the evidence, *Journal of Adolescent Health*, Volume 33, Issue 5, November 2003, Pages 324-348, ISSN 1054-139X

INTERNATIONAL MEDICINE RESEARCH

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Perceptions of Food Inequality and Community Interventions in Rural Malawi

Introduction

Food insecurity, defined as existing “when all people at all times [do not] have access to sufficient, safe, nutritious food to maintain a healthy and active life,” has been an issue for many countries in Sub-Saharan Africa (1). In Malawi, food insecurity became a serious issue in the early 2000s as the result of growing problems that had been building since the early 1980s (2). Several reasons have been proposed to explain the food insecurity problem, including farming practices, political policies, agricultural issues, and a high dependence on foreign aid (3). This food crisis has had a large effect on the overall health of the country. The country has a high infant mortality rate of 53 deaths per 1,000 births, as well as a low life expectancy at birth (54 years) (4). Additionally, Malawi also has a high adult prevalence of HIV, affecting 10.0% of the population.

In the last decade, the food insecurity problem in Malawi has gained the world’s attention and international efforts have begun to try and improve the situation. However, the implementation of these efforts has struggled greatly over the past decade. One of the many problems faced is the lack of planning and research to address the root of the issue. One study writes, “Humanitarian assistance has become the *de facto* policy of a world that is unwilling to take decisive action to address the underlying causes of global poverty...Providing humanitarian aid is at best a small part of what we should do to address the plight of the poor. It is not the solution to global poverty” (5). Studies have only recently begun looking at how to solve the actual problem of famine, both globally and specifically in Malawi. These studies have shown that the problem is not simply that governments do not have enough funds. In fact, giving funds directly to the government has been shown to be ineffective and sometimes detrimental due to government corruption and the lack of knowledge of what to do with these funds (5). Programs also often focus on interventions that are easier for aid workers, rather than providing heavier emphasis on cultural norms. Messer and Shipton write, “The question throughout Africa is not just how to ensure that Africans produce more food, but how to help ensure that people in Africa

have the means to acquire food and other necessities by their own chosen means” (6). Specifically, practices and resources that already exist in the community must be examined. As rural communities make up 80% of the population in Malawi, proper research, must involve going into these rural communities, examining the normal practices, and begin learning cultural norms within the community. Then, these normal practices should be examined in a more holistic approach, looking at the overall trends within the community. Only after this has been completed can aid workers begin implementing new strategies and practices that can become part of everyday life within the community (8). This approach will lead to a more sustainable intervention, ultimately decreasing a community’s reliance on international aid.

Objectives

We focused on the perceptions of individuals residing in the community. The purpose of this research project included three major objectives. First, we looked to identify perceptions directed towards the timeframe of food insecurity. Next, we wanted to identify available assistance currently in place among community members. Lastly, we wanted to determine perceptions of community food insecurity vs. individual household insecurity.

Methods

The survey was administered in several villages in the Ntcheu district of Malawi between June and July of 2014. Food insecurity levels and perceptions were measured based on a four-page survey. The survey was translated from English to Chichewa by a translator on site, and then back translated by a second translator to ensure consistency in wording. The first section of the survey was ten questions that asked about food insecurity perceptions at both an individual and community level. The same ten questions had been asked to the participants at two prior timeframes (January/February 2014 and June/July 2013). The second section focused on collecting qualitative information regarding an individual’s experience with food insecurity. Individuals were also asked about their food insecurity perception scores from the two previous timeframes in relation to the third collection. The third section consisted of diet diversity questions. The final section collected income and employment information for the household. Questions for the survey were developed from current research literature on the topic.

Forty households were surveyed, and were drawn from a sample of ninety individuals that had been interviewed during previous timeframes. Inclusion criteria required that the individual surveyed must be considered the head of household, and a minimum age of 18. Participants were selected based on convenience sampling, requiring that they were at home and available to sit for an interview. The survey was read orally in Chichewa by a translator, and then responses were orally translated back to English for the interviewers. Responses were hand recorded on the surveys.

Results

Results of the study are pending. Current analysis shows that individuals perceive themselves to be less food insecure than the community (based on quantitative scoring through survey questions). This has been consistent between the dry and rainy seasons. Analysis from the qualitative section of the survey indicate that a variety of factors influence participants’ responses. Common themes from the qualitative questions include ganyu (working in neighbors’ fields for food or money), planning, family, coping mechanisms, and preventative mechanisms.

Conclusion

Food insecurity is a complex problem, with a variety of contributing factors. As such, these factors must be considered when trying to define a population as food insecure. This is especially true when determining if a household is food insecure. Heads of households may state they are less food insecure than others in the community, but could still be food insecure and in need of assistance. Current and future interventions must take this into account before implementing new strategies and programs in Malawi.

References

1. *Food Security*. (2014, Jan 12). Retrieved from The World Health Organization: <http://www.who.int/trade/glossary/story028/en/>
2. Stambuli, Kalonga. "A Descriptive Analysis of the Food Crisis in Malawi". *The Society of Malawi Journal*. 55, 2 (2002), 1-30.
3. Dorward, Andrew and Kydd, Jonathan. "The Malawi 2002 food crisis: the rural development challenge". *The Journal of Modern African Studies*. 42, 3 (2004), 343-361.
4. *Malawi Statistics*. (2014, Jan 12). Retrieved from unicef: http://www.unicef.org/infobycountry/malawi_statistics.html
5. Jamieson, Dale. "Duties to the Distant: Aid, Assistance, and Intervention in the Developing World". *The Journal of Ethics*. 9, 1/2 (2005), 151-170.
6. Messer, Ellen and Shipton, Parker. *Hunger in Africa: Untangling its Human Roots*.
7. *The World Factbook: Malawi*. (2014, Jan 12). Retrieved from Central Intelligence Agency: <https://www.cia.gov/library/publications/the-world-factbook/geos/mi.html>
8. Ellis, F. "A framework for livelihood analysis". *Rural Livelihoods and Diversity in Developing Countries* (28-51). Oxford: Oxford University Press.

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Local Community Response to a National Public Smoking Ban in Ladakh, India

Introduction

While tobacco control has seen great international success as a public health measure over the last 5 decades, India is expected to lose more than 1.5 million lives per year due to tobacco (ITC Project, 2013; Ng, et al., 2014). Recently, India has actively engaged in tobacco control efforts and is considered an international leader in tobacco control policy. In 2008, the government enacted a nation-wide ban on public smoking (ITC Project, 2013). Nevertheless, the in-country diversity makes it challenging to create acceptable programs for the variety of specific, local populations. The region of Ladakh is one such population area in India.

Objectives

This project investigated a local public response to a national ban on smoking in public areas in Ladakh, a culturally diverse and geographically remote region of Northern India. This mixed methods community-based participatory research explored knowledge and attitudes, observed enforcement, and perceived harms and benefits of the ban through quantitative survey and in-depth qualitative interviews. The research is hypothesis generating rather than hypothesis testing and will be useful in informing tobacco control experts in India of the scope of reactions nationally, as well as guiding collaborating partners in Ladakh in the local enforcement and supplementation of this policy.

Background

The 2008 ban is not well known among certain sub-populations of the Ladakhi community – specifically tourists and merchants – and is inconsistently enforced (Dara et al., 2012). Other findings beyond Ladakh show “systematic heterogeneity in the attitudes and behaviors of smokers and non-smokers” regarding tobacco control policy (Poland et al., 2000). This work suggests that distinct patterns can be used to design specific interventions for different types of smokers and non-smokers, and calls for further research to investigate the heterogeneity of attitudes regarding policies and behaviors towards them. Further, these findings have significant implications and raise interesting questions about how public knowledge and attitudes may affect local implementation of a national policy, and how this affects community members. How national policies are practiced on the local level and supplemented with community-based interventions requires empiric data and calls for a community-engaged approach of investigation.

Ladakh, India lies in the mountainous northern province of Jammu and Kashmir, and was extremely isolated until the later half of the twentieth century when it saw a large increase in basic infrastructure and tourism. The rapid development of Ladakh has had major effects on

public health, including an increase in access to biomedical care, but also to harmful goods like tobacco. Ladakh's unique path of development raises interesting questions regarding how a national tobacco control policy might be played out on the local level. After rapid globalization occurred in the 1970s, a Ladakhi movement for regional political autonomy began. Some outside observers characterize this movement as a local fight against the damaging influence of Western development, while others argue that it embraces development and seeks to fight instead against the state government, which holds Ladakhi development back (Norberg-Hodge, 1991; van Beek, 2000; Chin, Dye & Lee, 2008). These complex political factors are further complicated by the Ladakhi economy's reliance on tourism. Opposing forces of globalization and local autonomy create an interesting environment to explore how national policy inspired by international sanctions (WHO FCTC, 2014) is applied on the local level.

This project explored the local perspective of the national policy in Ladakh, both to gauge its effectiveness and acceptability in the community and to contribute to literature that informs tobacco control experts in India on the scope of attitudes nationally. Data was gathered through survey and interview data using a community-engaged approach that continued the University of Rochester's collaborative partnership with the local health department and hospital. At this point in project development, this work was hypothesis generating rather than hypothesis testing, and will lay groundwork for future research in this area.

Research Design and Methodology

This research used mixed methodology combining in-depth qualitative interviewing with a brief quantitative survey to identify attitudes and awareness regarding smoking policies among people of the general Ladakh population, as well as among itinerant merchants, business owners, other community members and tourists in Leh, Ladakh. Preliminary study findings were presented at the Leh Department of Health before departure from Ladakh.

A critical component of this work was the application of principles of community-based participatory research (CBPR) to project development and implementation. CBPR is a collaborative approach that actively engages communities in a research process, utilizing the unique strengths of communities and academic institutions in the process and outcomes of research (University of Washington, 2013). It is specifically well designed to study and develop solutions to health care issues within the context of social, political and economic systems (Israel, Schulz, Parker & Becker, 2001). As a part of the application of these principles in my research, I hired a local Ladakhi college student, Punchok Namgial, as a research assistant. This gave my work a more authentic cultural context and increased research capacity in Ladakh.

Survey Protocol

The survey instrument was adapted from an existing instrument used by the International Tobacco Control (ITC) Policy Evaluation Project (ITC Project India Surveys, 2013). ITC is a partnership between international health organizations and policymakers in over 20 countries, including India, whose goal is to measure the psychosocial and behavioral effect of national level tobacco control policies (ITC Project, 2013). Survey questions used as a template are from the tool used in four states in southern India, which is specifically designed for Indian populations. Finalized questions were developed in collaboration with partners at the Leh Department of Health and Punchok Namgial, the study's hired research assistant.

A convenience sample of 52 adults were surveyed, including shop owners, restaurant managers, taxi drivers, tourists, Internet café managers, and local people in the streets of Leh.

Surveys were administered in English, the common language of tourists, businessmen, and professional Ladakhis, and responses recorded by myself with pen and paper. The hired research assistant, who is tri-lingual in English, Hindi and the local language of Ladakhi acted as a translator when necessary. Data was entered into an Excel spreadsheet on a password protected computer, and analyzed using the statistical program R.

In-depth Interviewing Protocol

10 in-depth interviews were conducted. Interviews were conducted in English when appropriate and the research assistant translated in the local Ladakhi language and Hindi when needed. Informants were recruited using purposive sampling. Interview questions explored general knowledge and attitudes, observed enforcement, and perceived benefits and harms regarding the ban, and were developed in collaboration with the Leh Department of Health and Punchok Namgial. Interviews were not recorded.

Results

Data analysis is ongoing, however some preliminary analyses have been completed.

Survey Results

60% of respondents expressed knowledge of the policy banning public smoking. Respondents' perceptions of the existence of smoking policies varied. For restaurants: 57.7% of respondents reported that smoking was banned in all indoor areas, 25.0% reported that smoking was not allowed in some indoor areas, and 3.8% reported no rules or restrictions in restaurants. Respondents answered that smoking should not be allowed in various public places: public transportation (92.3%), hospitals (90.3%), schools (88.5%), restaurants (82.7%), and restaurants (65.3%). 42.3% of respondents believed that smoking should be banned in all outdoor eating areas.

In-depth Interview Results

Many respondents expressed approval of the law and suggested that the local government should enforce the law more strictly. Most respondents expressed that enforcement of the law would help both smokers and non-smokers but few perceive direct harm from second-hand smoke.

Conclusions

The population represented by this sample shows low knowledge of the existence of this policy and reports low observed enforcement, especially in restaurants. However, respondents do express belief that smoking should be banned in many public places. In-depth interviews show that the ban does have support in the community and many respondents recommend stricter enforcement of this policy and express an attitude that the policy must be supplemented with education about the health risks of smoking. Perceptions of second-hand smoke are rare and suggest that community-based education is required to engage non-smokers in advocacy for their own health regarding the enforcement of this policy. Further analysis is ongoing.

References

- Bandura, A, 2001. Social cognitive theory: An agentic perspective. *Annual Reviews of Psychology*. 52, 1-26.
- Chin, N.P., Dye, T.D. & Lee, R.M., 2008. "Women's life narratives: Implications for child survival in Himalayan Buddhist villages". *Modern Ladakh: Continuity and change in anthropological perspective*. F. Pirie and M. van Beek, (Eds.) Leiden: Brill.
- Dara K, Caldwell E, Gewali A, Lewis C, Ullah A, Weber E, Ossip D, & Chin NP. "Tobacco moving across borders: A symbol of freedom among Ladakhi teens." Paper presentation at Society for Applied Anthropology, Baltimore, MD. March 2012
- Israel, BA, Schulz, SJ, Parker, EA, Becker, AB, 2001. Community-based participatory research: Policy recommendations promoting a partnership approach in health research. *Education for Health*, 14:2, 182-187. Retrieved from: https://depts.washington.edu/ccph/pdf_files/EducforHealthIsrael.pdf
- ITC Project, 2013. TCP India National Report. Findings from the Wave 1 Survey (2010-2011). University of Waterloo, Waterloo, Ontario, Canada; Healix-Sekhsaria Institute for Public Health, Navi Mumbai, India. Retrieved from: http://www.itcproject.org/files/ITC_IN1_Smoked_f2f_EN.pdf
- ITC Project India Surveys, 2013. *ITC Project*. Retrieved from: http://www.itcproject.org/files/ITC_IN1_Smoked_f2f_EN.pdf
- Ng M, Freeman MK, Fleming TD, Robinson M, Dwyer-Lindgren L, Thomson B, Wollum A, Sanman E, Wulf S, Lopez AD, Murray CJL, Gakidou E, 2014. Smoking Prevalence and Cigarette Consumption in 187 Countries, 1980-2012. *Journal of the American Medical Association*. 311(2):183-192. Retrieved from: 10.1001/jama.2013.284692.
- Norberg-Hodge, H, 1991. *Ancient futures: Learning from Ladakh*, San Francisco, Sierra Club Books.
- Poland, BD, Cohen, JE, Ashley, MJ, Adlaf, E, Ferrence, R, Pederson, LL, Bull, SB, & Raphael, D. Heterogeneity among smokers and non-smokers in attitudes and behavior regarding smoking and smoking restrictions. *Tobacco Control*, 9, 364-371. Retrieved from: <http://tobaccocontrol.bmj.com.ezpminer.urmc.rochester.edu/content/9/4/364.long>
- Pope, C, Ziebland, S, Mays, N, 2000. Qualitative research in health care: Analysing Qualitative data. *BMJ*, 320, 114-6.
- van Beek, M, 2000. *Lessons from Ladakh? Local responses to globalization and social change*. Schmidt JD, & Hersch (Eds.) *J. Globalization and Social Change* (250-266). London, Routledge.
- University of Washington, 2013. Community-Campus Partnerships for Health: Community-based participatory research. Retrieved from <https://depts.washington.edu/ccph/commbas.html>
- WHO FCTC, 2014. WHO Framework Convention on Tobacco Control. Retrieved from <http://www.who.int/fctc/en/>

INTERNATIONAL MEDICINE RESEARCH

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Medical, Health Sciences, and Social Work Students' Perspectives on the Health of Disadvantaged Minorities and Community Outreach in Hungary

Introduction:

Despite universal healthcare coverage in many countries of Europe, some populations are still left at the margins and excluded from this basic human right. The Roma remain the most disadvantaged and underserved minority across Europe.¹⁻³ It is estimated that 5-10 million Roma people live in Europe, with the highest concentration living in the Central Eastern Europe countries of Romania, Slovakia, Bulgaria, and Hungary.⁴ The extremely poor health outcomes of the Roma are reflective of their highly marginalized status in society. On average, Roma people have a life expectancy 10-15 years less than non-Roma people in Hungary.⁵ Roma infants in Hungary are twice as likely to be born prematurely and be underweight at birth.⁶ Forced sterilization of Roma women without informed consent is still practiced.^{1,5-7} Furthermore, rates of communicable and non-communicable diseases are significantly higher amongst the Roma than in the general population.^{1,5-7}

These health issues are further exacerbated by their lack of access to education, healthcare providers, and high unemployment rates. The Roma usually reside in very poor, segregated living conditions and face discrimination in the health care system.^{1,4,5} Their communities lack basic sanitation services, adequate housing, and access to health care services. Documented discrimination against the Roma by healthcare providers resulting in significantly lower quality of care has not improved in recent years.^{1,5-7}

In Hungary, the perspectives of medical, health sciences, and social work students regarding the Roma and other disadvantaged minorities have not been studied. Although there has been some investigation of healthcare provider attitudes towards the Roma, there has been no such study of this within the medical student and social work student population. The student participation and/or interest in working with disadvantaged populations is also understudied. These groups of students have a great opportunity and capability to affect change in the outreach to the Roma population and other underserved groups. Medical student-run clinics in the United States have already been successful at providing quality healthcare to underserved and disadvantaged populations.⁸⁻¹⁰ This model may also be applicable to another context.

Furthermore, as shortage of physicians in primary care worsens, the need for students who understand health disparities and how to address them in practice is also paramount. These circumstances lend themselves to an excellent opportunity to examine the perspectives of medical students and social work students in Hungary regarding the health of disadvantaged minorities and community outreach.

Objectives and Hypothesis:

This study aims to quantitatively and qualitatively explore the perspectives of medical student and social work students with regards to the health of disadvantaged minorities and community outreach in Hungary. The research questions that we would like to address are: 1) What is the knowledge of medical and social work students on the health disparities of disadvantaged minorities, specifically the Roma, in Hungary? 2) What is the students' participation and involvement in community outreach with disadvantaged minorities? 3) What do students propose as solutions to the healthcare disparities faced by the Roma and other minorities?

We anticipate that the social work students will have had greater contact and experience with disadvantaged minorities, and thus have a better understanding of the health care issues that these populations face and a greater involvement in community outreach with the Roma and other minorities. We also hypothesize that medical students will suggest different solutions than social work students to remedy the healthcare disparities faced by minorities. We believe that medical students will have had less training in sociological factors of health, and thus be less aware of the magnitude of the effect that they have on the health of a population. Therefore, they may be more likely to emphasize genetic or biological factors of disease and respective treatment. On the other hand, we believe social work students will emphasize the social determinants of health and measures to improve these conditions as a means to better health for minorities.

Methods:

This multi-method approach used surveys and focus group interviews to collect data. The site of the study was the University of Szeged Faculty of Medicine in the Great Southern Plain of Hungary. The subjects of the study were students in their final 3 years of schooling from the Faculty of Health Sciences and Social Studies (in the Social Work program) and from the Faculty of Medicine. The survey was translated by Edit Paulik, M.D., Ph.D. and Andrea Szabo, Ph.D., DrPharm. In addition to approval by the RSRB, the survey was approved by the University of Szeged Ethical Approval Committee. After explanation of the purpose of the survey, paper copies of surveys were distributed to students at the end of the semester and their participation was completely voluntary. Completed and uncompleted surveys were returned to investigators in envelopes. If students were interested in participating in the focus group interview, they were asked to leave contact information on a separate page from the survey.

The focus group interviews were organized with a small number of students who and two investigators. After explaining the purpose of the interview and receiving verbal consent, the interviews were audio recorded. Discussion in the focus group interview revolved around expanding upon topics that were elucidated in the survey. The focus groups will be organized and conducted in accordance with methodology outlined by McLafferty¹⁸ and Kitzinger¹⁹ in their respective analyses of focus group methodology.

Results:

A total of 143 surveys were collected from students of the University of Szeged. Of the respondents, 67% were between the ages of 22-24 (inclusive). The majority of respondents (68%) were female. There were 91 medical students, 31 health sciences students, 18 social work students, and 3 nursing students who completed the survey. Almost all students surveyed were in their 4th year of study (94%) and 67% were Hungarian. A total of 14 students were interviewed for the focus groups interviews.

The results are divided into three sections, corresponding to the three main research questions of this study.

1) What is the knowledge of medical and social work students on the health disparities of disadvantaged minorities, specifically the Roma, in Hungary?

A large majority (75% of respondents) ranked the Roma people as having the worst health outcomes. However, only about half of respondents (51%) indicated that they believed access to healthcare was equal for all people in Hungary. Regarding life expectancy, 80% of respondents indicated that they did not believe life expectancies at birth are the same for all groups of people in Hungary. The majority (67%) of respondents believed that a healthy lifestyle was the most important factor affecting health outcomes, followed by not smoking or drinking alcohol (10%), having a healthy family history and living in a safe neighborhood (both 7%). Only 18% of respondents believed that access to healthcare was the most important factor in disease outcomes for the Roma people.

2) What is the students' participation and involvement in community outreach with disadvantaged minorities?

The majority of students (66%) believed that there were volunteer opportunities at the University, but 41% of respondents believed that there were few opportunities. Despite these opportunities, 85% of students reported never participating in volunteer activities. Furthermore, 69% of students believed that students should be more involved. When asked if they would be interested in volunteering if there were more organized volunteer opportunities, only 9% said they would be very interested and 61% said they would be somewhat interested. When asked about how effective they believed community outreach to be in affecting change, 20% responded very effective and 64% responded somewhat effective. However, 50% of respondents said that addressing healthcare disparities is very important.

3) What do students propose as solutions to the healthcare disparities faced by the Roma and other minorities?

When asked which governing body or community organization should be held most responsible for addressing healthcare disparities, 56% reported the national government, 1% reported community organizations, and 27% reported the healthcare system. However, 57% of students believed that the community organizations were the ones doing the most to address healthcare disparities. About 73% of respondents believed that students should be very responsible or somewhat responsible for addressing healthcare disparities in Hungary. Students seemed to largely believe that good health outcomes are mostly due to positive lifestyle factors, rather than access to healthcare.

The results of the interviews largely supported the results garnered from the surveys. Further statistical analyses of the data are pending.

Conclusions:

Students recognized the marginalized status of the Roma people and understood that they suffered more from poor health outcomes than the rest of the population in Hungary. However, it was not clear whether students believed that the Roma people had equal access to healthcare as the rest of the population. From the interviews, there was a lot of discussion surrounding the universal healthcare system of Hungary. After some talk, students seemed to discover some pitfalls of the system, by which the Roma people get lost in the system.

Respondents reported that there did exist some volunteer opportunities for students at the University of Szeged. In the interviews, many students expressed the belief that these opportunities were scarce and ambiguous. Volunteer participation was very low amongst the respondents, but they expressed some interest in participating in volunteer work if there were more organized and interesting volunteer experiences. Students reported the biggest barrier to participation was time. Students didn't want to work for free when they already had a lot to worry about with academic responsibilities. There was the

understanding amongst many students that addressing healthcare disparities is important, and that community outreach is fairly effective at improving these problems.

Students believed that the national government and the healthcare system should be most responsible for addressing the issues that the Roma people and other minorities in Hungary face. Only 2 respondents said that community organizations should be responsible, yet 57% believed that community organizations were doing the most, presenting some ambiguity here. Students placed a lot of responsibility on outside organizations, which might explain the low participation rate in volunteer work and the low motivation to participate in volunteer work.

At the University of Szeged, the students surveyed demonstrated a strong knowledge of the health disparities that the Roma people face. However, this knowledge didn't always correlate with the principle causes responsible for these differences in health outcomes. Students also expressed interest in participating in volunteer work, but cited several barriers to participation, mainly the lack of interesting and organized activities and the lack of time. Students believed that the government and healthcare system should be the most responsible for addressing the differences in health outcomes for the Roma people and other minorities, but did not place themselves as students responsible for this.

References:

1. Ambulance Not On The Way: The Disgrace of Healthcare for Roma in Europe. Budapest, Hungary: European Roma Rights Centre; 2006.
2. Timmer AD. Dealing with Difference: Hungarian Civil Sector Efforts to Aid the Roma. *Anthropology of East Europe Review*;26:73-81.
3. Fesus G, Ostlin P, McKee M, Adany R. Policies to improve the health and well-being of Roma people: The European experience. *Health Policy* 2012;105:25-32.
4. Kosa Z, Szeles G, Kardos L, et al. A Comparative Health Survey of the Inhabitants of Roma Settlements in Hungary. *American Journal of Public Health*;97:853-9.
5. Puporka L, Zadori Z. The Health Status of Romas in Hungary. Budapest: The World Bank Regional Office Hungary; 1999.
6. Hajioff S, McKee M. The health of the Roma people: a review of the published literature. *Journal of Epidemiology and Community Health* 2000;54:864-9.
7. Parekh N, Rose T. Health inequalities of the Roma in Europe: A literature review. *Central Europe Journal of Public Health* 2011;19:139-42.
8. Simpson SA, Long JA. Medical Student-Run Health Clinics: important Contributors to Patient Care and Medical Education. *Journal of General Internal Medicine* 2007;22:352-6.
9. Dehaven M, Gimpel N, Dallo F, Billmeier T. Reaching the underserved through community-based participatory research and service learning: description and evaluation of a unique medical student training program. *Journal of Public Health Management and Practice* 2011;17:363-8.
10. Holmqvist M, Courtney C, Meili R, Dick A. Student-Run Clinics: Opportunities for Interprofessional Education and Increasing Social Accountability. *Journal of Research in Interprofessional Practice and Education* 2012;2:264-77.
11. Ellett J, Campbell J, Consalves W. Patient satisfaction in a student-run free medical clinic. *Family Medicine* 2010;42:16-8.
12. Meah Y, Smith E, Thomas D. Student-run health clinic: novel arena to educate medical students on systems-based practice. *Mt Sinai J Med* 2009;76:344-56.
13. Meili R, Fuller D, Lydiate J. Teaching social accountability by making the links: Qualitative evaluation of student experiences in a service-learning project. *Medical Teacher* 2010;32:1-8.
14. Kosa K, Darago L, Adany R. Environmental survey of segregated habitats of Roma in Hungary: a way to be empowering and reliable in minority research. *European Journal of Public Health* 2009;21:463-8.

15. Masseria C, Mladovsky P, Hernandez-Quevedo C. The socio-economic determinants of the health status of Roma in comparison with non-Roma in Bulgaria, Hungary and Romania. *European Journal of Public Health* 2010;20:549-54.
16. Girasek E, Molnar R, Eke E, Szocska M. The medical career choice motivations: Results from a Hungarian study. *Central European Journal of Medicine* 2011;6:502-209.
17. National Roma Integration Strategies: What Next? *Journal of the European Roma Rights Centre* 2013.
18. McLafferty I. Focus group interviews as a data collecting strategy. *Journal of Advanced Nursing* 2004;48:187-94.
19. Kitzinger J. Qualitative Research: Introducing Focus Groups. *British Medical Journal* 1995;311:299-302.

YEAR-OUT RESEARCH

Marguerite Maguire

Objectives: Many women who receive a diagnosis of fetal anomaly in the second trimester choose to terminate. Grief over termination for fetal anomaly has been shown to be severe however, little is known about how women define and experience this grief over time.

Study Design: From March 2012 to October 2013, we conducted qualitative phone interviews of 17 women from UCSF and University of Michigan at 1-3 weeks, 3 months and 1 year after second-trimester termination for fetal anomaly. All women chose their method (D&E or induction). We used a generative thematic approach to analyze the transcripts using NVivo software program.

Results: Seventeen participants completed at least one interview. All women reported grief at their initial interview but moved to coping throughout the year. Themes throughout the interviews include self-blame, guilt, social isolation, and grief triggered by reminders of pregnancy. We observed no difference in grieving based on method.

Conclusions: Pregnancy termination in the second trimester for fetal anomaly represents a loss similar to miscarriage or death of a loved one. However, this type of pregnancy loss is unique in that certain aspects of grief are related to participants' active role in the decision to end the pregnancy. Unlike grief after miscarriage, grief after pregnancy termination is associated with real and perceived stigma around terminating a pregnancy. This stigma is associated with feelings of self-blame, guilt and social isolation, which have been shown to compound the grieving process.

YEAR-OUT RESEARCH

Tyrrell, Jamie

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Teaching Theatre and Medicine

Abstract: Doctors, patients, and diseases have been the subject of a number of popular, famous, and infamous plays and television shows. The representations of the practitioners, the medical scientists, the patients, the sickness, the treatments, and the ethical dilemmas in these stories reflect the historical moment and the cultural perceptions (and misperceptions?), expectations, and anxieties about the medical profession. By teaching medical students to appreciate the ability of theatre and television to both reflect and influence public perception, they will be to recognizing the impact of dramatic portrayals of medicine on their patients' expectations of a medical experience.

Objectives: To provide an overview of theatrical representations of doctors and medical experiences and an understanding of the historic context in which the plays were written. To provide medical students with a context for assessing dramatic representations of doctors and medical experiences in contemporary media.

Methods: The "Playing Doctor from Shakespeare to Scrubs" medical humanities seminar exposed second-year medical students to medically-themed theatrical texts from the sixteenth through twenty-first centuries. Students presented dramatic readings from plays such as *All's Well That Ends Well* by William Shakespeare, *The Doctor's Dilemma* by George Bernard Shaw, *Angels in America* by Tony Kushner, and *Wit* by Margaret Edson. Students presented excerpts from television and film portrayals of medicine and facilitated discussions about the historical context and medical themes.

YEAR-OUT RESEARCH

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Toxicity Study of anti-VEGF Treatments for Macular Degeneration

Abstract:

Age-related macular degeneration (AMD) is the leading cause of blindness in developed countries, affecting about 2% of Americans⁹. Current treatment includes intraocular injections of ranibizumab (Lucentis, Genentech), aflibercept (VEGF Trap-Eye, Regeneron), and bevacizumab (Avastin, Genentech). Ranibizumab was the first of the three to be FDA approved and was shown to be safe and superior to previous treatments in 2005 clinical trials^{2,10}. Later, aflibercept was found to be of similar effectiveness and safety as ranibizumab in 2012 RCTs^{4,16}. Avastin, FDA approved to treat colon cancer, has been used off label for intraocular use since 2005 but does not have similarly large clinical trials as Lucentis and VEGF Trap-Eye to support its safe intraocular use, though a large retrospective study³ and an RCT⁵ showed bevacizumab to be no more harmful than ranibizumab. Some *in vitro* studies have found no differences between the three treatments on cell morphology, viability, or cell death in a variety of cornea and retinal cell lines^{1,7,8,13,15,18}. However, for unknown reasons, other studies have demonstrated a cytotoxic effect of bevacizumab on retinal pigment epithelial cells, choroidal endothelial cells, fibroblasts, and trabecular meshwork^{6,10} while ranibizumab had no adverse affects on the same cell lines^{12,15}.

Objectives: To determine *in vitro* cytotoxicity of bevacizumab, ranibizumab, and aflibercept on ARPE-19 cells.

Methods: Cellular toxicity was assessed through cell viability (MTT), proliferation (BrdU), permeability (TER), apoptosis (TUNEL), and intracellular accumulation (Cy3 conjugation).

Results: Bevacizumab inhibited cellular proliferation in BrdU studies, and along with aflibercept accumulated intracellularly 1.5 fold compared to control. No differences were found in MTT, TER, or TUNEL assays between the three treatments.

Conclusions: Bevacizumab may inhibit RPE cell proliferation, possibly related to its intracellular accumulation. Although aflibercept was found to accumulate as well, no adverse affects on RPE cells were observed. Though no direct correlation can be made with clinical safety, this data shows that future work on anti-VEGF toxicity should continue with these relatively new drugs.

References

1. Brar VS1, Sharma RK, Murthy RK, Chalam KV. Mol Vis. 2010 Sep 12;16:1848-53. Bevacizumab neutralizes the protective effect of vascular endothelial growth factor on retinal ganglion cells.
2. Brown DM, Kaiser PK, Michels M, et al. Ranibizumab versus verteporfin for neovascular age-related macular degeneration. N Engl J Med 2006;355:1432-1444
3. Curtis et al. Risks of mortality, myocardial infarction, bleeding, and stroke associated with therapies for age-related macular degeneration. Arch Ophthalmol. 2010 Oct;128(10):1273-9. doi: 10.1001/archophthalmol.2010.223.
4. Heier et al. Intravitreal aflibercept (VEGF trap-eye) in wet age-related macular degeneration. Ophthalmology. 2012 Dec;119(12):2537-48. doi: 10.1016/j.optha.2012.09.006. Epub 2012 Oct 17.
5. IVAN Study Investigators. Ranibizumab versus bevacizumab to treat neovascular age-related macular degeneration: one-year findings from the IVAN randomized trial. Ophthalmology. 2012 Jul;119(7):1399-411. doi: 10.1016/j.optha.2012.04.015. Epub 2012 May 11.
6. Kernt. Bevacizumab is not toxic to human anterior- and posterior-segment cultured cells. Ophthalmologie. 2007 Nov;104(11):965-71.
7. Klettner et al. Different properties of VEGF-antagonists: Bevacizumab but not Ranibizumab accumulates in RPE cells. Graefes Arch Clin Exp Ophthalmol. 2009 Dec;247(12):1601-8. doi: 10.1007/s00417-009-1136-0. Epub 2009 Jul 14.
8. Luthra et al. Retina. Evaluation of in vitro effects of bevacizumab (Avastin) on retinal pigment epithelial, neurosensory retinal, and microvascular endothelial cells. 2006 May-Jun;26(5):512-8.
9. National Eye Institute . <https://www.nei.nih.gov/eyedata/amd.asp#1>. Accessed Sept 5, 2014.
10. O'Neill et al. Antifibrotic Activity of Bevacizumab on Human Tenon's Fibroblasts In Vitro. Invest. Ophthalmol. Vis. Sci. December 2010 vol. 51 no. 12 6524-6532
11. Rosenfeld PJ, Brown DM, Heier JS, et al. Ranibizumab for neovascular age-related macular degeneration. N Engl J Med 2006;355:1419-1431
12. Rusovici et al. Evaluation of cytotoxicity of bevacizumab on VEGF-enriched corneal endothelial cells. Mol Vis. 2011;17:3339-46. Epub 2011 Dec 20.
13. Schnichels et al. Comparative toxicity and proliferation testing of aflibercept, bevacizumab and ranibizuman on different ocular cells. Br J Ophthalmol. 2013 Jul;97(7):917-23. doi: 10.1136/bjophthalmol-2013-303130. Epub 2013 May 17.
14. Spitzer et al. Antiproliferative and cytotoxic properties of bevacizumab on different ocular cells. Br J Ophthalmol. 2006 Oct;90(10):1316-21. Epub 2006 May 24.
15. Spitzer et al. Graefes Arch Clin Exp Ophthalmol. Comparative antiproliferative and cytotoxic profile of bevacizumab (Avastin), pegaptanib (Macugen) and ranibizumab (Lucentis) on different ocular cells. 2007 Dec;245(12):1837-42. Epub 2007 Mar 9.
16. Stewart et al. Clinical and differential utility of VEGF inhibitors in wet age-related macular degeneration: focus on aflibercept. Clin Ophthalmol. 2012;6:1175-86. doi: 10.2147/OPHTH.S33372. Epub 2012 Jul 26.
17. The CATT Research Group. Ranibizumab and Bevacizumab for Neovascular Age-Related Macular Degeneration N Engl J Med 2011; 364:1897-1908 May 19, 2011 DOI: 10.1056/NEJMoa1102673
18. Yoeruek et al. Safety profile of bevacizumab on cultured human corneal cells. Cornea. 2007 Sep;26(8):977-82.

YEAR-OUT RESEARCH

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The Affect of Late Infection and Antibiotic Treatment on Capsular Contracture in Silicone Breast Implants: A Rat Model

Objective

Despite strides being made in current research to combat capsular contracture via disruption of biofilms and reduced contamination at the time of implant,^{1,2,3} capsular contracture continues to occur months to years after implantation with no sign of these early complications.^{4,5} Up until this point, no research has been carried out to attempt to identify a link between a remote infection established well after implantation, the hematogenous spread of bacteria to a capsule, and capsular contracture, leaving a gap in clinical guidelines for the treatment of breast implant patients. This experiment is the first to assess whether late infections increase the incidence of capsular contracture and if treatment of these infections can reverse this effect in an in vivo rat model.

Methods

Three groups of female Wistar rats (n=42) received two silicone implants in separate dorsal, subcutaneous pockets. All groups except control underwent injection of a human strain of Methicillin-sensitive *Staphylococcus aureus* (MSSA) at least 30 days after implantation, allowing for physiologic capsule formation. The infection group received a peritoneal injection, inducing a transient bacteremia, the treated group received a course of antibiotics following bacterial inoculation, and a final group received no intervention and served as control.

Results

Implants were removed 4 months after insertion with capsules measured for thickness and sent for bacterial quantification. Compared to both the control and treated groups, capsule thickness in the infection group was statistically greater ($p < 0.05$), a difference not observed between treated and control groups. Additionally, a statistically significant positive correlation was found between capsule thickness and bacterial count ($R=0.614$, $p<0.01$).

Conclusions

The difference in thickness between the control capsules and those from the infection group is an indication that bacterial contamination of a capsule from a late infection may increase the incidence of capsular contracture and suggests that treating these late infections could in fact prevent this complication.

References

1. Steiert AE, Boyce M, Sorg H. Capsular contracture by silicone breast implants: possible causes, biocompatibility, and prophylactic strategies. *Medical Devices: Evidence and Research*. 2013;6:211-218.
2. Schreml S, Heine N, Eisenmann-Klein M, Prantl L. Bacterial colonization is of major relevance for high-grade capsular contracture after augmentation mammoplasty. *Ann Plast Surg*. 2007;59:126–130.
3. Jacombs A, Allan J, Hu H, et al. Prevention of Biofilm-Induced Capsular Contracture with Antibiotic-Impregnated Mesh in a Porcine Model. *Aesthetic Surgery Journal*. 2012;32:886-891.
4. Hunter JG, Padilla M, Cooper-Vastola S. Late *Clostridium perfringens* breast implant infection after dental treatment. *Ann Plast Surg*. 1996;36:309–312.
5. Chang J, Lee GW. Late Hematogenous Bacterial Infections of Breast Implants: Two Case Reports of Unique Bacterial Infections. *Ann Plast Surg*. 2001;67:14-16.

YEAR-OUT RESEARCH

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Human Vection Perception Using Inertial Nulling and Certainty Estimation

Abstract: When an object is moved in visual space there are two possible perceptions: 1) the viewer perceives external object motion or 2) the viewer perceives self-motion (vection). The latter occurs if the object motion involves a significant portion of the visual field. Individuals with visual motion sensitivity disorders such as migraine may be especially susceptible to vection. We aimed to expand the current understanding of vection by examining the effect of visual field movement (VFM) duration on the perception of subsequent self-motion. We hypothesized that longer duration VFM would produce greater vection and would thus require greater vestibular stimulation to null the perception of self-motion. To test this, we examined how VFM influenced threshold and bias. We also collected subject-reported estimations of vection, and hypothesized that longer duration VFM would be perceived as stronger. The relationship of migraine and vection was examined. We recruited 12 healthy adult subjects and examined for history of migraine. Subjects sat on a motion platform. A visual star-field stimulus was presented for varying durations and fore-aft platform motion occurred in the final 1 s of the visual stimulus. Subjects reported the perceived direction of platform motion using a pushbutton device. The magnitude of platform motion was varied across trials in a staircase manner to determine the point of subjective equality (PSE). We calculated the peak velocity of the platform motion stimulus at the PSE as a measurement of bias, and examined relationship of PSE and VFM duration. In a separate trial using identical visual stimuli but no platform motion stimulus, subjects reported certainty and direction of perceived self-motion. The relationship of certainty estimation (CE) and VFM duration was examined. Increased VFM duration significantly increased PSE ($p = .007$) and CE ($p < .0001$). The net effect of direction was not significant in either condition. Diagnosis of migraine significantly increased perception of self-motion by CE ($p = .01$) but not PSE. These results suggest that vection is increased by longer duration visual stimuli, and that history of migraine plays a significant role in self-motion perception.

Objectives: This project aims to expand our current understanding of vection by quantifying it using actual motion and comparing this value to subjects' subjective estimations of vection strength. Individuals with motion sensitivity disorders and other vestibular disorders, such as migraine, may be especially susceptible to migraine. If this is the case, the accurate measurement of vection may serve as part of a diagnostic test for vestibular disorders.

Methods: Twelve healthy individuals (7M, 5F) aged 19 to 67 (mean 39.25 ± 18.32) were recruited. In Part One of the experiment, motion stimuli were delivered in complete darkness using a 6-degree of freedom Hexapod Motion Platform (HMP) coupled to the visual display. Subjects were secured in place with the head anchored. A visual stimulus consistent with moving through a star field was presented at a constant velocity of ± 20 cm/s for 0 (no visual stimulus), 1, 2, 4, or 8 seconds. Platform motion in the forwards or backwards direction occurred in the final 1s of the visual stimulus. Subjects reported perceived direction using a pushbutton device. The magnitude of platform motion was varied in a staircase manner. Peak platform velocity at the PSE was determined. In Part Two of the experiment, identical visual stimuli to those previously described were delivered with no motion stimulus. Subjects reported the perceived direction and magnitude of self-motion on a scale of 0 (none) to 100 (very compelling).

Results: Increased visual stimulus duration significantly increased vection by our two methods of measurement, PSE ($p = .007$) and CE ($p < .0001$). The diagnosis of migraine was significantly increased by measurement of vection by CE ($p = .01$) but not PSE.

Conclusions: These results suggest that vection is increased by longer duration visual stimuli, and that history of migraine plays a significant role in self-motion perception.