SCHOOL OF MEDICINE & DENTISTRY
UNIVERSITY of ROCHESTER MEDICAL CENTER

Medicine of the Highest Order

2015

Annual Medical Student Abstract Journal

Sponsored by:

Center for Advocacy, Community Health, Education and Diversity

Offices for Medical Education

Medical Student Research Faculty Advisory Committee

Community Outreach Faculty Advisory Committee

International Medicine Faculty Advisory Committee

Medical Humanities Faculty Advisory Committee

Aaserude, Eric & Hong, Steven

Preceptor: Beau Abar, Ph.D.
University of Rochester School of Medicine and Dentistry
Department of Emergency Medicine

Access to care and depression among emergency department patients

Introduction:

Major depressive disorder is a serious, common public health concern that is characterized by a series of symptoms including depressed mood and diminished interest or pleasure in most activities of the day (DSM-V). The prevalence of depression during a lifetime is 16.2% and the 12-month prevalence is 6.6%. [1] In particular, several studies have shown that among patients in the Emergency Department (ED), the prevalence of depression is even higher than in the general population.[2-3] One study showed that the prevalence of a positive depression screen is approximately 33%, and using a 33% positive predictive value, an estimated 10.5% would met the diagnostic criteria for major depressive disorder.[2] Because of the high concentration of patients with depression, the ED may serve as an important forum for the identification of depression and the intervention in the disease process.[4]

Concomitant to identification of potential concerns regarding depression is the issue of patient access to appropriate care. Many patients lack the ability to affordably receive efficacious treatment due to insurance-related barriers.[5] Furthermore, other individuals may be unaware of their level of access for primary and behavioral health services, and this lack of awareness will lead to patients in need not receiving the care appropriate to their concerns. Finally, other individuals may have insurance coverage and be aware of their access to care, but not know who they should contact to initiate treatment. This study will seek to establish prevalence estimates regarding these kinds of potential barriers to care, and will relate these problematic situations with patient demographic characteristics and symptoms of depression.

Objective:

The primary purpose of this study is to examine the extent to which patients in the emergency department perceive their access to primary and behavioral health care. We will also seek to relate this perceived access to self-reported symptoms of depression as a way to demonstrate unmet behavioral health needs. Finally, we will examine potential differences in perceived access to care across age groups: 18-26 years (i.e., insurance coverage potentially provided through parents), 27-64 (i.e., insurance coverage likely the responsibility of the patient), and 65+ (i.e., Medicare coverage eligible).

Methods:

Two medical students (Steven Hong, Eric Aaserude) stationed in the SMH ED conducted brief surveys on all patients 18 years or older that presented to the ED and who demonstrated decisional capacity. Representatives of the Emergency Department Research Associates program approached patients, introduced the study, and asked if they would be willing to speak with the medical student representatives of the study. The medical students would assess the subject's decisional capacity during the process of consent using standardized procedures employed in previous screening protocols in the emergency department. Following obtaining consent, the medical students would conduct a brief questionnaire which included demographic characteristics, questions on access to care, and a PHQ-9 depression screening tool. Subjects' responses were recorded directly into REDCap by the medical students using a tablet computer. Subjects were advised during the consent process that they had the right to withdraw from the study at any time without prejudice. If a participant reported severe depression (PHQ-9 scores greater than 20) and/or current thoughts of self-harm (Yes to item 9a on the PHQ-9), the medical students reported these levels to the physician providing care to the participant.

Results:

A total of 637 subjects were enrolled in the study and completed the brief survey over the course of the summer. The percentage of patients in the emergency department presenting with mild depression or greater was 42%, which is consistent with previously recorded incidence of depression in emergency department patients[2] (Table 1). Access to care metrics were reported on a scale of 1-5. The majority of patients reported experiencing some barriers to care (mean=1.32, SD=0.42), with the most prominent barriers being difficulty finding transportation (mean=1.44, SD=1.02), work responsibilities (mean=1.47, SD=0.99), and the feeling that the doctor is not responsive to patients' concerns (mean=1.41, SD=0.93) (Table 1).

Table 1: Descriptive statistics of study participants

	M (SD)	Frequency (%) [a]
PHQ-9 Score	5.30 (5.47)	
No depression (0)		103 (17%)
Minimal depression (1-4)		252 (41%)
Mild depression (5-9)		150 (24%)
Moderate depression (10-14)		59 (10%)
Moderately severe depression (15-19)		35 (6%)
Severe depression (20-27)		15 (2%)
Access to Care Mean Score	1.32 (0.42)	
Barrier: taking care of others	1.35 (0.91)	
Barrier: lack of insurance	1.33 (0.94)	
Barrier: difficulty finding transportation	1.44 (1.02)	
Barrier: doctor, clinic, or hospital bills	1.30 (0.84)	
Barrier: work responsibilities	1.47 (0.99)	
Barrier: fear that the doctor will discover a serious illness	1.26 (0.78)	
Barrier: your feeling that the doctor is not responsive to your concerns	1.41 (0.93)	
Barrier: has embarrassment about a potential illness	1.15 (0.59)	
Barrier: confusion trying to schedule an appointment	1.20 (0.61)	

Bivariate correlations suggested multiple correlations between increasing PHQ-9 score and access the healthcare. Higher PHQ-9 scores were associated with higher access to care mean scores, less access to doctors or doctor's assistants as well as providers to contact for depression, suggesting that the greater the barriers to care present the higher the levels of depression. In addition, patients that reported longer wait times to see a physician also reported greater barriers to care. The pattern of correlations seems to hold when eliminating the least or most depressed individuals, which strengthens the case made considerably (Table 2).

Table 2. *Bivariate correlations*

	1	2	3	4	5
1. PHQ-9 Score	1	0.44***	-0.09*	-0.10*	0.08
2. Access to Care Mean Score		1	-0.16***	-0.17***	0.16***
3. Doctor/Doctor's Assistant (0 = No, 1 = Yes)			1	0.38***	0.02
4. Provider to contact for depression (0 = No, 1 = Yes)				1	-0.10*
5. Normal time to be seen by a provider					1

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.00$

Bivariate spearman correlations were also calculated with respect to PHQ-9 score and specific barriers to care and provided further evidence for positive correlation. Particularly strong correlations were observed between PHQ-9 score and difficulty finding transportation (PHQ-9 score=0.30), the feeling that the doctor is not responsive to patients' concerns (PHQ-9 score=0.29), embarrassment about a potential illness (PHQ-9 score=0.28) and confusion trying to schedule an appointment (PHQ-9 score=0.29).

Discussion:

While there have been great strides in the development of effective pharmacologic and psychotherapy treatment for depression, the question still remains of how to eliminate the barriers blocking patients from accessing the resources available to them. The data here provides additional evidence showing the heightened prevalence of depression in the Emergency Department setting and initial evidence demonstrating the association between a greater prevalence of depression and perceived barriers to mental and primary health care. Across all barriers analyzed, there was a greater incidence of depression associated with a greater perception of barriers. Depression was particularly highly correlated with the following specific barriers: difficulty finding transportation, feeling that the doctor is not responsive to your concerns, embarrassment about a potential illness, and confusion trying to schedule an appointment. These barriers may be used as potential targets for intervention to increase access to health care resources. Continued analysis is currently being done to analyze the influence of age and varying severities of depression on the perception of barriers.

References

1. Kessler R.C. et al. (2003). The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). *JAMA, 289,* 3095-3105.
2. Boudreaux E.D. et al. (2008). Mood disorder screening among adult emergency department patients: a multicenter study of prevalence, associations and interest in treatment. *General Hospital Psychiatry, 30,* 4-13.
3. Kumar A. et al. (2004). A Multicenter Study of Depression among Emergency Department Patients. *Academy of Emergency Medicine, 11,* 1284-1289.
4. Kowalenko T. & Khare R.K. (2004). Should we screen for depression in the emergency department? *Academy of Emergency Medicine*, *11,* 177-178.
5. Shi, L. & Singh, D.A. (2015). *Delivering Health Care in America: A Systems Approach*. Jones & Bartlett Learning: Burlington, MA.

Asad Arastu

Preceptor(s) Name: Dr. Ricardo Basurto-Davila
Title: Health Economist
Institution: Los Angeles Department of Public Health
Department: Office of Health Assessment and Epidemiology

Utilizing a Health and Economic Perspective to Evaluate Hepatitis C Treatment Policies in Los Angeles County

Objective:
The aim of this study is to evaluate the health and economic effects of the Los Angeles County (LAC) Department of Health Service (DHS) HCV Initiative. Study tasks included meetings with relevant stakeholders, gathering data, and the development of a preliminary mathematical model to better understand the clinical and cost effectiveness of a 24-week treatment and follow-up plan for genotype-1 Hepatitis C virus (HCV) infections using direct-acting antiviral (DAA) medications at DHS sites in LAC.

Background:
With over 16,627 deaths attributed to HCV in the United States in 2010, a 75% increase in reported cases of acute HCV between 2010 and 2012, and nearly 4.1 million infected with the virus in the United States, HCV has become a serious public health concern. [1,2] HCV is a contagious liver disease caused by a viral infection and spread via blood of an infected individual. Whilst there are vaccinations to prevent Hepatitis A and Hepatitis B, no such vaccination exists for HCV, but it can be treated with medication. Infections may be asymptomatic, but it is common for the acute infection to progress to the chronic state. In the most severe cases, HCV results in cirrhosis and/ or liver cancer. [3]

A recent Centers for Disease Control and Prevention (CDC) update recommends that all adults born between 1945 and 1965 (baby boomers) be tested for HCV at least one time, regardless of risk factors present. More than 75% of infected adults are from this cohort. [4] There are approximately 2.5 million “baby boomers” currently residing in LAC and DHS provides health care services for nearly 300,000 of them. With some degree of uncertainty, DHS estimates HCV prevalence amongst its patient population at up to 5%, significantly higher than the national average. [6]

HCV treatment dosage and duration depends on a few factors: the viral load, genotype of HCV variant, and liver damage level. Current standard of treatment is a 12-week treatment with a combination of drugs: Sofosbuvir, Ribavirin, and peg-interferons. Interferon-based treatments have presented challenges because of significant side effects, poor response rates, and significant variation in terms of responses based on genetic predisposition. The Food and Drug

Administration recently approved a new generation of DAA medications, including Gilead's Harvoni, which address some of these challenges: they have shown lower rates of side effects and higher positive response and compliance rates. [8] One concern, however, is the significant costs of these medications and lack of real-world clinical effectiveness data.

DHS has launched a treatment protocol that tracks a patient from the point of initial contact with a primary care physician, through 12 weeks of therapy, and 12-week followup to assess sustained virologic response. The protocol details a specific flow for each patient identified as having HCV and following through the complete therapy regimen. This evaluation will assess the (1) efficiency of the referral and treatment process, (2) costs of the program, and (3) effectiveness of DAA agents in a real-world clinical setting.

Methods:
The study team met with relevant stakeholders to determine the data needed to generate the appropriate cost-effectiveness model. As this is an evaluation of a new protocol, data from previous HCV treatment outcomes will not be used. Instead, the team determined what data would be needed at each step. Process efficiency will be measured by the length of time required for each step of the referral and treatment process, as well as the proportion of individuals who complete each step. Effectiveness will be measured by full completion of treatment regimen and sustained virologic response 24 weeks after treatment start. Program costs will be measured using micro-costing data, including the value of the medications, staff time, laboratory tests, training costs, etc.

A preliminary decision tree was constructed in TreeAge Pro 2012 to model the HCV protocol pathways. This model will capture costs and outcomes for patients as they navigate the HCV Initiative's referral and treatment process, and will produce costeffectiveness estimates of the program. In addition, the model will be used to conduct sensitivity analysis, in order to assess the robustness of baseline results to uncertainty in the model's parameters.

Results:
As this will be a retrospective analysis and data collection only started recently, the appropriate data points for probabilities, outcomes, and costs have not been collected to appropriately populate the model.

Conclusion:
The high costs of new generations of medications underscore the importance of examining their cost-effectiveness in real-world clinical settings. This study will provide a unique assessment of the value of direct-acting agents for treatment of Hepatitis C infections in a large patient population with high prevalence of infection.

References:

1) "Surveillance for Viral Hepatitis – United States, 2012." Centers for Disease Control and Prevention, 5 Jan. 2015. Web. <http://www.cdc.gov/hepatitis/Statistics/2012Surveillance/Commentary.htm>.
2) "Viral Hepatitis Statistics & Surveillance." Centers for Disease Control and Prevention, 24 Aug. 2014. Web. <http://www.cdc.gov/hepatitis/Statistics/>.
3) "Hepatitis C Information for the Public." Centers for Disease Control and Prevention, 9 Dec. 2014. Web. <http://www.cdc.gov/hepatitis/c/cfaq.htm>.
4) "Hepatitis Why Baby Boomers Should Get C Tested." Centers for Disease Control and Prevention, 1 May 2013. Web. <http://www.cdc.gov/knowmorehepatitis/Media/PDFs/FactSheet-Boomers.pdf>.
5) "Hepatitis C and Baby Boomers (1945-1965)." Centers for Disease Control and Prevention, 27 Jan. 2015. Web. <http://www.cdc.gov/knowmorehepatitis/LearnMore.htm>.
6) Personal communication with Dr. Ricardo Basurto-Davila.
7) "Hepatitis C Diagnostic Testing." Hepatitis C Online. Web. <http://www.hepatitisc.uw.edu/pdf/screening-diagnosis/diagnostictesting/ coreconcept/all>.
8) "What Medications Are Used to Treat Hepatitis C?" American Liver Foundation. Web. 30 Jan. 2015. <http://hepc.liverfoundation.org/treatment/the-basicsabouthepatitisc-treatment/what-medications-are-used-to-treat-hepatitis-c/>.
9) "Gilead Gets U.S. Approval to Sell New Hepatitis C Drug." WSJ. Web. 17 Jan. 2015. <http://www.wsj.com/articles/gilead-gets-u-s-approval-to-sell-newhepatitiscdrug-1412963083>.
10) Weinstein MC, Siegel JE, Gold MR, Kamlet MS, Russell LB. Recommendations of the Panel on Cost-effectiveness in Health and Medicine. JAMA.1996;276(15):1253-8.
11) Tsochatzis, Emmanuel A., Catriona Crossan, Louise Longworth, Kurinchi Gurusamy, Manolo Rodriguez-Peralvarez, Konstantinos Mantzoukis, Julia O'brien, Evangelos Thalassinos, Vassilios Papastergiou, Anna Noel-Storr, Brian Davidson, and Andrew K. Burroughs. "Cost-effectiveness of Noninvasive Liver Fibrosis Tests for Treatment Decisions in Patients with Chronic Hepatitis C." Hepatology: 832-43. Print.

Allison Arp

Preceptor
Michael T. Sellix, Ph.D
Assistant Professor
University of Rochester School of Medicine
Department of Medicine, Endocrine/Metabolism

The Influence of Androgen on Clock Controlled Gene Expression in Granulosa Cells from Women with Polycystic Ovary Syndrome

Introduction

Despite the fact that polycystic ovary syndrome (PCOS) is one of the most commonly diagnosed fertility disorders, the etiology of the disease remains controversial (1). Developmental programming due to excess fetal androgen exposure, of maternal or fetal origin, is widely considered causative in PCOS (2). The disease is often co-morbid with metabolic syndrome (3). In mammals, reproductive physiology and metabolism are directly and indirectly regulated by the circadian timing system (4, 5). Evidence suggests that mutations disrupting clock function have dramatic impacts on reproductive function and metabolism (6-8). Dr. Sellix's lab and others have shown that the clock in the ovary contributes to hormone synthesis and ovulation timing (9, 10). Thus, a link exists between circadian timing system stability and fertility.

Objective

Our aim is to determine the influence of hyperandrogenemia in women with PCOS on the timing of clock and putative clock controlled gene expression in isolated ovarian granulosa cells. We hypothesize that women suffering with PCOS and confirmed hyperandrogenemia will have more dramatic circadian disruption in the ovary than healthy controls or women with PCOS and normal serum androgen levels.

Background

Circadian rhythms are driven at the molecular level by an autoregulatory transcriptional-translational feedback loop (TTFL) of rhythmic clock gene transcription factors (5). The primary feedback loop involves the regulation of the three period genes (per 1-3) and two cryptochrome genes (cry1 and cry2). Per and cry expression is driven by a complex including the activators BMAL1 and CLOCK. PER and CRY act as negative regulators in the feedback loop, directly suppressing their own transcription and the transcription of other BMAL1:CLOCK target genes. BMAL1:CLOCK also directly regulate the timing of output genes or clock-controlled genes (CCGs). CCGs are the effector molecules of the clock, mediating its temporal control over physiological function (11, 12). While the suprachiasmatic nucleus (SCN) is the primary central pacemaker, gonadotropin-releasing hormone (GnRH) neurons, pituitary and ovarian cells are also considered cell-autonomous clocks (11, 13-14). It is widely believed that synchronization among central and peripheral oscillators (e.g. SCN, ovary), or “internal circadian organization”, is a fundamental property of physiological homeostasis (15).

Many of the reproductive and metabolic features of PCOS have been described in animal models using developmental stage-specific androgen exposure (16, 17). Prenatal androgen excess (PNA) mice and mice exposed to androgen during puberty are anovulatory with hyperandrogenemia and metabolic dysfunction including insulin resistance (IR; 18-20). The PNA mouse is widely considered a representative model as it mimics the direct effects of excess androgen in utero on the developing HPO axis.

Methods

To contrast the effects of PCOS with or without excess serum androgen on clock function in the ovary we will measure the timing and amplitude of clock and CCG expression in ovarian GC cultures from humans. Cells will be recovered from healthy women seeking IVF for male cause infertility or egg donors (controls n=15), women with a confirmed diagnosis of PCOS and elevated free androgen index (FAI; n=15) or PCOS diagnosis without hyperandrogenism (n=15). At the time of in vitro fertilization, GCs will be recovered, cultured at $5x10^5$ cells/dish in 6 well culture plates, synchronized with DEX (200nM) and recovered (three wells per collection) every 6h for 24h. Cells are washed once in sterile PBS, scraped in PBS and pelleted. Pellets are then snap frozen in liquid nitrogen and stored at -80C. RNA will be extracted using RNAeasy kits with on-column DNAse digestion (Qiagen). After cDNA synthesis samples will be analyzed with the RT^2 Profiler PCR Array qPCR system (Qiagen) on a Bio-Rad CFX386 qPCR thermocycler. GC cDNA will be analyzed in triplicate across time and treatment using the following human PCR arrays: (A) the Circadian Rhythms PCR array, (B) the G-protein coupled receptor array and (C) the Female Infertility PCR. Gene expression level will be quantified relative to the housekeeper b-actin using the □ CT method and rhythms will be analyzed with CircWave software for rhythm phase and amplitude as a function of treatment (R.A. Hut, Groningen, NL). The phase and amplitude of clock gene and CCG expression will be analyzed as a function of time and treatment.

Results

Due to the dependency on donations of human ovarian granulosa cells, we have not collected enough data to begin analysis yet.

Conclusion

There is not enough data to make any meaningful conclusions at this time. If the findings of this proposal indicate that clock gene and CCG expression in the ovary are affected by androgen, they will contribute to a more accurate understanding of the etiology of developmentally programmed disease, such as PCOS, that is linked to circadian clock function.

References

1. Padmanabhan V, Veiga-Lopez A 2011 Developmental origin of reproductive and metabolic dysfunctions: androgenic versus estrogenic reprogramming. Seminars in reproductive medicine 29:173-186

2. Franks S, Berga SL 2012 Does PCOS have developmental origins? Fertility and Sterility 97:2-6
3. Dunaif A 1997 Insulin resistance and the polycystic ovary syndrome: mechanism and implications for pathogenesis. Endocr Rev 18:774-800
4. Dibner C, Schibler U, Albrecht U 2010 The mammalian circadian timing system: organization and coordination of central and peripheral clocks. Annual Review of Physiology 72:517-549
5. Albrecht U 2012 Timing to perfection: the biology of central and peripheral circadian clocks. Neuron 74:246-260
6. Kennaway DJ 2005 The role of circadian rhythmicity in reproduction. HumReprodUpdate 11:91
7. Bass J, Takahashi JS 2010 Circadian integration of metabolism and energetics. Science 330:1349-1354
8. Arble DM, Ramsey KM, Bass J, Turek FW 2010 Circadian disruption and metabolic disease: findings from animal models. Best Pract Res Clin Endocrinol Metab 24:785-800
9. Sellix MT, Yoshikawa T, Menaker M 2010 A circadian egg timer gates ovulation. Curr Biol 20:R266-267
10. Alvarez JD, Hansen A, Ord T, Bebas P, Chappell PE, Giebultowicz JM, Williams C, Moss S, Sehgal A 2008 The circadian clock protein BMAL1 is necessary for fertility and proper testosterone production in mice. J Biol Rhythms 23:26-36
11. Kennaway DJ, Varcoe TJ, Mau VJ 2003 Rhythmic expression of clock and clock-controlled genes in the rat oviduct. Mol Hum Reprod 9:503-507
12. Hamada T, Antle MC, Silver R 2004 Temporal and spatial expression patterns of canonical clock genes and clock-controlled genes in the suprachiasmatic nucleus. European Journal of Neuroscience 19:1741
13. Sellix MT, Menaker M 2010 Circadian clocks in the ovary. Trends Endocrinol Metab 21:628-636
14. Gras S, Georg B, Jorgensen HL, Fahrenkrug J 2012 Expression of the clock genes Per1 and Bmal1 during follicle development in the rat ovary. Effects of gonadotropin stimulation and hypophysectomy. Cell and Tissue Research 350:539-548
15. Mohawk JA, Green CB, Takahashi JS 2012 Central and Peripheral Circadian Clocks in Mammals. Annual Review of Neuroscience
16. Abbott DH, Barnett DK, Bruns CM, Dumesic DA 2005 Androgen excess fetal programming of female reproduction: a developmental aetiology for polycystic ovary syndrome? Hum Reprod Update 11:357-374
17. Roland AV, Nunemaker CS, Keller SR, Moenter SM 2010 Prenatal androgen exposure programs metabolic dysfunction in female mice. J Endocrinol 207:213-223
18. Sullivan SD, Moenter SM 2004 Prenatal androgens alter GABAergic drive to gonadotropin-releasing hormone neurons: implications for a common fertility disorder. Proc Natl Acad Sci U S A 101:7129-7134
19. Manneras L, Cajander S, Holmang A, Seleskovic Z, Lystig T, Lonn M, Stener-Victorin E 2007 A new rat model exhibiting both ovarian and metabolic characteristics of polycystic ovary syndrome. Endocrinology 148:3781-3791
20. van Houten EL, Kramer P, McLuskey A, Karels B, Themmen AP, Visser JA 2012 Reproductive and metabolic phenotype of a mouse model of PCOS. Endocrinology 153:2861-2869

Anna Artymowicz, B.Sc.

Preceptor(s) Name: Nancy Chin Ph.D, M.P.H.
Title: A Rough Sketch of Sowa-Rigpa, Traditional Tibtean Medicine
Institution: CIBS, Central Institute of Buddhist Studies
Department: Department of Medical Humanities

A Rough Sketch of Sowa-Rigpa, Traditional Tibtean Medicine

Introduction: Our medical beliefs -accepted medical truths, ways of reasoning, definitions of sufferning an healing- are shaped by our personal and cultural context. Health care providers need to realize that many people will not share their own belief system, and that understanding another's values, beliefs, and concerns is necessary to effectively establish common goals.

Objective: To create, under the guidance of the teachers at the CIBS, a Thangka of my own. Together with a written overview of the traditonal Tibetan medicine system, I would like to use this piece as a way to introduce to those interested a currently active medical/healing system that is different from the one prevailing in North America.

Background: Thangka paintings are religious works used for spiritual enrichment and as teaching tools in the Buddhist tradition, laden with symbolism and created in accodance with guidelines found in Buddhist scripture.

Many Thangka paintings have been and continue to be used to supplement the medical teachings of Sowa Rigpa, a Tibetan medical system more than 2500 years old.

Methods: Thangkas are painted on cotton or sewn with silk. Painted Thangkas are most commonly created on loosely woven cotton using paint made of pigment in a water soluble medium. Traditionally, mineral and organic pigments are used, tempered with a herb and glue solution. The paint I used was manufactured using synthetic coloring agents. In Western terminology, this is a distemper technique.

References:

Sowa-Rigpa: Himalayan art of healing. Indian Journal of Traditional Medicine, 3(2), 212–218.

Asselin, Patrick

Preceptors:
Jeff Bazarian, MD, MPH
Associate Professor
Department of Emergency Medicine

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., & Povilshock, 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

Baman, Jayson

Preceptor:
Anthony K.L. Leung, Ph.D.
Assistant Professor
Department of Biochemistry and Molecular Biology
Bloomberg School of Public Health
Johns Hopkins University

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 degeneration[1]. 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 functions[2-4]. 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 pathology[1].

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 domains[7]. In fact, previous studies show that PARP-13 plays an integral role in the mediation of miRNA silencing under stress conditions[8]. 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 $1x10^5$ cells/mL were treated with sodium arsenite (250 µM 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 $1x10^5$ cells/mL were treated with 1µg/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, $1x10^5$ cells/mL were treated with an approximately 1.1µg/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) 1.Ramaswami, M., Taylor, J.P. & Parker, R. Altered ribostasis: RNA-protein granules in degenerative disorders. *Cell* **154**, 727-36 (2013).
2) 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) 3.Thedieck, K. et al. Inhibition of mTORC1 by astrin and stress granules prevents apoptosis in cancer cells. *Cell* **154**, 859-74 (2013).
4) 4.Dougherty, J.D., White, J.P. & Lloyd, R.E. Poliovirus-mediated disruption of cytoplasmic processing bodies. *J Virol* **85**, 64-75 (2011).
5) 5.Anderson, P. & Kedersha, N. Stress granules: the Tao of RNA triage. *Trends Biochem Sci* **33**, 141-50 (2008).
6) 6.Buchan, J.R. & Parker, R. Eukaryotic stress granules: the ins and outs of translation. *Mol Cell* **36**, 932-41 (2009).
7) 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).

Bevan, Graham

Jean-Philippe Couderc, PhD and Dr. Arthur Moss, M.D.
University of Rochester
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 predicative 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 ($\lambda 2/\lambda 1$)[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 λ2/λ1 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 λ2/λ1 (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 λ2/λ1 (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 disconcordant 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 λ2/λ1 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. riori, 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.

Bhagat, Dhristie

Preceptor: Jill Halterman
University of Rochester Department of Pediatrics

Interactive Physical Play and Behavioral and Academic Outcomes in Urban Children with Persistent Asthma

Introduction: Asthma disproportionately affects urban youth, and may lead to limited activity and reduced participation in interactive physical play (IPP) at school [5]. Urban youth with asthma are also at risk for behavioral and academic difficulties [1]. As participation in recess and physical activity is positively associated with school---based performance and behavior [3], it is crucial to explore these correlations for urban children with asthma.

Objective:
1) To describe participation in IPP among school---aged children with persistent asthma;
2) To determine if IPP varies with asthma severity
3) To evaluate the relationship between IPP and behavior/academic outcomes.

Background: Asthma is the most common chronic disease in children, with poor underserved youth at highest risk of developing it [5]. Children living in urban communities have also been shown to be at greater risk of decreased physical activity and interactive physical play (IPP), due to multiple social and environmental factors [5, 4]. Urban youth face more struggle with behavior and academics as well [1]. Research supports the idea of physical activity having a key role in child development, including social/emotional growth [2].

Methods: We analyzed baseline data from elementary school children (4---10 yrs) with persistent asthma enrolled in the SB---TEAM trial in urban Rochester, NY. In---home surveys were conducted with caregivers to assess asthma severity, level of participation in IPP at school (gym, running at recess, or sports team participation), academic performance, and social/emotional functioning via the Parent Appraisal of Children's Experiences (PACE) questionnaire. Bivariate and regression analyses assessed the relationship between asthma severity, IPP and behavior/academic outcomes.

Results: We enrolled 324 subjects (78% response rate); 59% Black, 31% Hispanic, mean age 7.9 yrs, 69% Medicaid. Overall, caregivers reported 50% of children experienced limitation in gym class, 34% ran at recess, and 18% were on sports teams, with only 53% participating in any IPP at school. Compared to those with mild persistent asthma, more children with moderate---severe asthma were limited in gym (56 v 42% p=.009), and fewer ran at recess (29 v 42% p=.007) or took part in any IPP (48 v 58% p=.046). Those who participated in IPP had better positive peer social skills and task orientation and less shy/anxious behavior (all p<.05); more had reading (72 v 58% p=.008) and math (80 v 68% p=.019) skills at grade level, and fewer needed learning services (25 v 35% p=.067). Results were consistent in multivariate analyses.

Conclusion: Many urban school children with asthma, especially those with moderate--- evere symptoms, do not partake in IPP at school and may suffer academic and behavioral consequences. Further efforts are needed to optimize asthma control for these children and encourage participation in IPP, with a broad view of health and development.

References:

1. Barros, R. M., E. J. Silver, and R. E. K. Stein. "School Recess and Group Classroom Behavior." Pediatrics 123.2(2009): 431---36. Pediatrics. American Academy of Pediatrics, Feb. 2009. Web. 1 June 2015.
2. Bulotsky---Shearer, Rebecca J., Elizabeth R. Bell, Sandy L. Romero, and Tracy M. Carter. "Preschool Interactive Peer Play Mediates Problem Behavior and Learning for Low---income Children." Journal of Applied Developmental Psychology 33.1 (2012): 53--- 65. Elsevier. Web. 1 June 2015.
3. Centers for Disease Control and Prevention. The association between school based physical activity, including physical education, and academic performance. Atlanta, GA: U.S. Department of Health and Human Services; 2010.
4. Farley, Thomas A., Rebecca A. Meriwether, Erin T. Baker, Liza T. Watkins, Carolyn C. Johnson, and Larry S. Webber. "Safe Play Spaces To Promote Physical Activity in Inner---City Children: Results from a Pilot Study of an Environmental Intervention." Am J Public Health American Journal of Public Health 97.9 (2007): 1625---631. Web. 4. Milteer, R. M., K. R. Ginsburg, and D. A. Mulligan. "The Importance of Play in Promoting Healthy Child Development and Maintaining Strong Parent---Child Bond: Focus on Children in Poverty." Pediatrics 129.1 (2011): E204---213. Pediatrics. American Academy of Pediatrics, 26 Dec. 2011. Web. 1 June 2015.
5. Weil, C. M., S. L. Wade, L. J. Bauman, H. Lynn, H. Mitchell, and J. Lavigne. "The Relationship Between Psychosocial Factors and Asthma Morbidity in Inner---City Children With Asthma." Pediatrics 104.6 (1999): 1274---280. Pediatrics. American Academy of Pediatrics, Dec. 1999. Web. 1 June 2015.

Bragg, Andrew

Preceptor:
Adit Ginde, MD, MPH
University of Colorado School of Medicine
Department of Emergency Medicine

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 $PaCO_2$ < 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

Michael Bux

Carla Casulo, MD
Assistant Professor of Medicine
University of Rochester Medical Center
Wilmot Cancer Center, Hematology/Oncology

Identifying the high risk follicular lymphoma population for clinical and biological investigation

Introduction:

Follicular lymphoma (FL) is the second most common adult B-cell lymphoma typically affecting older adults. Follicular lymphoma is considered an incurable disease, however modern medical treatments including anti-CD20 antibody, rituximab, have provided good prognosis to FL diagnosis. Many patients will achieve remission lasting 3-5 years, with subsequent periods of relapse and remission. Patients live many years with their disease, with most dying from other causes. A subpopulation has been identified, however, with high-risk disease whose mortality is significantly higher than the rest of the population of follicular lymphoma. This population is poorly understood, and the mechanism conferring increased mortality is yet unknown. Much work is needed to study the genetic, biochemical, and clinical nature of the high-risk FL population.

Objective:

The nature of this work was to create a clinical database of all FL patients treated at the Wilmot Cancer Center in order to have a pool of data from which to identify patients whose disease could be classified as high risk. This work is a necessary first step in order to determine the population of interest for further investigation.

Methods:

A database was created using REDCap software that included domains such as demographics, date and age of diagnosis, classification of tumor at diagnosis, treatment, date of relapse, etc. A list of preserved tissue samples was provided by the Department of Pathology at SMH, and clinical data was extracted from the electronic medical record of each patient whose sample was on the list. Patients were excluded from the database if original diagnosis was not FL or transformed disease. This was approved by the RSRB.

Results:

The database was completed containing a total of 127 patients. Of these 127 patients, 102 have complete and usable database records. The male:female ratio is 2:1 with 93% of patients identifying as White/Caucasian. Fifty-three percent of patients relapsed, with 22 patients relapsing within two years of initial treatment. Since patients with high-risk FL typically experience their first relapse within two years of being treated, it is this set of 22 patients that has been preliminarily identified as the target population for further study. This means approximately 20% of patients in the dataset meet the screening criteria of high-risk disease, which is consistent with the proportion of patients described as high-risk in the medical literature.

Conclusion:

Follicular lymphoma is a B-cell malignancy that affects older adults. Although the disease is generally considered incurable, modern treatments provide a favorable prognosis to the majority of patients. With this improved treatment, a subpopulation has been identified with high-risk disease that experience early and more frequent relapse as well as greater mortality. In the FL patient population treated at the Wilmot Cancer center, approximately 20% meet the preliminary screening criteria of high-risk disease. Tissue samples from these patients are currently under genetic investigation with future plans for histopathological and clinical investigation. The long-term goal of this work is to understand the mechanism that confers high-risk disease so that treatment strategies can be improved in order to decrease morbidity and mortality.

References:

Byrtek, Michelle, et al. "Early relapse of follicular lymphoma after R-CHOP uniquely defines patients at high risk for death: An analysis from the National LymphoCare Study." *Blood* 122.21 (2013): 510-510.

Salles, Gilles, et al. "Rituximab maintenance for 2 years in patients with high tumour burden follicular lymphoma responding to rituximab plus chemotherapy (PRIMA): a phase 3, randomised controlled trial." *The Lancet* 377.9759 (2011): 42-51.

Eric Chang, MS2

Preceptor:
Scott E. Liebman, M.D., M.P.H.
University of Rochester
Department of Nephrology

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 catheters[3]. 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 septicemia[7], 43% lower risk for cardiovascular-related mortality[6], reduced rates of infection[8] and reduced rates of all-cause mortality[5]. AVGs are considered suboptimal when compared to AVFs but are still safer than catheters[4].

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 URMC 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.

Hamza Chengazi

Preceptor Name: Dr. Laurel Carney
Institution: University of Rochester
Department: Neurobiology and Anatomy

Neural Responses in Awake and Behaving Budgerigars

Introduction:

Amplitude modulation (AM) is a common characteristic of acoustic envelopes found both in natural sound and vocalizations (Rosen, 1992; Beckers and ten Cate, 2001; Nelson and Carney, 2007; Carney et al., 2013). The information carried in these modulations has biological significance, as it plays an important role in speech recognition and processing of acoustic stimuli. Previous research has shown that such envelope information is sufficient for speech recognition (Shannon et al., 2007). The ability of neurons to recognize and respond to changes in AM may help to explain differences in hearing ability as well. The present study examined the budgerigar (*Melopsittacus undulatus*), a vocal mimic known to have complex vocalizations and similar AM detection ability as humans (Carney et al., 2013). Birds were trained to perform a behavioral task via operant conditioning (similar to Carney et al 2013), while also having neuronal responses from the IC recorded.

Objective:

The objective of the study was to use choice probability to examine the role of IC neurons in amplitude modulation coding within the brain. Increased understanding of the neuronal basis of AM processing may have implications of cochlear neuropathy and hidden hearing loss. Though most hearing loss has been considered a function of hair cell damage, new research suggests that nerve fibers and upstream damage may play a role as well (Plack et al., 2014). Damage or degradation within the midbrain may then play a large role in hearing loss by having behavioral consequences via the reduction of AM coding and use of this significant auditory characteristic.

Background:

In the past, auditory neuroscience has focused on either the beginning of the auditory pathway (for example: the cochlea and auditory nerve fibers) or the highest levels of the pathway in the auditory cortex (Joris et al., 2004; Niwa et al., 2012). The inferior colliculus (IC), however, shows increasing promise as a structure to study, since its neurons are the first within the ascending auditory pathway tuned to amplitude modulations (Carney et al., 2014). The IC is located within the midbrain and acts as a bottleneck for auditory information: all of the auditory information coming from ascending projections of the periphery pass through the IC (Nelson and Carney, 2007). Additionally, the IC has also been shown to receive top-down projections from higher cortical regions (Krishna and Semple, 2000). Thus, it seems as though the midbrain may play an important role in processing and the resultant behavior that comes from acoustic stimuli.

Neuronal coding of AM information can occur via two different processing schemes in the IC: temporal coding, in which neurons synchronize firing to the modulations of the amplitude envelope, and rate coding, in which the average firing rate of the neurons changes in response to the presence of modulation (Nelson and Carney, 2007). Previous studies of the neural bases of AM coding in the IC are all limited in that none of them compare the physiological responses of neurons in an animal to the consequent behavior of that same animal. By observing the physiological responses of neurons in an animal that is also performing a task, one can better understand the role of neuronal processing and its effects on the decision making process. Choice probability is the attempt to correlate neurons' firing rates to the subject's perceptual decisions (Niwa et al., 2012; Haefner et al., 2013). By comparing neural response patterns during correct responses and those during incorrect responses, one can gain insight on the possible effect of specific neurons' on the whole organisms behavior.

Methods:

Two budgerigars (*Melopsittacus undulatus* [1 male: 1 female]) were used in this study. For the behavioral portion of the study, the birds were trained to perform a simple choice task within a booth: birds initiated a noise with a central button and then responded with a right or left button depending on if the bird recognized the sound as modulated or unmodulated. Correct responses were reinforced by giving the bird a seed, and incorrect responses caused a 5 second time out. Bias was controlled for by releasing two seeds for a correct answer on a side that the bird was biased against. Responses were tracked and the depth of modulation was decreased as the birds correctly responded to determine their threshold for detection. Throughout the task, a head-mounted Microdrive allowed recording of neural firing patterns (rate and synchronicity) from cells in the IC. The technique for implantation and recording is the same as that of research done by Henry et al (paper is in review), as the same birds were used in this study. The firing patterns of neurons are then to be analyzed in relation to behavior.

Results and Conclusion:

The study is still ongoing, and results have not yet been obtained. Birds have adequately been trained however, and the process of performing the task and recording from neurons has been commenced. The ultimate goal is to correlate the firing patterns of neurons and look for a relationship between these patterns and the bird's behavior. A positive finding would show that IC cells are directly correlated with the bird's behavior and thus the AM coding in the midbrain plays a role in decision making and perception.

References:

Beckers GJL, ten Cate C (2001) Perceptual relevance of species-specific differences in acoustic signal structure in Streptopelia doves. Anim Behav 62:511–518.

Carney LH, Ketterer AD, Abrams KS, Schwarz DM, Idrobo F (2013) Detection Thresholds for Amplitude Modulations of Tones in Budgerigar, Rabbit, and Human. 787:109–118 Available at: http://link.springer.com/10.1007/978-1-4614-1590-9.

Carney LH, Zilany MS a., Huang NJ, Abrams KS, Idrobo F (2014) Suboptimal Use of Neural Information in a Mammalian Auditory System. J Neurosci 34:1306–1313 Available at: http://www.jneurosci.org/cgi/doi/10.1523/JNEUROSCI.3031-13.2014.

Haefner RM, Gerwinn S, Macke JH, Bethge M (2013) Inferring decoding strategies from choice probabilities in the presence of correlated variability. Nat Neurosci 16:235–242 Available at: http://www.ncbi.nlm.nih.gov/pubmed/23313912.

Joris PX, Schreiner CE, Rees A (2004) Neural Processing of Amplitude-Modulated Sounds. :541–577.

Krishna BS, Semple MN (2000) Auditory temporal processing: responses to sinusoidally amplitude-modulated tones in the inferior colliculus. J Neurophysiol 84:255–273.

Nelson PC, Carney LH (2007) Neural rate and timing cues for detection and discrimination of amplitude-modulated tones in the awake rabbit inferior colliculus. J Neurophysiol 97:522–539.

Niwa M, Johnson JS, O'Connor KN, Sutter ML (2012) Activity Related to Perceptual Judgment and Action in Primary Auditory Cortex. J Neurosci 32:3193–3210.

Plack CJ, Barker D, Prendergast G (2014) Perceptual Consequences of "Hidden" Hearing Loss. Trends Hear 18:1–11.

Rosen S (1992) Temporal information in speech: acoustic, auditory and linguistic aspects. Phil Trans R Soc Lond 336:367–373 Available at: http://rstb.royalsocietypublishing.org/content/336/1278/367.abstract.

Shannon R V, Zeng F, Kamath V, Wygonski J, Ekelid M (2007) Temporal Cues. Science (80-) 270:303–304.

Dauphin, Leah

Preceptor:
Julia A. Margenthaler, MD
Washington University School of Medicine, St. Louis, Missouri
Department of Surgery

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 pro

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.

DeHority, Rebecca

Preceptor:
John Elfar, MD
University of Rochester Medical Center
Center for Musculoskeletal Research
Department of Orthopedics

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, axonoetmesis, or neuroetmesis[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 outcome[5]. 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 function[6.] 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 nerves[7]. We hypothesize that this transient improvement represents the portion of the nerve that retains it 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:

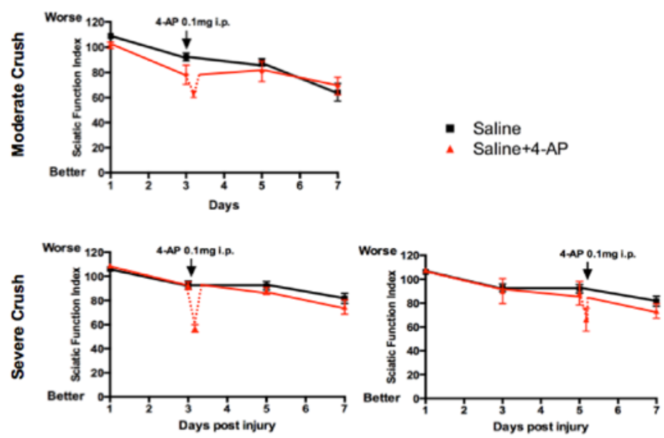
To describe the architecture of the nerve that underlies the transient functional improvement seen in systemic administration of 4-AP to a mouse with a peripheral nerve crush injury. Furthermore, to characterize the changes in the amount myelin and neurofilament at the site of the crush injury, and proximal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

Samuel Donovan
URSMD Class of 2018

Exploring Patients' Decisions to Seek Emergency Department Care for Non-Emergent Health Concerns in East Boston

Introduction

The East Boston Neighborhood Health Center (EBNHC) is a Federally Qualified Health Center (FQHC) that has provided a wide range of health-related services to the East Boston community since 1970. Originally founded as an Urgent Care clinic, the organization has expanded over the last several decades to include primary care, several outpatient specialty practices, and numerous community-based health and wellness interventions. In 2010, EBNHC became the only FQHC in the continental United States to operate a satellite Emergency Department (ED) that is open 24 hours per day, 7 days per week. Though the ED has only 12 beds, high demand and rapid turnover allow the department to serve approximately 130 patients per day, leading to a total of 44,000 visits in 2014. EBNHC operates under the clinical license of Boston Medical Center (BMC), and ED physicians have direct admitting privileges for inpatient surgical, catheterization, and radiology services at BMC's main hospital in Boston's South End. Additional "ED to ED" transfer is also available from EBNHC to Massachusetts General Hospital (MGH), which offers high-level care across all medical and surgical specialties.

East Boston is geographically isolated from the rest of the city by Boston Harbor, meaning the neighborhood's largely under-served population has limited access to the city's premier academic medical centers. The high quality, multi-lingual services provided by EBNHC, as well as the ED's capacity to facilitate transfer to high-level hospitals, make EBNHC a lifeline for many patients. With this responsibility in mind, EBNHC continually performs internal Quality Improvement (QI) studies with the goal of providing the highest quality of care to an expanding patient population. The Access Project is one such study, which examines the balance between supply and demand for both ED and outpatient services. During the first round of data collection, an analysis of ED visits over two weeks found that 56% of the 1,244 visits during the study period were "triage green," pertaining to non-acute issues that could likely be addressed at lower cost in the outpatient setting. The study also showed that 86% of those "triage green" patients were followed regularly by a primary care provider at EBNHC, and that the organization's capacity to accommodate same-day outpatient appointments considerably exceeded appointment requests. This data reveals an opportunity to reduce unnecessary ED visits while simultaneously maximizing the efficiency of outpatient services, which are beginning to move towards "advanced access" model geared towards higher availability of same-day appointments.[1] In order to design an intervention that would improve efficiency, however, a better understanding is needed of the factors that drive this sub-optimal utilization EBNHC's clinical resources.

This project aimed to explore why patients with non-acute medical issues who are regularly seen by a local PCP seek care from EBNHC's ED instead of making a same-day appointment at their PCP's outpatient clinic. A literature review reveals numerous qualitative and quantitative studies examining similar questions in EDs at large academic medical centers,[2,3] and one study exploring ED usage among immigrants that share some demographic similarities with East Boston's population.[4] Some common themes exist between these studies, including problems with access to non-ED treatment and patients' perceptions of non-emergent medical issues to be genuine emergencies. However, even a brief analysis shows that ED usage patterns are highly context-specific. For this reason, EBNHC wished to use qualitative methods to gain a deeper understanding of why their patients in particular choose the ED over their primary care providers.

Methods

Project participants were chosen based on their status as current or former "triage green" patients in the EBNHC Emergency Department who also had a primary care provider at one of EBNHC's outpatient clinics. Purposeful sampling techniques were used to ensure that participants adequately reflect the demographic diversity of EBNHC's patient population, and that each of EBNHC's major outpatient clinics (Family Medicine, Adult Medicine, and Pediatrics) are represented among participants' primary care providers.[5] Because the study involved qualitative interviews, a relatively small sample size was needed; targeted enrollment was between 10 and 20 interviews. Comparable qualitative studies examining attitudes and beliefs about Emergency Department usage have achieved meaningful results with a similar sample size.[3] Minors under the age of 18 were not interviewed, and participants were excluded if they had any form of decisional incapacity. Interviewees were approached and interviewed after triage, often while they waited for the results of lab tests. Interviews were conducted in English, Spanish, and Italian, and were digitally recorded, de-identified, securely stored, and transcribed. An interview guide was elaborated with input from Emergency Department staff, and the interviewer added follow-up questions not included in the guide during interviews in order to clarify answers or probe on certain subjects. Analysis involved examining all transcripts and summarizing key themes and concepts related to the study's central aims.

Results

Fifteen interviews were performed, with a mean duration of 13 minutes. The shortest interview was four minutes (the patient had to leave before the interview was complete), and the longest interview lasted 30 minutes. Interviews took place in the primary language of the interviewee (nine in Spanish, four in English, one in Italian), with one exception: a native Arabic speaker who was comfortable speaking in English. Interviewee ages ranged from 19 to 77 years, and participants' primary care providers included physicians from EBNHC's Family Medicine, Adult Medicine, Pediatrics, and OB/GYN clinics.

Analysis

As with many health behaviors, the decision to seek care at the Emergency Department rather than a PCP for non-emergent health issues was often difficult to explain, even for the patients themselves:

I: So you have doctor Sharma [your PCP], and there's also the emergency department. What kind of sickness is a doctor Sharma sickness, and what kind of sickness is an emergency sickness? Like for example, if I have a stuffy nose and a sore throat.
P: Emergency.
I: Ok, and if I have a broken leg?
P: Emergency.
I: And if I have a stomach ache?
P: Doctor Sharma (laughing)
I: Ok, and if I have a headache, but it's a really bad headache?
P: Doctor Sharma
I: Ok. So why would you say doctor Sharma for the headache for example?
P: (long pause, then laughing) Last time I had a headache I came over to the emergency, and then they gave me ibuprofen (laughing). I hate them when they give me ibuprofen. All the time when I take ibuprofen, 800, 600. I don't know…

Despite this patient's difficulty in articulating her reasoning, she brings up a number of salient themes that arose during interviews with other study participants. Past experiences ("I hate them when they give me ibuprofen") were important drivers for many patients. This occasionally included negative experiences with PCPs; but more often, patients described very positive past experiences with the ED as a main factor in their decision to return.

Additionally, several participants appeared to subconsciously categorize illness by type rather than severity. As with the above patient, some participants initially struggled to explain why they would choose their PCP only for certain illnesses; but probing often revealed that they would often seek care form their PCP only for complications arising from chronic issues that they had previously discussed in a regular checkup:

Well, if it was something involving something that we discussed when I go [to my PCP], say like a blood pressure thing or whatever, yeah I think I would call him first before I would come in here. Definitely, you know. Anything that we normally talk about, if something came up in that area, I would try to get in contact with him.

The perceived convenience of accessing the Emergency Department, or lack thereof in accessing care at their PCP office was the third major factor that often explained patients' care-seeking pattern. Some patients did not even attempt to make appointments with their PCP because they assumed availability of same-day or next-day appointments would be limited or non-existent. Others did call, and were told that availability was in fact limited, and still others appeared to choose the Emergency Department precisely because they could simply walk in, which they perceived as more convenient than calling to make an appointment.

Any one of these major drivers—past experiences, type of illness, and perceived convenience—could singlehandedly explain a given patient's decision to choose the Emergency Department. However, most patients' decisions were driven by some combination of these factors, as well as several other related inputs. A conceptual model was elaborated to reflect these findings (see **Figure 1**). When asked directly about their reasons for choosing the ED over their PCP, almost every patient alluded in some way to their belief that the ED was simply more convenient. Sometimes this was based on experience, but it was often based on a preconceived notion that same-day PCP appointments are rarely available. Similarly, past experience occasionally had a role in patients' categorization of their illnesses; but oftentimes patients categorized illnesses independently of previous experience.

Several themes relating to these three principal thematic axes arose across patient interviews. Among them, time was most frequently mentioned. One patient eloquently described the importance of time as it related to his own health as well as any patient's capacity to seek appropriate medical attention (translated from Spanish):

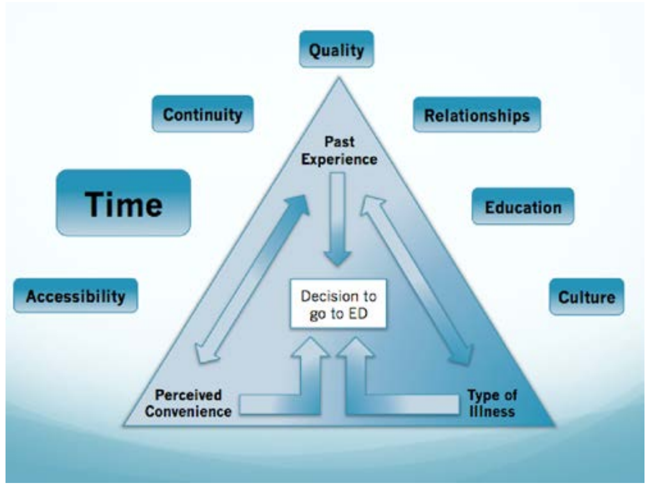


Figure 1: Factors affecting the decision to seek care in the EBNHC Emergency Department. Three principal factors (past experience, perceived convenience, and type of illness) often interact with each other and a number of additional drivers to influence patient behavior.

> *"Time is the enemy for everything. Clearly. Time is the enemy when you want to cure yourself of anything. In many cases, there is no time. And it's worse for one's health (chuckles). Sometimes I'm taking care of other things and there is no time for that."*

As a theme, time was closely related to perceived convenience: patients mentioned either the amount of time they would have to spend before talking to a physician, or—as in the above example—that they believed their PCP's availability was constricted such that it did not fit in with their own work schedule. With the ED's "24/7" availability, accessibility was another factor that arose during interviews, closely related to both time and perceived convenience.

Continuity of care emerged as a significant factor during a number of interviews. Some patients, after receiving a letter from EBNHC informing them that their PCP was retiring or moving to another practice, had yet to make contact with the new PCP to whom they were assigned. This was true not only for several study participants, but also for many more ED patients who were screened for the study during triage.

Very few patients cited dissatisfaction with their PCP as a reason for visiting the ED. However, conversations about quality of care revealed an interesting and somewhat paradoxical finding, exemplified in two excerpts from this patient's interview:

> *I: So tell me a little bit about your PCP here in East Boston.*
> *P: Ah, I think he's very competent. We have a good chat when I come in and cover, you know, anything that's happened, any change in medication or, you know…and it's been a very stable relationship. I know what to expect from him…*
> Later in the interview:

I: Ok. Alright. Any other comments or anything you want to add?
P: No, I'm very satisfied with the way things went today [in the ED]. You know, I have been here when it's been a long wait, but today it moved along very well

This exchange illustrates a common finding from many interviews: when describing their PCP, patients positively associate the amount of time spent on a visit with quality of care. Primary providers are commended for thoroughness, thoughtfulness, and a desire to know the patient as a whole. This contrasts sharply with the inverse association between time spent and quality of care in the ED. Patients describing an ED visit cited short wait times and efficiency as the principal measures for evaluating their experiences.

This is not to say, however, that patients were unappreciative of ED personnel. Several participants cited the close connections they had formed with ED staff:

They help me a lot. When I came here first, I didn't speak English, I don't understand nothing. And when I need someone to explain to me, I found one girl, she works here, Karima. Yeah, she helped me a lot, she's my best friend.

In describing positive ED experiences, many patients mentioned the staff's linguistic competence as well as their kindness and personal touch, all of which allowed them to feel more comfortable at EBNHC's ED than they did visiting other hospitals and health centers in Boston.

As with any health-related decision, both culture and education played a significant role in patients' choice to seek care at the ED. A majority of patients interviewed for this study were born outside the United States, and some of them described their experiences with the health system in their native countries. These accounts varied depending on country of origin; but a number of participants drew parallels between EBNHC's ED and their home countries' health clinics. As in those clinics, ED patients can walk in without an appointment, speak their own language, and pick up medications in the same building immediately after receiving treatment. Given this natural tendency to seek out a familiar solution to their health problems, it will likely fall on EBNHC's professionals to educate their patients on the best way to seek care for non-urgent issues. Some participants were asked whether they had received this kind of information from either their PCP or the ED staff, and all who were asked said they did not recall such a conversation.

Possible Next Steps

Results from this study highlight the need for future research, as well as several opportunities for programmatic interventions. Due to time restrictions, the study focused only on patients in the Emergency Department. However, further insight may be gained from conducting a similar qualitative study among those patients who choose to seek care from their PCP for non-urgent complaints. By studying these "positive deviants," EBNHC might identify factors that differentiate those who choose their PCP from patients who prefer the ED.[6] Additionally, a larger scale quantitative analysis—using a survey tool based on the qualitative results of this study—would allow EBNHC to get a more statistically representative picture of the decision-making factors that drive patients to choose the ED.

Despite the limitations resulting from this study's small sample size, three themes that arose during analysis reveal areas for potentially effective intervention. Firstly, patients who chose the ED due to limited **accessibility** of their Primary Care Providers may benefit from a shift towards more evening hours, allowing them to seek care after work. Moving towards an "Advanced Access" model, in which a certain number of appointments at each PCP are reserved for same-day appointments, may also give EBNHC the ability to better cater to patients that do not wish to wait more than a few hours to be seen by a provider. However, given the difficult logistics and considerable up-front costs of correctly implementing Advanced Access, it would be prudent to pilot the model with a small number of providers before rolling out on an organizational level.[1]

Continuity may represent an additional opportunity for EBNHC to prevent unnecessary ED visits. Though patients were often aware of a recent change in PCP, many did not take the initiative to contact their new provider for an appointment. This study showed that when these patients had a non-emergent health concern, they often chose walking into the ED over contacting a new PCP for the first time. A more "hands-on" approach to transitions in care might change this calculus. For example, patients might benefit from a phone call from the new provider's office soon after they are transferred. By welcoming them to the practice, encouraging them to schedule their first regular check-up, and informing them of the provider's same-day appointment availability, a provider's nurse or administrative assistant could initiate the kind of personal connection that drive patients' care-seeking decisions.

Finally, patient **education** could significantly improve utilization of EBNHC's PCP services. Study participants did not recall receiving educational materials or anticipatory guidance from their providers on the best place to seek treatment for non-urgent health problems. Regular visits with a PCP and ED visits both represent opportunities for EBNHC staff—providers, nurses, or administrators—to educate patients on the benefits of calling their PCP for minor health concerns. Care-seeking decisions could also be significantly influenced by something as simple as a small pamphlet or refrigerator magnet emphasizing the PCP's same-day appointment availability and providing appropriate contact information.

Acknowledgements
I am extremely grateful for the support and assistance I received from all of the EBNHC staff with whom I worked this summer. Bernadette Thomas was my first contact at EBNHC, and provided expert guidance from study design through data collection and analysis. In the Emergency Department, Laurie Falaro-Shoemaker, Michael Mancusi, and Stylianos Maheras all welcomed me and greatly assisted with the logistics of time-consuming data collection in a busy clinical setting; and the entire nursing, administrative, and clinical staff of the department were equally welcoming, providing me with invaluable insight into the patients to which they are incredibly dedicated. Last and certainly not least I would like to thank the study participants themselves, who generously volunteered their time and thoughtful opinions. Funding for this study was provided by the Office for Medical Education at the University of Rochester School of Medicine and Dentistry.

References

1. Rose KD, Ross JS, Horwitz LI. Advanced access scheduling outcomes: a systematic review. *Arch Intern Med*. 2011;171(13):1150-1159. doi:10.1001/archinternmed.2011.168.

2. Lucas R, Sanford S. An analysis of frequent users of emergency care at an urban university hospital. *Ann Emerg Med*. 1998;32(5):563-568.

3. Olsson M, Hansagi H. Repeated use of the emergency department: qualitative study of the patient's perspective. *Emerg Med J*. 2001;18(6):430-434. doi:10.1136/emj.18.6.430.

4. Chan TC, Krishel SJ, Bramwell KJ, Clark RF. Survey of illegal immigrants seen in an emergency department. *West J Med*. 1996;164(3):212-216.

5. Marshall M. Sampling for qualitative research. *Fam Pract*. 1996.

6. Pascale R, Sternin J, Sternin M. *The Power of Positive Deviance: How Unlikely Innovators Solve the World's Toughest Problems*.; 2010.

Andrew Forrestel and Amanda L. Mereness

PI: Michael Sellix, Ph.D.
Assistant Professor of Medicine
University of Rochester School of Medicine and Dentistry
Department of Endocrinology and Metabolism

Evidence for Non-Genomic Influence of Androgen on Clock Gene Expression in Mouse Ovarian Granulosa Cells

Internal biological or circadian clocks play an intricate role in the timing of female reproductive physiology. Molecular clock gene expression, including the repressor Period2, has been described in each tissue of the hypothalamo-pituitary-ovarian (HPO) axis and its' function is linked to steroid hormone synthesis and ovulation. Despite the fact that the clock clearly plays a role in ovarian physiology, the role of the timing mechanism in fertility disorders remains largely unknown. One such disease is polycystic ovary syndrome (PCOS), an exceptionally devastating endocrinopathy that produces infertility in roughly 10% of women. Developmental programming by excess fetal androgen, most likely of ovarian origin, plays a primary role in the etiology of PCOS. We have shown that fetal androgen programs altered clock function in the ovary, indicating that circadian disruption may be a factor in the etiology and progression of the disease. Treatment of ovarian granulosa cells (GCs) from immature gonadotropin primed female C57BL/6 Period2::Luciferase (PER2::LUC) transgenic mice with androgen shortens the period of PER2::LUC expression. Though not known, it is presumed these effects in the clock are mediated by a direct transcriptional influence of androgens through classic androgen receptor (AR) signaling. However, recent evidence suggests that androgens may also influence the timing system through novel non-genomic signaling mechanisms involving the membrane bound AR, Epidermal Growth Factor Receptor (EGFR) and Akt/PI3K/AMPK signaling.

To address this hypothesis, we have determined the effects of androgen on rhythms of PER2 expression in isolated GCs recovered from immature gonadotropin primed PER2::LUC transgenic mice. Briefly, 3-4 week old mice were given an i.p. injection (10IU) of pregnant mare serum gonadotropin to induce follicular growth. Forty-eight hours later mice were euthanized and granulosa cells were removed via needle puncture and cultured in 35mm dishes. After a period of incubation (72hr) cells were synchronized with dexamethasone (200nM) followed by culture in the presence of the non-aromatizable androgen 5α-dihydrotestosterone [DHT; 5 µM concentration (n=3-5 cultures per conc.)]. Cells were then treated with LY294002 (PI3K inhibitor; 10µM), Compound C (AMPK inhibitor; 10µM), Erlotinib (EGFR inhibitor; 10µM), AG1478 (EGFR inhibitor; 10µM), or Erlotinib + AG1478 (5µM; 5µM). As previously observed, DHT treatment dose-dependently shortened the period of PER2::LUC expression in the cells; the effects of DHT were attenuated following co-treatment with PI3K, AMPK or EGFR inhibitors. These data suggest that abnormally high androgen levels may affect clock gene expression directly in target tissue via non-genomic membrane-dependent AR-activated EGFR signaling pathways.

Fowler, Xavier

Preceptor:
John Elfar, MD
University of Rochester Medical Center
Center for Musculoskeletal Research
Department of Orthopaedics
Rochester Institute of Technology
Department of Mechanical and Manufacturing Technology

A Non-destructive Model of Measuring Joint Reactive Force at the Patellofemoral Joint

Introduction:
The patellofemoral joint (PFJ) represents one of the most commonly implicated joints in persons presenting with knee pain.[1-5] Pathologies of this joint are frequently attributed to structural changes that ultimately cause an increase in the joint reactive force (JRF).[6-9] Furthermore, surgical interventions around this joint present a concern for changes that may occur to the patellofemoral joint reactive force (PFJRF).[10] In particular, elevated PFJRFs can contribute to articular cartilage degeneration at the PFJ, creating significant risk for pain and arthritis.[10-14] An accurate means to measure such forces has much clinical significance, but presents many technical challenges.

To date, there have been many studies that have quantified the PFJRF.[6,10,15-17] In these previous studies, the joint reactive force is largely based on angle measurements and/or computerized modeling of joint kinetics. The methods employed in these studies are limited by their inability to capture the mechanical features of the surrounding soft tissues (e.g. the extensibility of a given tendon) and may not accurately represent the in vivo qualities of the PFJ.

Recreating and non-invasively measuring the JRF of any joint creates a number of logistical challenges. Ideally, a measure of the JRF would respect as much of the native architecture as possible while allowing for discrete quantification of the force across a given joint. While cadaveric approaches to measuring the PFJRF are lacking in the literature, previous studies on other joints have utilized cadavers to calculate the JRF.[18-22] Previous works have demonstrated that by introducing a linear distracting force across the joint of interest, force and displacement can be used to identify the point where the distracting and compressive forces of the joint are equal – the JRF.[18,22]

Objective:
The purpose of our study was to create a model capable of obtaining in-vivo-like measures of the PFJRF without violating the native architecture of the PFJ. We hypothesized that accurate

and reproducible measures could be made of the PFJRF without disrupting the joint using a linear distracting force.

Methods:

Specimen Preparation

12 fresh-frozen cadaver lower limbs were obtained following standard institutional protocols. Physical examination was used to rule out gross deformity or prior surgeries to the knee.

A vertical incision was made on the anterior surface of the knee to allow for retraction of the skin and connective tissues covering the anterior surface of the patella. Once the patella was revealed, a custom patellar plate was attached to the patella perpendicular to the PFJ using three extra fine screws measuring approximately 15 mm in length. Use of these screws allowed us to prevent entry into the sub-patellar space. Four 6.0 mm fixation pins were then placed transversely in both the tibia and femur for application of the bi-planar medio-lateral external fixator (Large External Fixator Set, Synthes Inc., West Chester, PA). A final 6.0 mm pin was placed transversely through the lateral epicondyles of the femur. This pin was connected to a u-shaped traction ring to allow for secure placement of the limb into the lower jaw of the tensile tester.

The specimens were then suspended within a tensile tester (MTS Insight 100, MTS Systems, Eden Prarie, MN) using a custom apparatus, with the leg fixed at 90° by external fixation rods (Large External Fixator Set, Synthes Inc., West Chester, PA). A unidirectional distracting force was then applied perpendicularly over the PFJ. Throughout the range of distraction, force and displacement were simultaneously and constantly measured. During each trial, the patella was displaced 1.25 mm at a rate of 0.5 mm/s. During pilot testing, distraction to 3.05 mm was found to be sufficient enough to reach the inflection point. Each measurement was performed three times to ensure consistency, with 2 minutes provided between each measure to allow for soft tissue relaxation. 2 minutes for relaxation was chosen based on previous works demonstrating the return of soft tissues to baseline length in this time frame.[18] Following three trials at 90°, three more sets of measures were taken with the legs repositioned and fixed at 60°, 30°, and 0°.

Calculation of the JRF

Given the time required to extract the thousands of data points from the force-displacement curves, efforts are still underway regarding the calculation of the experimental JRFs.

Using the data sets from the force-displacement curves, a best-fit polynomial will be generated to fit the force-displacement curves. To ensure accuracy in determining the inflection point, or JRF, the second derivative of this polynomial will be set to zero and its root solved to determine the inflection point. This will give us added accuracy over visual estimation of the inflection point on the graphs produced.

Statistical Analysis

Statistical analysis will follow the completion of data extraction. We plan on calculating the mean and SD for all specimens. To assess the reliability of our measures, and to ensure distraction did not result in permanent insult to the soft tissues of the PFJ, we plan to take the repeated measurements and calculate the intraclass correlation coefficient (ICC).

Results

Final results are still being extracted and calculated from the data gathered. From the pilot data collected, distraction of the PFJ at all angles seems to demonstrate an initial phase with a steeper slope where greater amounts of force appear to be required to distract the joint than is required beyond the (visually) estimated inflection point. Beyond the perceived inflection point, relatively linear phases are observed with lower slopes. This pattern was expected and proves consistent with previous works using this method to determine the JRF.[18,22]

Discussion

As data analysis is ongoing, we cannot yet draw any meaningful conclusions regarding the validity of our approach to measuring the PFJRF. We hope to complete data analysis over the next several months and are hopeful that this approach will confirm our hypothesis that this will be a reliably reproducible and non-destructive method of determining the joint reactive force. If this holds true, this method will offer a reliable means to study the PFJRF in additional contexts, such as before and after various surgical interventions.

References:

1. Glaviano NR, Kew M, Hart JM, Saliba S. Demographic and Epidemiological Trends in Patellofemoral Pain. *Int J Sports Phys Ther.* 2015;10(3):281-290.
2. DeHaven KE, Lintner DM. Athletic injuries: comparison by age, sport, and gender. *Am J Sports Med.* 1986;14(3):218-224.
3. Boling M, Padua D, Marshall S, Guskiewicz K, Pyne S, Beutler A. Gender differences in the incidence and prevalence of patellofemoral pain syndrome. *Scand J Med Sci Sports.* 2010;20(5):725-730.
4. Devereaux MD, Parr GR, Lachmann SM, Thomas DP, Hazleman BL. Thermographic diagnosis in athletes with patellofemoral arthralgia. *J Bone Joint Surg Br.* 1986;68(1):42-44.
5. Sheehan FT, Derasari A, Brindle TJ, Alter KE. Understanding patellofemoral pain with maltracking in the presence of joint laxity: complete 3D in vivo patellofemoral and tibiofemoral kinematics. *J Orthop Res.* 2009;27(5):561-570.
6. Mostamand J, Bader DL, Hudson Z. Reliability testing of the patellofemoral joint reaction force (PFJRF) measurement during double-legged squatting in healthy subjects: a pilot study. *J Bodyw Mov Ther.* 2012;16(2):217-223.
7. Mostamand J, Bader DL, Hudson Z. Reliability testing of the patellofemoral joint reaction force (PFJRF) measurement in taped and untaped patellofemoral conditions during single leg squatting: a pilot study. *J Bodyw Mov Ther.* 2011;15(4):502-506.

8. Ho KY, Blanchette MG, Powers CM. The influence of heel height on patellofemoral joint kinetics during walking. *Gait Posture.* 2012;36(2):271-275.
9. Chinkulprasert C, Vachalathiti R, Powers CM. Patellofemoral joint forces and stress during forward step-up, lateral step-up, and forward step-down exercises. *J Orthop Sports Phys Ther.* 2011;41(4):241-248.
10. Edmonds EW, Glaser DA. Adolescent Patella Instability Extensor Mechanics: Insall Extensor Realignment Versus Medial Patellofemoral Ligament Reconstruction. *J Pediatr Orthop.* 2015.
11. Grana WA, Kriegshauser LA. Scientific basis of extensor mechanism disorders. *Clin Sports Med.* 1985;4(2):247-257.
12. Heino Brechter J, Powers CM. Patellofemoral stress during walking in persons with and without patellofemoral pain. *Med Sci Sports Exerc.* 2002;34(10):1582-1593.
13. Steinkamp LA, Dillingham MF, Markel MD, Hill JA, Kaufman KR. Biomechanical considerations in patellofemoral joint rehabilitation. *Am J Sports Med.* 1993;21(3):438-444.
14. Panagopoulos A, van Niekerk L, Triantafillopoulos IK. MPFL reconstruction for recurrent patella dislocation: a new surgical technique and review of the literature. *Int J Sports Med.* 2008;29(5):359-365.
15. Koehle MJ, Hull ML. A method of calculating physiologically relevant joint reaction forces during forward dynamic simulations of movement from an existing knee model. *J Biomech.* 2008;41(5):1143-1146.
16. Lenhart RL, Thelen DG, Wille CM, Chumanov ES, Heiderscheit BC. Increasing running step rate reduces patellofemoral joint forces. *Med Sci Sports Exerc.* 2014;46(3):557-564.
17. Willson JD, Ratcliff OM, Meardon SA, Willy RW. Influence of step length and landing pattern on patellofemoral joint kinetics during running. *Scand J Med Sci Sports.* 2015.
18. Canham CD, Schreck MJ, Maqsoodi N, Doolittle M, Olles M, Elfar JC. A nondestructive, reproducible method of measuring joint reaction force at the distal radioulnar joint. *J Hand Surg Am.* 2015;40(6):1138-1144.
19. Ishii S, Palmer AK, Werner FW, Short WH, Fortino MD. Pressure distribution in the distal radioulnar joint. *J Hand Surg Am.* 1998;23(5):909-913.
20. Lapner PC, Poitras P, Backman D, Giachino AA, Conway AF. The effect of the wafer procedure on pressure in the distal radioulnar joint. *J Hand Surg Am.* 2004;29(1):80-84.
21. Miura T, Firoozbakhsh K, Cheema T, Moneim MS, Edmunds M, Meltzer S. Dynamic effects of joint-leveling procedure on pressure at the distal radioulnar joint. *J Hand Surg Am.* 2005;30(4):711-718.
22. Yang L, Cai G, Coulton L, Saleh M. Knee joint reaction force during tibial diaphyseal lengthening: a study on a rabbit model. *J Biomech.* 2004;37(7):1053-1059.

Derrick German

Preceptor(s) Name: Supriya Mohile, MD
Title: Understanding Barriers to Obtaining Oral Cancer Treatment and Their Impact on Patient Cancer Experience
Institution: University of Rochester Medical Center
Department: Geriatric Oncology

Understanding Barriers to Obtaining Oral Cancer Treatment and Their Impact on Patient Cancer Experience

Introduction:
The benefits of oral oncolytics include their ease of use, convenience, and generally well-tolerated side effect profiles as compared to traditional intravenous chemotherapy. Although the cost associated with oral oncolytic therapy is high and growing, research into patient preferences and quality of life issues indicates that patients prefer them to traditional intravenous chemotherapies. Studies evaluating adherence and oral oncolytics show an association between out of pocket expense, social support, treatment adherence, and treatment success. Currently there is little data describing the psychosocial impact of the financial burden associated with oral cancer medication and its influence on patient satisfaction and medication adherence.

Objective:
Through this study we hope to:
1. Assess how financial health impacts patient satisfaction and distress during oral oncolytic treatment.
2. Measure the psychosocial burden of financial toxicity in patient undergoing oral cancer treatment.
3. Identify patient characteristics or other factors associated with patterns of treatment satisfaction.
4. Document total time and resources used by healthcare professionals in assisting patients obtain oral cancer therapy.

Background:
Oral oncolytics are a relatively new form of anti-cancer therapy that account for roughly 25% of the oncology drug market.1 As insurance providers devise methods of controlling their use and cost, patients are placed at higher risk of out of pocket spending and consequently poor adherence and compliance to their cancer treatment plans.2 Although the cost associated with cancer care and oral oncotic therapy is high and growing, research into patient preferences and quality of life issue indicates that patients prefer oral chemotherapies as opposed to traditional intravenous chemotherapies.3

The benefits of oral oncolytics include their ease of use, convenience, and generally well-tolerated side effect profiles. It is important to note that because of the increased independence associated with oral oncolytic therapy, patients require a greater level of responsibility to properly and safely administer their own oral cancer treatments. Studies evaluating adherence and oral oncolytics show an association between adherence, cost, and treatment success.4 Studies have also shown that factors such as related side effects, out of pocket expense, and social support affect patient adherence.5

Methods:
The study population includes patients 18 years and older with solid tumor malignancy, other than breast cancer, who are prescribed an oral oncolytic at the University of Rochester Medical Center. Study participants are followed from the time oral cancer medication is prescribed until approximately 3 months after receipt of medication. Details are shown in figures 1 and 2 below.

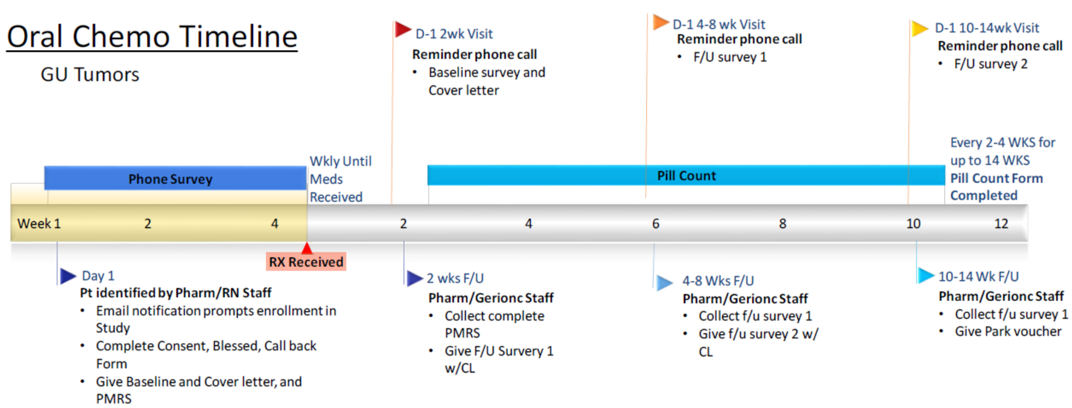


Figure 1: Oral chemo study time line for GU Tumors

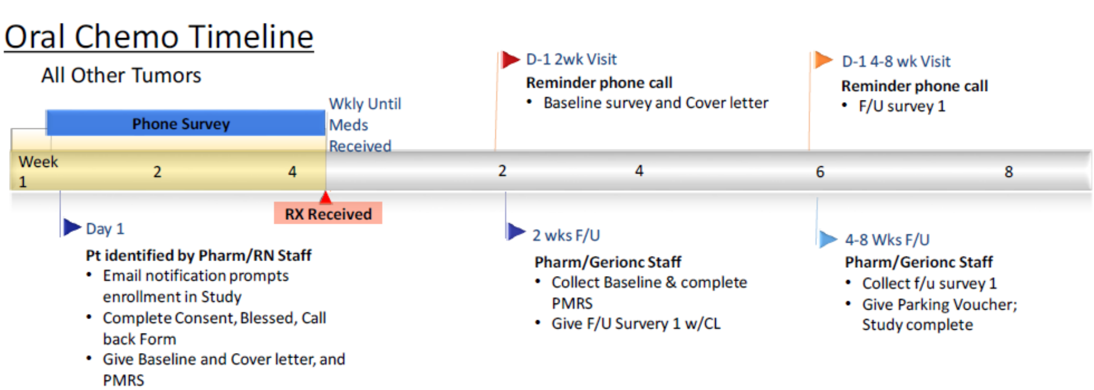


Figure 2: Oral chemo study time line for All other non-GU Tumors.

As illustrated in the figures, validated patient reported outcomes tools and interviews are used to measure the psychosocial impact of prescription wait time and to quantify financial burden, document side effect profile, and describe patient experience while taking medication.

Evaluation of medication adherence for patients with genitourinary malignancy was done by utilizing pill counts and a comprehensive review of medication regiment at monthly intervals.

Name	Assessment Components
Baseline Survey	Demographics, Finances, Geriatric Depression Scale, Distress Scale, OARS Medial Social Support, Comorbidity, Instrumental Activities of Daily Living
Telephone Survey	10-point worry scale regarding wait for oral cancer medication
Post Medication Receipt Survey	Medication Adherence Questionnaire, finances, healthcare related resources, NCNN Distress Management Survey, Press Gainey Questionnaire, PRO-CTCAE
Follow-up Survey	Medication Adherence Questionnaire, finances, healthcare related resources, NCNN Distress Management Survey, Press Ganey Questionnaire, PRO-CTCAE, CTSQ

	Patient Reported Outcomes Tool
BLESSED	Screening tool for cognitive impairment: Score >10 consistent with impairment
PRO-CTCAE	Patient self reporting medication side effect tool
Press-Ganey	Patient satisfaction survey on entire healthcare experience
CTSQ	Cancer Therapy Satisfaction Questionnaire: Evaluates patient's perspective on cancer specific therapy

Tables 1 and 2: Patient recorded outcome tools used to measure the psychosocial impact of prescription wait time and to quantify financial burden, document side effect profile, and describe patient experience while taking medication

Documentation of health care professional workload in assisting patients to receive oral cancer treatment is quantified using a questionnaire.

Bivariate and multivariable analyses will be incorporated to evaluate potential associations among clinical factors, patient reports, financial burdens, and psychosocial impacts of out of pocket costs, medication adherence, and certain patterns for prescription wait times or certain treatment recommendations.

Preliminary Results and Conclusions:

We anticipate finding that patients experience significant costs associated with taking oral oncolytic medications. We also expected to find that increased cost sharing and wait time for delivery of medication would result in higher psychosocial stress. Preliminary data however suggest that once medication is received, there is decreased in worry among study participants (average baseline worry scale score of 4.6 as compared to an average follow-up worry scale score of 2, where 10=extremely worried) (Table 3).

Characteristics	Frequency
Uroligoc Malignancy	N=17
Non-urologic Malignancy	N=26
Average Age	63.1 (48-81)
Race	
Caucasian	N=21
Non-caucasian	N=22
Health Care Provider Subjects	N=20
Baseline Worrry Scale 10=extremely worried	4.6 (0-10)
Follow Up Worry Scale 10=extremely worried	2 (0-10)

Table 3. Preliminary Study participant characteristics.

Preliminary findings examining personal characteristics and distress show that:

1. More patients with >80k reported no distress vs. distress. This association is not statistically significant but a bigger sample size might be warranted to determine an association.
2. There is no statistically significant association between marital status and distress.
3. Participants reporting distress had a mean age of 64.8 years old while those that did not report distress were on average 60.5 years old. There is no statistically significant relationship between the two groups (p=0.3795).

It is important to note these results are based on a small sample size and incomplete data set, and that further data analyze is needed.

Household Income	Not Distress	Distress
$0-19,000	0	1
$20,000-$39,000	2	1
$40,000-$59,000	1	1
$60,000-$80,000	0	1
> $80,000	8	3
Prefer Not to answer	0	1
Total	11	19
Fisher's test P=.4577		

Marital Status	Not Distressed	Distress
Married	9	9
Divorced	2	1
Total	11	10
	Fisher's test P= .4135	

	Mean Age of Particpants Reporting
Distress	64.8
Not Distressed	60.4545
	Satterthwaite P= 0.3795

Table 4-6. Preliminary results findings examining the association of distress with personal characteristics.

Although provider data was not assessed, we expect to find that assisting patients procure oral cancer medication is burdensome and time consuming for health care professionals.

Future work should look at further evaluating factors associated with poor medication adherence in patients taking oral cancer medications.

References

1-3. *Raborn ML, Pelletier EM, Smith DB, Reyes CM:* **Patient Out-of-Pocket Payments for Oral Oncolytics: Results From a 2009 US Claims Data Analysis**. J Oncol Pract 8(3 Suppl):9s-15s, 2012

4. Timmers L, Boons C, Magnus, D, Moes, JE, Swart EL, Boven E, Smit EF, Hugtenburg JG. **The Use of Erlotinib in daily Practice: a Study on Adherence and Patients' Experiences**. BMC Cancer 11:284, 2011

5. *Verbrugghe A, Verhaeghe S, Lauwaert K, Beekman D, Van Hecke A.* **Determinants and Associated Factors Influencing Medication Adherence and persistence to Oral Anticancer Drugs: A Systematic Review**. Cancer Treatment Reviews 39:610-621, 2013

6. *Teno JM, Lima JC, Lyons KD*. **Cancer patient assessment and reports of excellence: reliability and validity of advanced cancer patient perceptions of the quality of care.** Journal of clinical oncology : official journal of the American Society of Clinical Oncology 27:1621-6, 2009
7. Thi-MY-Uyen Nguyen, Adam La Caze, Neil Cottrell. **What are validated self-report adherence scales really measuring?: a systematic review.** British Journal of Clinical Pharmacology. 77:427-445, 2013
8. *Hay JL, Atkinson TM, Reeve BB, Mitchell SA, Mendoza TR, Willis G, Minasian LM, Clauser SB, Denicoff A, O'Mara A, Chen A, Bennett AV, Paul DB, Gagne J, Rogak L, Sit L, Viswanath V, Schrag D, Basch E; NCI PRO-CTCAE Study Group*. **Cognitive interviewing of the US National Cancer Institute's Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE).** Qual Life Res 23(1): 257-269, 2014
9. *Abetz L, Coombs JH, Keininger DL, Earle CC, Wade C, Bury-Maynard D, Copley-Merriman K, Hsu MA.* **Development of the cancer therapy satisfaction questionnaire: item generation and content validity testing**. Value Health. Dec;8 Suppl 1:S41-53, 2

Gold, Jillian and Piper, Keaton

Camille A. Martina, PhD,[1] Erik A. Rueckmann, MD,[2] and Ryan P. Bodkin, MD.[2]
University of Rochester Medical Center
[1]Department of Public Health Sciences
[2]Department of Emergency Medicine

Advanced rock climbers' management of climbing-related hand injuries.

Background and Introduction

Rock climbing is quickly becoming a popular sport. It is one of the fastest growing sports, with over six million people climbing in the United States alone (1). Although the sport is known for the potential for high impact falls, traumatic injuries are rare and much less common than overuse hand injuries (2). The sport has adopted remarkable safety practices, yet research studies still commonly report up to 80% injury rates (4, 5). These injuries primarily involve the hand, predominantly the A2 pulley.(5, 6). Climbing-related hand injuries often demand close attention to care and proper treatment for full recovery, yet most climbers fail to seek any medical care for their injuries, risking future debilitating conditions such as muscle contractures, invasive orthopedic surgeries, limited range of motion, and chronic pain that affects their everyday lives (2, 8, 9). In 2013, a study at the University of Vermont College of Medicine reported that of climbers with chronic injuries, 93% of them lived with significant pain and/or functional limitations (2). In an internal study at the University Rochester School of Medicine and Dentistry, more than 70% of climbers in the study reported injuries, of which only 31% were examined by a physician (10). Hand injuries negatively impact climbers' ability to pursue their lifelong passion and affect their day to day lives. With the increasing popularity in the sport, the importance of understanding, preventing and effectively treating these unique injuries becomes significant.

There are means of reducing the duration and intensity of these injuries. One study showed that all climbers with pulley injuries recovered to full strength and range of motion within one year when complying with the physician recommendations (6). There are effective means to facilitate full recovery from climbing-related hand injuries yet rates of seeking professional medical care as low as 31% in injured climbers (10). In order to connect injured climbers with effective healthcare, the first step is to identify the unknown barriers that prevent climbers from seeking healthcare for their injuries.

Therefore we asked two questions: 1) What informs advanced climbers' decisions to seek or not seek professional healthcare? 2) How do those who do not seek healthcare manage their injuries?

Objective

This study sought to determine the reasons why climbers decide to seek or not seek professional healthcare for their hand injuries as well as identify alternative treatment methods climbers are using.

Methods

Participants and setting

After Institutional Review Board approval, individuals were approached to participate in the study between May and July 2015. The study was conducted in the United States at seven popular climbing sites in Colorado and California (Table 1). Preliminary data was also collected at a climbing gym in Western New York State. The climbers were screened verbally by inclusion criteria: age above 18, have sustained a hand injury caused by climbing, climb at the advanced level (described below), and willingness and consent to participate in the study. The climbers were then asked to read an information sheet detailing the study and consent orally to a survey and interview

Advanced climbers were identified and determined for eligibility in our study based on these criteria: 1) climbing *onsight* at least at an ability of 5.10 on the *Yosemite Decimal System (YDS)*, or 2) bouldering *onsight* at least at an ability of V6 or above

Onsight climbing refers to a climber who completes a climbing route on a vertical face without having previously attempted the route, or had any information to direct the climber where/how to climb the route. The YDS is a method of rating the difficulty of climbs that commonly need a rope from 5.0 being the easiest to 5.15 being the most difficult. At the 5.10 level and above, routes are further divided into 5.10a, b, c, and d, with 5.10a being the easiest and 5.10d being the most difficult before 5.11. The YDS is used primarily for climbers with ropes including sport climbers (who attach their rope to fixed bolts on the wall for safety) and traditional climbers (who place their own gear, such as nuts and cams, rather than using pre-fixed bolts). The other type of advanced climbers included in this study included *boulderers* (climbers that do not use ropes or gear of any type and only climb up to a height at which they could safely come down from, commonly less than 20 feet). To assess the level of of an advanced *boulderer, the V Scale* is used rather than the YDS scale. The *V Scale* ranges from V0 (easiest) to V16 (most difficult). The *boulderers* included in this study could climb at or above a V6 level.

The eligible advanced climbers participating in the study were interviewed about why they chose to seek or not seek medical care for their injuries and what were the outcomes. For those who chose not to seek medical care, they were asked about their personal treatment regimens and sources of information.

Preliminary questionnaire
A preliminary questionnaire asked about the climber's demographics, climbing habits, general ideology on medical care and injuries, and each of their specific climbing-related hand injuries. The purpose of the questionnaire was to better define the sample population interviewed and guide the interview in a more efficient manner.

Quantitative Methodology
The responses to the questionnaires were compiled to detail the demographics of our participants as well as trends relating to their injuries and correlating management of care.

Qualitative Methodology
The surveys were quickly reviewed by the researchers before conducting the interviews. The interviews were conducted using an interview script as well as follow up questions regarding specific answers to the questionnaire and interview. The follow-up questions included respondent verification questions, to confirm appropriate interpretations of the responses. All interviews were recorded and transcribed. The transcripts were read and coded by two researchers, separately. The codes were compared and discussed for each interview and compiled into agreed-upon themes into a template. Themes were then condensed into categories. The main codes were then generated by tallying the number of climbers whose responses fell under each category.

Results
Response Rate
Sixty climbers were approached and 28 eligible participants consented to participate in the study.

Demographics
Twenty eight climbers participated in the study, 26 men and 2 women ranging from age 22 to 66. The average climber was 33 years old began climbing at age 19, climbs 13 hours a week for 41 weeks per year and climbed at this frequency for 10 years. Climbers reported *onsight* climbing between 5.10c and 5.13b on YDS. *Boulderers'* skill level ranged from *onsight* climbing V7 to V14. Of the 28 climbers interviewed, 13 had occupations that required them to rock climb at an advanced level. Nine reported not having health insurance at the time of injury.

Study participants were from 11 U.S. states (CO, CA, NC, GA, OH, UT, NY, NM, WV, MN, & TX) and reported they most often climbed in 11 U.S. states (CO, CA, AZ, UT, NV,VA, NC, WV, NY, NM, AL).

Coding Results

Why, and under what conditions, do climbers seek professional healthcare for their hand injuries?

1. A serious medical intervention is required, including stitches, surgery, trauma, dislocation (16 climbers)
2. If self-treatment has not yielded the desired results, including seeing a doctor as a last resort, and seeing a doctor for the purpose of faster recovery in competitive situations (15 climbers)
3. If there were a provider whom the climber trusted, including providers the climber has had a previous relationship with, providers who are open to learning about climbing, and providers who themselves are climbers (6 climbers)

Why, and under what conditions, do climbers choose not to seek professional healthcare?

1. Trust in their own knowledge and the knowledge of the climbing community (16 climbers)
2. Belief that seeing a professional is not necessary, including the belief that the injury will heal on its own, and the belief that the injury is not serious (10 climbers)
3. Belief that doctors do not know how to help with these types of injuries (10 climbers)

Where do climbers seek care and information on how to treat their climbing related hand injuries?

1. Own knowledge and peer knowledge, including personal experience with previous injuries applied to current injuries, knowledge gained from medical classes, friends' experience with injuries, and general advice from other climbers. (20 climbers)
2. Media, including climbing magazines, podcasts, books, google searches (17 climbers)
3. Physical therapists, including 3 who have seen PT in the past, and 9 who indicated they would theoretically in the future but have not in the past (12 climbers)

What are the main lessons climbers have learned from their experiences with hand injuries?

1. Take more rest after the injury, with varied definitions of rest (16 climbers)
2. Rest immediately after the injury, with emphasis on not doing another route to finish the day (7 climbers)
3. Importance of avoiding certain hand positions or moves to prevent injury (7 climbers)

Conclusion

Seventeen out of 28 climbers chose not to seek any professional healthcare for their hand injuries. These climbers preferred to seek treatment and advice from within the climbing community. They trusted their peers and climbing media for information more than they trusted medical providers. Climbers who did seek medical attention for their hand injuries were more likely to do so after repeated or worsening injuries, and were more likely to seek care from a physical therapist over other types of healthcare providers.

This data is important because it confirms the high prevalence of climbers with climbing-related hand injuries that fail to seek professional medical care. Along with the high incidence of retrospective adjustments the participants would implement to their treatment plan, this data shows that many climbing-related hand injuries are being sub-optimally treated. Furthermore, the study showed that climbers were seeking care through other venues which could be used as future means to disseminating treatment and prevention therapies

References

1. Outdoor Industry Foundation. 2013 Outdoor Recreation Participation Study, Boulder CO. Outdoor Industry Foundation, 2013
2. Schoffl V, Morrison A, Schwarz U, Schoffl I, and Kupper T. Evaluation of injury and fatality risk in rock and ice climbing. *Sports Medicine.* 2010:20:8 657-679.
3. Folkl AA. Characterizing the consequences of chronic climbing related injury in sport climbers and boulderers. *Wilderness & Environmental Medicine*. 2013:24:153-158.
4. Logan AJ, Makwana N, Mason G, and Dias J. Acute hand and wrist injuries in experienced rock climbers. *British Journal Sports Medicine*. 2004:38:545-548.
5. Zafonte B, Rendulic D, and Szabo RM. Flexor pulley system: anatomy, injury, and management. *Journal of Hand Surgery.* 2014:39:12:2525-2533.
6. Kubiak EN, Klugman JA, and Bosco JA. Hand injuries in rock climbers. *Bulletin of NYU Hospital for Joint Diseases.* 2006:64:3(3):172-177.
7. Schoffl VR, Einwag F, Strecker W, and Schoffl I. Strength measurement and clinical outcome after pulley ruptures in climbers. *Medicine & Science in Sports and Exercise*. 2006:38:4:637-43.
8. Logan AJ, Mason G, Dias J, and Makwana N. Can rock climbing lead to Dupuytren's disease? *British Journal of Sports Medicine*. 2005:39:639-44.
9. Wyatt JP, McNaughton GW, and Grant PT. A prospective study of rock climbing injuries. *British Journal of Sports Medicine*. 1996:30:148-150.
10. Furst-Nichol N, and Mirabelli M. Injury patterns and healthcare utilization among rock climbers in North America. Abstracts from Basic Science, Clinical, & Translational Research Summer Funding at University of Rochester. 2012:24-25.
11. Cohen RA, and Martinez ME. Health insurance coverage: early release of estimates from the national health interview survey January-March 2015. "*National Health Interview Survey Early Release Program CDC*. Division of Health Interview Statistics, National Center for Health Sciences. 2015.

Jennifer Hu

PI: Dr. Peter Wyman
Professor
University of Rochester School of Medicine
Department of Psychiatry

Motivating Factors for Youth Peer Leader Involvement in a School-Based, Suicide Prevention Program: A Qualitative Interview Study

Introduction: Peer-led health intervention programs are an innovative, community-based approach to disseminating information and improving health outcomes. The number of peer leaders recruited, the quality of their training sessions, and the setting for intervention conversations have all been shown to impact the effectiveness of such programs, though specific motivators for peer leader engagement and retention have received little attention in the literature.

Objectives: We examined motivators behind youth peer leaders' initial engagement and sustained participation (1-2 years) in a school-based, suicide prevention program, 'Sources of Strength.'

Methods: Structured interviews were conducted with thirty-five peer leaders from six different schools in upstate New York (these schools and peer leaders were identified from a larger study population, consisting of 798 peer leaders from 20 schools). All interviews were recorded and transcribed verbatim. Responses to questions pertinent to the study were identified and coded. We used Self-Determination Theory as a foundation because it provided a useful framework for intrinsic motivation analysis; operationalizations based on Ryan and Deci's definitions were developed, and exemplar quotes identified to guide our coding process. We left the option of "open coding" available for any additional themes.

Results: Youth peer leaders reported competence (34/35), relatedness (29/35), and the desire to help others (29/35) were the major reasons why they joined and continue to participate in Sources of Strength. Several noted they were proud of being able to help others and make a difference in their schools. Autonomy (10/35) and having fun (10/35) also emerged as themes and, to a lesser extent, an increase in status (4/35).

Conclusions: This study suggests competence, relatedness, and the desire to help others are particularly important for youth peer leader engagement, though having fun, autonomy, and an increase in status may play a role. Future peer-led health intervention programs should seek to directly address these sources of motivation to improve their recruitment, sustainability, and outcomes.

This qualitative study will supplement a larger mixed methods project. The research team is currently in the process of using social network analysis and quantitative methods to provide additional information on strong peer leader involvement among high-school aged youth.

References:

Kelly, J.A. (2004). Popular opinion leaders and HIV prevention peer education: resolving discrepant findings, and implications for the development of effective community programmes. *AIDS Care*, 16(2): 139-50.

Ryan R.M. & Deci E.L. (2000). Self-determination theory and the facilitation of intrinsic motivation, social development, and well-being. *American Psychologist*, 55(1): 68-78.

Wyman P.A., Brown C.H., LoMurray M., Schmeelk-Cone K., Petrova M., Yu Q., Walk E., Tu X., Wang W. (2010). An outcome evaluation of the Sources of Strength suicide prevention program delivered by adolescent peer leaders in high schools. *American Journal of Public Health*, 100(9): 1653-16661.

Kantorowska, Agata

Preceptors:
Henry C. Lee, MD, MS
Stanford University
Assistant Professor, Department of Pediatrics (Neonatology)
Director of Research, California Perinatal Quality Care Collaborative

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) infants[7], 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) <u>Donor human milk availability in California NICUs is increasing overall</u>. 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) <u>The availability of donor human milk in a hospital is correlated with an increase in the rate of breastfeeding at discharge among VLBW infants</u>. 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) <u>The availability of donor human milk in a hospital is correlated with a decrease in the rate of NEC among VLBW infants</u>. 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) <u>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</u>. 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.

Michael Kelly

Preceptor(s) Name: Dr. Aaron Boes MD, PhD
Title: Baer Fellow for Non-invasive Brain Stimulation
Institution: Berenson Allen Center for Non-invasive Brain Stimulation,
Beth Israel Deaconess Hospital, Boston, MA
Department: Neurology

Response to first course of TMS treatment for depression predicts subsequent response

Abstract:
Multiple trials have established the efficacy of using repetitive transcranial magnetic stimulation (rTMS) for the treatment of major depression. For those who respond favorably to rTMS it remains an open question how best to maintain the therapeutic response over time. One possibility is initiating a second rTMS treatment course when symptoms recur (reinduction), but the efficacy of this approach has not been systematically investigated. Here, we performed a retrospective review of our clinical database to assess the efficacy of reinduction for recurrence of depression symptoms, as assessed by change in the Beck Depression Inventory (BDI). 16 courses of reinduction were performed in 13 patients. This cohort was enriched with patients that had a favorable response to the initial treatment course with an average reduction in BDI of 60%. Importantly, treatment response to reinduction as assessed by the BDI was significantly predicted by the response to the initial course. As such, patients who achieve therapeutic benefit from rTMS on their initial treatment course are likely to achieve similar benefits if symptoms recur.

Introduction:
Major depressive disorder (MDD) is highly prevalent and has a devastating impact on the depressed individual, as well as a major societal impact[1]. Of individuals with MDD, 20-30% do not respond to available treatment[2] and often develop treatment resistant depression (TRD). Repetitive transcranial magnetic stimulation (rTMS) has emerged as a safe and effective therapeutic option for TRD[3–7]. RTMS is a noninvasive brain stimulation technique that uses electromagnetic energy to induce an electric current in the brain, using a magnetic field to penetrate the scalp and skull[8]. Current guidelines recommend 30 sessions of 10 Hz rTMS of the left dorsolateral prefrontal cortex (DLPFC) over the course of 4-6 weeks as a treatment for patients with TRD,[3] with three devices with FDA clearance for this indication. Using these treatment guidelines in patients who have failed at least one anti-depressive medication has shown that about half of the patients will have a 50% or greater reduction in depressive symptoms, and 29% will achieve a full remission of symptoms[9,10]. The efficacy of rTMS therapy, along with its low side-effect profile[11], makes it an appealing treatment option for the TRD.

The vast majority of evidence regarding the use of rTMS for TRD has focused on response to a 4 – 6 week course of treatment relative to a sham treatment[3]. Much less has been done to assess how best to maintain the therapeutic benefits in those who have a favorable response. There are reports of the effects lasting several months, typically in patients who also take medications[12]. There have been a few reports suggesting that less frequent rTMS treatment sessions at weekly or biweekly intervals may be helpful[13,14]. A topic that has received less research is the efficacy of initiating another treatment course of rTMS upon symptom recurrence. It has been suggested that those who respond to the initial TMS treatment are more likely to respond to TMS if it is reintroduced. For example, Dunner et al showed that the effects of rTMS were more favorable in those who previously responded to a course of rTMS relative to those in whom rTMS was previously less successful[12].

In this article we perform a retrospective chart review to identify patients who received two or more treatment courses of rTMS from our Center. We evaluated whether the response to the first treatment course predicts response to subsequent courses, which we term reinduction.

Methods:

A retrospective chart review of 225 patients receiving rTMS for treatment resistant depression was performed. We identified all patients who underwent a course of rTMS using standard treatment protocols (4 – 6 weeks of daily high frequency 10 - 20 Hz rTMS to the left dorsolateral prefrontal cortex) and underwent subsequent reinduction, defined here as ≥3 treatment sessions per week for at least 2 weeks and up to 2 months, or 30 sessions. Only patients with pre- and post-treatment Beck Depression Inventory (BDI) data were included. Responders were defined as having a 50% reduction in BDI scores over the course of treatment[15].

A multivariate regression model was used to identify variables that predict percent BDI change during a course of reinduction. Variables evaluated included: age, number of treatment sessions, days between inductions, presence of maintenance sessions, and severity of depression. Variables with some predictive value ($p \leq 0.20$) were entered into the final regression model. Statistical analyses were performed using PSPP (psppire 0.8.3, Free Software Foundation).

Results:

Data from 225 patients was reviewed and 13 met the inclusion criteria as outlined above, with two or more courses of rTMS. Of these, 3 patients had more than one reinduction course and thus 16 courses of reinduction were analyzed. Patient demographic and response to treatment data are provided in Table 1.

Of the 12 patients with a significant response to the reinduction rTMS course (>50% reduction in BDI), 9 came from patients who were responders to the first induction. The remaining three cases were from patients who had a mild response (40-49.9% reduction in BDI) to first induction (Figure 1). 82% (9/11) of responders to initial treatment also responded to the reinduction course. The results of the statistical analyses further underscored the relationship between first induction response and reinduction response. The Pearson correlation coefficient between percentage change in BDI across the first induction and percentage change in BDI across the reinduction was found to be 0.50 ($p=0.05$). The strongest predictor of percentage change in BDI at reinduction was the change in BDI with the initial treatment session, based on multiple regression model (Table 2). The overall model predicting re-induction percentage was shown to be significant, with an R value of 0.77 ($p=0.03$), and explained 44% of the variance in the primary outcome variable (adjusted $R^2 = 0.44$).

Anyalysis performed using only each patient's second TMS induction yielded similar results. Pearson correlation coefficient, as described above, was 0.47 ($p=0.11$). The multiple linear regression model using the same variables as above was significant and explained 51% of the variability in the primary outcome (adjusted $R^2=0.51$, $p=0.04$). However, while the predictive value of first induction percentage reduction in BDI was the largest of the studied variables, it was not statistically significant ($p=0.06$).

Discussion:

These results support and extend Dunner's prior conclusion that benefit from an initial course of rTMS for TRD is a predictor of response to subsequent courses of treatment[12].

We have shown that change in BDI over the course of an initial course of rTMS is correlated with the change in BDI over subsequent courses, and this variable is more predictive than other variables that could be predictive, such as pre-treatment BDI. This finding makes intuitive sense, that responders in the past are likely to be responders in the future, yet is necessary to establish as this result has definite implications for determining treatment plans for patients with TRD that have previously responded to rTMS. The results were similar using only patients second inductions as well as when using all subsequent rTMS inductions, supporting this notion.

This work has a number of limitations. Foremost, this is a small sample that is skewed toward those who were initially successful with their TMS treatment course. As such, our analysis is not well powered to assess whether a lack of response to the initial rTMS course is a predictor of not responding to subsequent courses of rTMS. Furthermore, the patients studied wherein were identified via chart review and represent a heterogeneous group that received open-label treatments using non-uniform treatment protocols. Despite these issues, we believe this result if noteworthy and should spur further investigation of this topic, ideally in a prospective trial with controlled treatment parameters. Doing so would represent a great step forward for the field.

Table 1. Demographic information showing differences between initial and subsequent rTMS inductions.
The table shows the similarity between the first and subsequent rTMS inductions. All differences between the inductions were within the calculated standard deviation. Overall the average reduction in BDI across both the first treatment course and reinduction was 60%.

	Unstandardized Coefficents B	Standardized Coefficients Beta
Constant	111.05±44.23	0.00*
Gender	12.72±14.19	0.20
Age at reinduction	-1.61±0.86	-0.45
Days between inductions	0.00±0.01	-0.11
Percent response to first induction	0.61±0.23	0.60*

Table 2. Multiple regression model including all eligible reinducitons.
The multiple regression model predicted 44% of the variability in percent change of BDI over a course of reinduction rTMS and was statistically significant ($p=0.03$). Percent response to first induction exhibited the largest standardized coefficient (0.60), which was significant at ($p=0.03$). No other variable was shown to exhibit significant predictive value in the model.

	First Treatment Course	Reinduction
Age (years, mean±SD)	52.9±9.9	55.1±9.0
rTMS sessions in treatment (mean±SD)	21.1±6.6	22.1±7.9
Initial BDI (mean±SD)	31.7±11.6	26.7±11.4
% Change in BDI (mean±SD)	60.1±31.1	59.6±31.8
Responder (%)	68.8	75.0

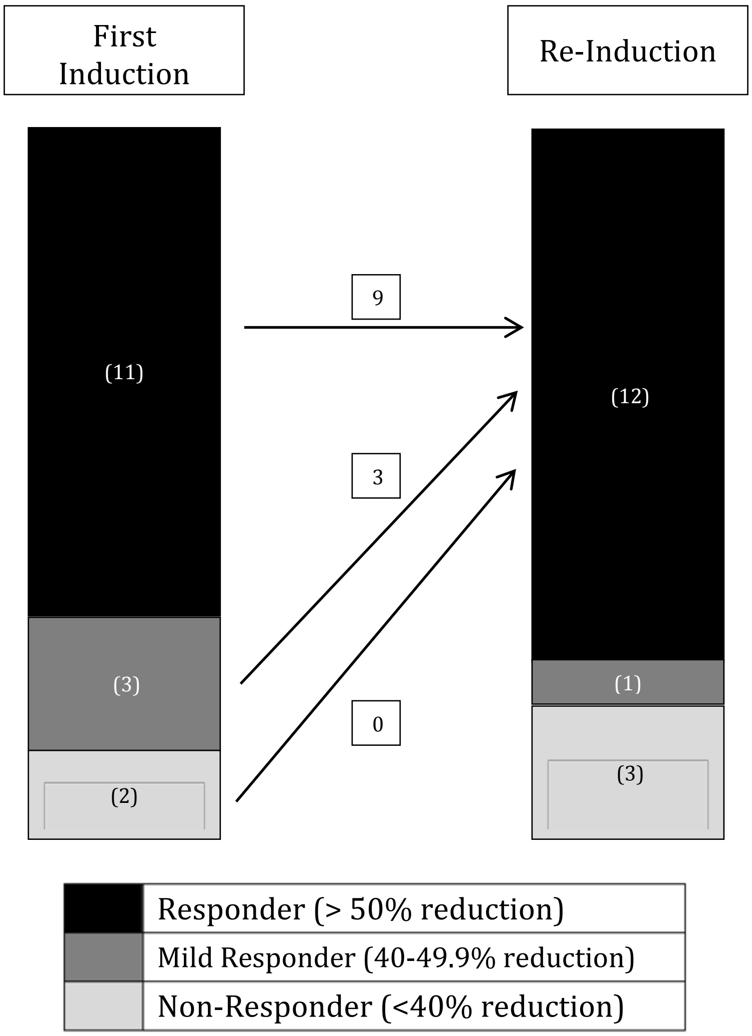


Figure 1. Responses to Reinduction. There were 12 cases of response to reinduction and 9 came from those who responded initially, while the other 3 were from near responders. No patients who were non-responders initially became responders upon reinduction. Overall, 9/11 responders to the initial course of rTMS were responders to reinduction.

References:

1. Kessler RC, Berglund P, Demler O, et al. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). *JAMA*. 2003;289(23):3095-3105. doi:10.1001/jama.289.23.3095.

2. Bentley SM, Pagalilauan GL, Simpson S a. Major Depression. *Med Clin North Am*. 2014;98(5):981-1005. doi:10.1016/j.mcna.2014.06.013.

3. Lefaucheur J-P, André-Obadia N, Antal A, et al. Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS). *Clin Neurophysiol*. 2014;125(11):2150-2206. doi:10.1016/j.clinph.2014.05.021.

4. Rossi S, Hallett M, Rossini PM, Pascual-Leone A. Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. *Clin Neurophysiol*. 2009;120(12):2008-2039. doi:10.1016/j.clinph.2009.08.016.

5. Magstim. Rapid2 Therapy System. *510(k) Summ*. 2015. http://www.accessdata.fda.gov/cdrh_docs/pdf14/K143531.pdf. Accessed January 1, 2015.

6. Neuronetics. Neuronetics: NEUROSTAR TMS THERAPY® SYSTEM. *510(k) Summ*. 2008:0027-0031. http://www.accessdata.fda.gov/cdrh_docs/pdf8/k083538.pdf. Accessed July 1, 2015.

7. Brainsway. BRAINSWAY DEEP TMS SYSTEM. *510(k) Summ*. 2013.

8. Wagner T, Valero-Cabre A, Pascual-Leone A. Noninvasive human brain stimulation. *Annu Rev Biomed Eng*. 2007;9:527-565. doi:10.1146/annurev.bioeng.9.061206.133100.

9. Liu B, Zhang Y, Zhang L, Li L. Repetitive transcranial magnetic stimulation as an augmentative strategy for treatment-resistant depression, a meta-analysis of randomized, double-blind and sham-controlled study. *BMC Psychiatry*. 2014;14:342. doi:10.1186/s12888-014-0342-4.

10. Carpenter LL, Janicak PG, Aaronson ST, et al. Transcranial magnetic stimulation (TMS) for major depression: a multisite, naturalistic, observational study of acute treatment outcomes in clinical practice. *Depress Anxiety*. 2012;29(7):587-596. doi:10.1002/da.21969.

11. Janicak PG, O'Reardon JP, Sampson SM, et al. Transcranial magnetic stimulation in the treatment of major depressive disorder: a comprehensive summary of safety experience from acute exposure, extended exposure, and during reintroduction treatment. *J Clin Psychiatry*. 2008;69(2):222-232. http://www.ncbi.nlm.nih.gov/pubmed/18232722. Accessed July 27, 2015.

12. Dunner DL, Aaronson ST, Sackeim HA, et al. A multisite, naturalistic, observational study of transcranial magnetic stimulation for patients with pharmacoresistant major depressive disorder: durability of benefit over a 1-year follow-up period. *J Clin Psychiatry*. 2014;75(12):1394-1401. doi:10.4088/JCP.13m08977.

13. Richieri R, Guedj E, Michel P, et al. Maintenance transcranial magnetic stimulation reduces depression relapse: a propensity-adjusted analysis. *J Affect Disord*. 2013;151(1):129-135. doi:10.1016/j.jad.2013.05.062.

14. Levkovitz Y, Isserles M, Padberg F, et al. Efficacy and safety of deep transcranial magnetic stimulation for major depression: a prospective multicenter randomized controlled trial. *World Psychiatry*. 2015;14(1):64-73. doi:10.1002/wps.20199.

15. Reeves GM, Rohan KJ, Langenberg P, Snitker S, Postolache TT. Calibration of response and remission cut-points on the Beck Depression Inventory-Second Edition for monitoring seasonal affective disorder treatment outcomes. *J Affect Disord*. 2012;138(1-2):123-127. doi:10.1016/j.jad.2011.12.003.

Thomas Kemp and Deborah Paul

Preceptors Name: John Elfar, MD; Wejiing Zeng, MD
Title: Associate Professor, Department of Orthopaedics; PGY4 Orthopaedic Resident
Institution: University of Rochester School of Medicine and Dentistry
Department: Orthopaedics

Prosthetic Joint Infections in Patients Undergoing Carpal Tunnel Release

Introduction: According to the National Center for Health Statistics, there are approximately 260,000 Americans affected by carpal tunnel syndrome each year. For carpal tunnel patients, it is suggested that risks for postoperative infections increase with a history of a past prosthetic joint replacement. The American Academy of Orthopedic Surgeons recommends antibiotic prophylaxis for patients undergoing an invasive procedure who have had a prosthetic joint replacement. Prosthetic joint infections are possible complications of upper and lower extremity arthroplasty where a pathogen affects the area surrounding the prosthetic joint or where a small open channel is found in communication with the prosthetic joint. The consequences of prosthetic joint infection can be devastating, including multiple surgeries, prolonged antibiotic therapy, and loss of limb, or death. However, recent trends in hand surgery have moved away from antibiotic prophylaxis for routine carpal tunnel releases, as the rate of surgical site infection is 0.35%, and has not been demonstrated to be improved with prophylaxis.

Objective: It is our hypothesis that the rate of prosthetic joint infection is no greater from the reported incidence in the literature of 2% or is negligible in patients undergoing carpal tunnel release despite the lack of antibiotic prophylaxis. It is our hope that findings from this project will have significant implications in hand surgery and total joint arthroplasty to help guide the standard of care for the thousands of patients that have total joint arthroplasties and who will undergo a carpal tunnel release each year.

Methods: 2,914 patients aged 18 years or older were selected who have received a carpal tunnel release at the University of Rochester Medical Center between the dates of 1/1/2012 12/31/2014 with no gender, racial or ethnic origin restrictions. Patients were selected on the basis of having a history of total hip, knee and/or shoulder replacement along with a carpal tunnel release. Patient charts were evaluated and coded for relevant past medical and surgical history, risk factors and comorbidities, usage of perioperative antibiotics and the outcome of a prosthetic joint infection or upper extremity surgical wound infection within six months of having a carpal tunnel release.

Results: Out of 2,914 carpal tunnel release surgeries performed in the University of Rochester system between the dates of 1/1/2012-12/31/2014, 275 of those were of patients with previous total hip, knee, and/or shoulder arthroplasty. Of those 275 procedures, 43 received preoperative antibiotics, 12 received postoperative antibiotics. Of the 12 who received postoperative antibiotics, 2 were immunocompromised individuals and 5 had a surgical-site infection; none of the 12 lead to a post-operative prosthetic joint infection. One patient was excluded from the study for having a prosthetic joint infection prior to their carpal tunnel release. The remaining 220 cases received no perioperative antibiotics. There were no prosthetic joint infections in any group of patients, including those that received no prophylaxis and those who had received preor post-operative antibiotics. In up to 116 procedures, the surgeon was unaware of the patient's total joint arthroplasty.

Conclusion: The rate of prosthetic joint infection is 2%. In our population of patients with prosthetic joints undergoing carpal tunnel release, there was a 0% rate of prosthetic joint infection. There was no difference in outcome between patients who received preoperative antibiotics and those who received none, regardless of physician knowledge of prior total joint arthroplasty. Given these data, prophylactic antibiotics may not be indicated in carpal tunnel releases even with the presence of a prosthetic joint.

References:

1. American Academy of Orthopaedic Surgeons. Antibiotic Prophylaxis for Patients after Total Joint Replacement. (Type 1):1-3.
2. Berbari EF, Osmon DR, Carr A, et al. Dental procedures as risk factors for prosthetic hip or knee infection: a hospital-based prospective case-control study. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America. 2010;50(1):8-16.
3. Bykowski MR, Sivak WN, Cray J, et al. Assessing the impact of antibiotic prophylaxis in outpatient elective hand surgery: a single-center, retrospective review of 8,850 cases. The Journal of hand surgery. 2011;36(11):1741-7.
4. Illingworth KD, Mihalko WM, Parvizi J, et al. How to minimize infection and thereby maximize patient outcomes in total joint arthroplasty: a multicenter approach: AAOS exhibit selection. The Journal of bone and joint surgery. American volume. 2013;95(8):e50.
5. Kuehnert MJ, Kruszon-Moran D, Hill HA, et al. Prevalence of Staphylococcus aureus nasal colonization in the United States, 2001-2002. The Journal of infectious diseases. 2006;193(2):172-9.
6. Lalani T, Chu VH, Grussemeyer CA, et al. Clinical outcomes and costs among patients with Staphylococcus aureus bacteremia and orthopedic device infections. Scandinavian Journal of Infectious Diseases. 2008;40(11-12):973-977.
7. LaPorte DM, Waldman BJ, Mont MA, Hungerford DS. Infections associated with dental procedures in total hip arthroplasty. The Journal of bone and joint surgery. British volume. 1999;81(1):56-9.
8. Murdoch DR, Roberts SA, Fowler VG, et al. Infection of Orthopedic Prostheses after Staphylococcus aureus Bacteremia. Clinical Infectious Diseases. 2001; 32 (4):647-649.
9. Parvizi J, et al. Management of Periprosthetic Joint Infection: The Current Knowledge. The journal of bone and joint surgery. 2012 Jul 18;94(14):e104
10. Young H, Hirsh J, Hammerberg EM, Price CS. Dental disease and periprosthetic joint infection. The Journal of bone and joint surgery. American volume. 2014;96(2):162-8.
12. Zimmerli W. Infection and musculoskeletal conditions: Prosthetic-joint-associated infections. Best practice & research. Clinical rheumatology. 2006;20(6):1045-63.

Kim, Beom Soo

Precptor
Gerald I. Shulman, MD, Ph.D
Yale University School of Medicine
Departments of Internal Medicine, Cellular & Molecular Physiology, and HHMI

Antisense Oligonucleotide against Angiopoietin-Like 4 Reduces Body Weight Gain and Hepatic Steatosis in Fat-Fed Rats

Introduction

Non-alcoholic fatty liver disease (NAFLD) refers to hepatic steatosis due to causes other than excessive alcohol use. NAFLD is the most common liver disorder in developed countries, and its incidence is rising in parallel with that of obesity and diabetes.[1] NAFLD is associated with metabolic disease, and it has been shown that ectopic lipid deposition is directly linked with insulin resistance and diabetes.[2] Moreover, NAFLD can progress to non-alcoholic steatohepatitis (NASH), which is projected to overtake the viral hepatitis as the number one indication for liver transplant in the coming decades. In light of these trends, it will be critical to find new treatments for hepatic steatosis. .

Angiopoietin like 4 (ANGPTL4) is a multifunctional protein with several important roles in lipid metabolism. [3] As a PPARγ target, ANGPTL4 is induced during fasting to ensure proper distribution of fat over various tissues.[4] The full length ANGPTL4 molecule gets processed by proprotein convertase(PC) at the linker zone to produce an N-terminal coiled-coil domain and a C-terminal fibrinogen-like domain, each of which serves different functions.[5] Significant evidence has shown that the N-terminal coiled coil domain of ANGPTL4 inhibits lipoprotein lipase (LPL) inhibition by hindering the dimerization of LPL molecules.[4,6] Also, in vitro studies suggest that ANGPTL4 may play a synergistic role in activation of adipose lipolysis by glucocorticoids and catecholamines.[7] Thus, Angptl4 is a potential therapeutic target to alter lipid metabolism.

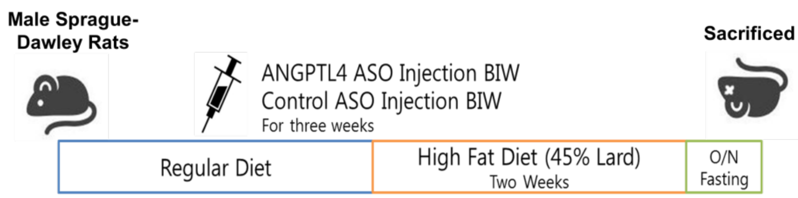
Objective

The objectives of this study were to assess the efficacy of an antisense ASO to decrease ANGPTL4 levels, and to assess the effect of ANGPTL4 knockdown on ectopic lipid deposition, PPAR target gene expression, and adipose lipolytic gene expression.

Methods

16 fat-fed (45% of calories from lard) male Sprague-Dawley rats received twice-weekly intraperitoneal injections of ANGPTL4 ASO or control ASO (40 mg/kg-week) for three weeks. Rats were fasted o/n and euthanized under isoflurane. Blood was collected from the IVC, and

tissues (liver, epididymal fat pad, and gastrocnemius) were collected and rapidly frozen in liquid nitrogen with pre-cooled aluminum tongs.



Blood samples were analyzed for plasma triglyceride, fasting plasma glucose, insulin, and free fatty acid concentrations with commercially available spectrophotometric assays. RNA was extracted from the collected tissues, and cDNA was prepared by reverse transcription PCR. mRNA expression was quantified by qPCR. Protein was extracted from each tissue, and protein abundance was assessed by Western immunoblotting.

Results

ANGPTL4 ASO treatment successfully knocked down ANGPTL4 RNA and protein expression in white adipose tissue and to a lesser degree in liver.

ANGPTL4 knockdown (KD) reduced body weight gain on high fat diet, and led to reduced epidydimal white adipose tissue mass. Also, hepatic triglyceride content was reduced by 36% ($P < 0.05$), while plasma triglycerides were reduced by 55% ($P < 0.001$). ANGPTL4 ASO treatment did not affect fasting glucose, fasting insulin, and non-esterified fatty acid (NEFA) contents in plasma. Additionally, PPARa target genes trended toward a decrease in liver (FGF21, ACSL1, ACSL3, G6Pase, ApoC3). Some PPARg target genes were significantly decreased in white adipose tissue (ATGL, DGAT), while others trended toward a decrease (c/ebp, LPL, srebp, scd1).

Enzymes that mediate adipocyte lipolysis, hormone sensitive lipase (Hsl) and Adipose Triglyceride lipase (ATGL) were found to be downregulated in ANGPTL4 ASO treated group. This led to reduced levels of phosphorylated adipocyte lipolytic enzymes, although there was no change in the ratio of the phosphorylated forms of the lipases to the total amount of the lipases.

The central genes of de novo lipogenesis (fatty acid synthase, steroyl CoA desaturase, and ATP citrate lyase) appear to be downregulated in the ANGPTL4 ASO treated rats.

Conclusion

ANGPTL4 ASO injection successfully knocked down ANGPTL4 expression in our animal model. This ANGPTL4 KD meaningfully brought down plasma and hepatic lipid content. Furthermore, the ANGPTL4 KD decreased adipocyte lipolytic machinery. Previous in vitro studies showed that

ANGPTL4 regulates intracellular lipases via phosphorylation. In contrast, our study showed that in vivo, the regulation of adipocyte intracellular lipases occurs at the level of gene and protein expression. Lastly, our study suggests that hepatic DNL pathways are also suppressed by ANGPTL4 KD. With the disinhibition of LPL activity, decreased intracellular lipolysis of adipocytes, and suppressed DNL activity, ANGPTL4 KD may successfully bring down plasma TG and consequently ectopic lipid deposition. However, the effect on body weight and WAT weight raises the concern for significant toxicity. Thus, further preclinical investigation is required before proposing ANGPTL4 inhibition as a viable pharmacologic target.

References

1. Rinella, Mary E. "Nonalcoholic Fatty Liver Disease." *Jama* 313.22 (2015): 2263. Web.

2. Shulman, Gerald I. "Ectopic Fat in Insulin Resistance, Dyslipidemia, and Cardiometabolic Disease." *New England Journal of Medicine N Engl J Med* 371.12 (2014): 1131-141. Web.

3. Zhu, Pengcheng, Yan Yih Goh, Hwee Fang Alison Chin, Sander Kersten, and Nguan Soon Tan. "Angiopoietin-like 4: A Decade of Research." *Bioscience Reports Biosci. Rep.* 32.3 (2011): 211-19. Web.

4. Dijk, Wieneke, and Sander Kersten. "Regulation of Lipoprotein Lipase by Angptl4." *Trends in Endocrinology & Metabolism* 25.3 (2014): 146-55. Web.

5. Lei, X., F. Shi, D. Basu, A. Huq, S. Routhier, R. Day, and W. Jin. "Proteolytic Processing of Angiopoietin-like Protein 4 by Proprotein Convertases Modulates Its Inhibitory Effects on Lipoprotein Lipase Activity." *Journal of Biological Chemistry* 286.18 (2011): 15747-5756. Web.

6. Yau, M.-H., Y. Wang, K. S. L. Lam, J. Zhang, D. Wu, and A. Xu. "A Highly Conserved Motif within the NH2-terminal Coiled-coil Domain of Angiopoietin-like Protein 4 Confers Its Inhibitory Effects on Lipoprotein Lipase by Disrupting the Enzyme Dimerization." *Journal of Biological Chemistry* 284.18 (2009): 11942-1952. Web.

7. Gray, N. E., L. N. Lam, K. Yang, A. Y. Zhou, S. Koliwad, and J.-C. Wang. "Angiopoietin-like 4 (Angptl4) Protein Is a Physiological Mediator of Intracellular Lipolysis in Murine Adipocytes." *Journal of Biological Chemistry* 287.11 (2012): 8444-456. Web.

Peter Krasniak

David Linehan
Chair, Department of Surgery
University of Rochester School of Medicine and Dentistry
Department of Surgery, Center for Tumor Immunology

Mechanism of Reduced Liver Metastasis in CCR2i Treatment of Pancreas Cancer

Introduction: Pancreas cancer (PC) has remained frustratingly difficult to treat despite advancements in therapeutics for many other malignancies, and PC with hepatic metastasis has a five-year survival of just 2.3%.[1]

Objective: Explore the mechanisms of reduction in liver metastasis during CCR2i treatment and develop a mouse model for the pre-metastatic and metastatic environment of the liver in pancreas cancer.

Background: The dense stroma of pancreas cancer and the cadre of immune cells that inhabit it help to confer the poor response to treatment of these cancers.[2] Specifically, tumor associated macrophages (TAMs), myeloid-derived cells differentiated from inflammatory monocytes (IMs), act to directly support tumor growth and suppress anti-tumor immunity.[3] Previously, the Linehan group has shown that increased IM egress from bone marrow, as measured by the ratio of blood IMs to bone marrow IMs, results in a poorer prognosis in patients with pancreas cancer. As IM mobilization is controlled via the CCL2/CCR2 chemokine axis, CCR2 blockade (CCR2i) was tested and shown in preclinical trials to decrease the blood to bone marrow IM ratio, reduce the size of the primary pancreatic tumor, and also to dramatically reduce the incidence of metastasis to the liver.[4]

Methods: For the pre-metastatic model, we injected cultured KCKO, a mice pancreas cancer cell line, into the tail of the pancreas of mice followed by CCR2i injection twice daily. After two weeks, livers were removed for analysis of pre-metastatic niche (macrophages and fibronection) and gene expression (RT-PCR). For the pancreas cancer liver metastasis model, we first established primary pancreatic tumors as in the previous model to induce pre-metastatic changes, making the liver hospitable to tumor cell colonization. Ten days post-implantation, we performed a hemisplenectomy followed by injection of luciferase labeled KCKO into the splenic blood vessels via the inferior pole of the hemispleen to establish micrometastatic disease. The primary tumor and inferior hemispleen were then resected. To study the efficacy of CCR2i in the treatment of micrometastatic disease, mice were randomized to treatment with vehicle, or CCR2i followed by luciferase imaging biweekly to detect recurrence in the liver. Liver specimens from CCR2i and vehicle treated mice were stained and assessed for immune cell composition (myeloid cells and lymphocytes) by FACS. Gene expression, including cytokines and chemokines were tested by real time PCR.

Results: The liver pre-metastasis model revealed that CCR2i creates a significant decrease in the cytokines IL10, TGFβ, and TNF, which overall implies a less tumorigenic environment in the liver. Additionally, pre-metastatic niche analysis displayed a dramatic decrease in macrophage infiltration and fibronectin deposition, indicating a liver with reduced metastatic potential in the treatment group. The liver metastasis model exhibited a significant decrease in immune cells associated with a pro-tumor environment (IMs, TAMs) in the CCR2i treatment group and a corresponding increase in $CD8^+$ cells, associated with an anti-tumor immune response. Finally, the gene expression of livers in the CCR2i group revealed a switch from a tumorigenic to an anti-tumor cytokine profile (decreased levels of IL6 and TNF) while also showing a dramatic increase in iNOS, again indicating the presence of a stronger anti-tumor immune response when treated with CCR2i.

Conclusions: In a preclinical mouse model, the treatment of pancreas cancer with CCR2 blockade shows promise as an immunotherapeutic regimen due to its ability to decrease incidence of liver metastasis. The most prominent mechanism indicated by these studies is the reversal of the suppression of anti-tumor immune responses through changing the cytokine profile as well as altering the immune cell composition in both the pre-metastatic and metastatic liver.

References: [1] R Siegel, et al. CA Cancer J Clin 2014;64:9–29. [2] C Clark, et al. Cancer Res 2007;78:9518-27. [3] J Mitchem, et al. Cancer Res 2013; 73:1128-41. [4] D Sanford, et al. Clin Cancer Res 2013;19:3404-13.

Kwak, Stephen

Joseph Miano, Ph.D.
Associate Professor
University of Rochester Medical Center
Department of Medicine, Aab Cardiovascular Research Institute

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 sequences[3]. 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 URMC 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, Coller 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)

Alcina Lidder

Bruce Tan, MD, MS, FACS
Assistant Professor, Department of Otolaryngology
Northwestern University- Feinberg School of Medicine

Li-Xing Man, MD, MPA
Assistant Professor, Department of Otolaryngology
University of Rochester School of Medicine and Dentistry

Evaluating Metrics of Responsiveness in Chronic Rhinosinusitis (CRS)

Introduction:

Chronic rhinosinusitis (CRS) is a heterogeneous disorder characterized by inflammation of the nose or paranasal sinuses for at least 12 weeks. It can be associated with nasal polyps (CRSwNP) or without nasal polyps (CRSsNP). The disease is defined based on the presence of specific symptoms, including facial pain or pressure, nasal discharge or post-nasal drip, nasal congestion, and loss of smell, and objective evidence of inflammation (1). CRS is a common disease: in 2007 an estimated 11 million adult patients reported having CRS, representing about five percent of the United States adult population (2). Living with CRS is often debilitating for patients and its primary morbidity is its effect on patients' quality of life (QOL).

Several disease-specific QOL instruments are commonly used in CRS, including the visual analog scale (VAS) and Sino-Nasal Outcome Test 22 (SNOT-22) (3). However there are limited studies examining general QOL impairment in CRS using measures of physical and social functioning and mental and emotional health. The Patient Reported Outcome Measurement Information System (PROMIS), developed by the NIH, has a validated question bank that can quantify the impact of CRS symptoms in the general QOL domains of physical function, fatigue, anxiety, depression, sleep disturbance, satisfaction with social role, pain interference, and pain intensity (4, 5). No existing studies examine the utility of the PROMIS-29 in CRS patients.

Objective:

We evaluated the responsiveness of disease-specific measures such as SNOT-22 and VAS scores in addition to PROMS-29 general QOL domains following standard-of-care (SOC) medical and surgical treatments for CRS.

Background:

Responsiveness, or sensitivity to clinical change, is an important consideration in the selection of patient reported outcome measures (PROMs) for research and clinical applications. While several PROMs have been used to measure outcomes in CRS, we are unaware of any

studies that examined the responsiveness of validated measures following medical or surgical therapy for CRS.

Methods:

Patients aged 18 to 89 with a CRS diagnosis who initiated SOC medical therapy (N=143) or underwent endoscopy sinus surgery (N=123) were recruited from a tertiary care center. Subjects completed the SNOT-22, VAS, and PROMIS-29 at baseline and three months following treatment. Responsiveness metrics such as Cohen's d (effect size) were calculated for these measures including individual SNOT-22 items and PROMIS-29 QOL domains.

Results:

Fifty-five (38.5%) subjects in the medical therapy group and 44 (35.8%) subjects in the surgical group completed both the baseline and post-treatment measures. Subjects who completed post-treatment questionnaires were similar with respect to baseline age, sex, polyp status, VAS score, and SNOT-22 total score compared to those who did not complete post-treatment questionnaires ($p > 0.05$). Disease-specific items were most responsive: VAS ($d = -0.58$, $p < .01$); total SNOT-22 score ($d = -0.70$, $p < .01$); and SNOT-22 Cardinal, a subset of SNOT-22 items including cardinal CRS symptoms ($d = -0.83$, $p < .01$) were most responsive for the medical therapy group and VAS ($d = -1.97$, $p < .01$); total SNOT-22 score ($d = -1.56$, $p < .01$); and SNOT-22 Cardinal ($d = -1.88$, $p < .01$) were most responsive for the surgery group. Responsiveness was greatest for the individual SNOT-22 items of runny nose ($d = -0.72$, $p < .01$); blockage/congestion of nose ($d = -0.69$, $p < .01$); and post-nasal drip ($d = -0.55$, $p < .01$) in the medical therapy group and blockage/congestion of nose ($d = -2.16$, $p < .01$); need to blow nose ($d = -1.16$, $p < .01$); runny nose ($d = -1.08$, $p < .01$); and sense of smell/taste ($d = -1.06$, $p < .01$) in the surgery group. Notably, every SNOT-22 item was significantly responsive in the surgical group. The general QOL domains of fatigue ($d = -0.82$, $p = .01$); sleep disturbance ($d = -0.83$, $p < .01$); and pain intensity ($d = -1.0$, $p < .01$) were most responsive in the surgical group.

Conclusions:

The most responsive measures were disease-specific QOL items such as SNOT-22 and VAS scores, with moderate to large effect sizes. The general QOL domains of fatigue, sleep disturbance, and pain intensity were significantly responsive in the surgical group but none were more responsive than disease-specific items. Our findings suggest that surgical management is associated with greater responsiveness, especially with respect to individual SNOT-22 items.

References:

1. Benninger MS, Ferguson BJ, Hadley JA, Hamilos DL, Jacobs M, Kennedy DW, et al. Adult chronic rhinosinusitis: definitions, diagnosis, epidemiology, and pathophysiology. *Otolaryngology- Head and Neck Surgery: Official Journal of American Academy of Otolaryngology-Head and Neck Surgery*. 2003;129(3 Suppl):S1-32.
2. Bhattacharyya N. Incremental health care utilization and expenditures for chronic rhinosinusitis in the United States. *Ann Otol Rhinol Laryngol.*Jul 2011; 120(7):423-7.

3. Rudmik L, Smith TL. Quality of life in patients with chronic rhinosinusitis. Curr Allergy Asthma Rep. Jun 2011;11(3):247-252.
4. Cella D, Riley W, Stone A, Rothrock N, Reeve B, Yount S, et al. Initial adult health item banks and first wave testing of the patient-reported outcomes measurement information system (PROMIS) network: 2005–2008. J Clin Epidemiol. Nov 2010;63(11):1179-94.
5. Gershon RC, Rothrock N, Hanrahan R, Bass M, Cella D. The use of PROMIS and assessment center to deliver patient-reported outcome measures in clinical research. J Appl Meas. 2010;11(3):304-14.

Jonathan Lin, BA; Lauren Broestl, BA, Kurtresha Worden, BA, Dan Wang, MD, MS.

Dena B, Dubal MD, PhD;
Department of Neurology, University of California San Francisco
Medical Student Training in Aging Research (MSTAR) Program
University of Rochester School of Medicine and Dentistry

Understanding the Function of Klotho in Alpha-Synuclein Transgenic Mice

Introduction: Epidemiologists estimate that Parkinson Disease (PD) affects over 4 million people worldwide and this number is projected to double by 2030 (2). Lewy bodies, aggregates of α-synuclein (α-syn) protein within neuronal cells, are suspected to contribute to PD by interfering with normal mitochondrial and synaptic functions (3). However, when longevity factor klotho (KL) is overexpressed in α-syn transgenic mice that model PD, our lab found that KL protects against cognitive and behavioral deficits.

Objective: The goal of my summer research was to study the molecular mechanism behind how KL protects against α-syn toxicity. Does overexpression of KL decrease pathogenic α-syn protein levels? Does KL preserve pre-synaptic proteins targeted by α-syn such as synapsin I? Or are other, unknown mechanisms involved?

Background: Previous work in our lab showed that elevating KL in mice that model Alzheimer's disease prevents premature morality and enhances cognition. KL did not alter human amyloid precursor protein or Aβ levels. However, KL did increase the number of GluN2B subunits of NMDA receptors in postsynaptic densities, enhancing long term potentiation, which is vital for learning and memory (1). We also found that KL is protective in a PD mouse model, however, it is unknown how KL exerts its effects at a molecular level.

Methods: We crossed hemizygous KL mice with hemizygous wild-type human α-syn (hSYN) mice to produce: non-transgenic (NTG), singly transgenic for KL or hSYN, and KL/ hSYN double transgenic mice. For our sample size we had 10-14 mice per experimental group. When these mice were between 8-13 months of age we perfused them with saline, extracted their brains and dissected out the hippocampus from the left hemisphere. The supernatant was then isolated from each sample and protein levels were assessed by BCA protein assay followed by Western Blot. Proteins were stained with primary antibodies against human α-syn, phosphorylated human α-syn, KL, synapsin I, actin, and β-tubulin. For each experiment, loading controls (tubulin and actin) were quantified independently to ensure that they did not differ among groups.

Results: We found that α-syn protein levels were equivalent among hSYN and KL/hSYN mice. We also found that hSYN decreases synapsin I levels (2 way ANOVA, $p<0.005$), and that KL fails to restore synapsin I back to NTG levels. Thus, despite high levels of α-syn and low levels of synapsin I, elevation of KL enhanced cognition and attenuated behavioral deficits in hSYN mice.

Conclusions. KL overexpression in mice confers resilience against α-syn toxicity through mechanisms that are independent of α-syn or synapsin I levels. Based off of our research, we believe that KL based therapeutics could counter the cognitive effects of α-syn in neurodegenerative diseases such as PD.

Funding was provided by the Medical Student Training in Aging Research Program (2T35AG026736-11) via AFAR (J.L.). Contributions from the NIA, AFAR, Glenn Foundation, and Weeks-Coulter and Bakar Foundations also supported the work (D.B.D.)

References

1. Dubal DB, Zhu L, Sanchez PE, Worden K, Broestl L, Johnson E, et al. Life extension factor klotho prevents mortality and enhances cognition in hAPP transgenic mice. J Neurosci. 2015;35: 2358–2371. doi: 10.1523/JNEUROSCI.5791-12.2015

2. Ross, G. W. and Abbott, R. D. (2014), Living and dying with Parkinson's disease. *Mov. Disord.*, 29: 1571–1573. doi: 10.1002/mds.25955

3. Xie, W. and Chung, K. K. K. (2012), Alpha-synuclein impairs normal dynamics of mitochondria in cell and animal models of Parkinson’s disease. Journal of Neurochemistry, 122: 404–414. doi: 10.1111/j.1471-4159.2012.07769.x

Magno, Jinno, MS2

Preceptor:
Jessica Shand, M.D., M.H.S.
Assistant Professor of Pediatrics
University of Rochester Medical Center
Pediatric Hematology/Oncology

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 children[1-3]. 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 ALL[4-6]. 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 (ΔMFI = 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 (ΔMFI = 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-kB pathways[9, 10]. Studies are underway to address whether chemotherapy treatment produces differences in NFkB 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 cancers[11], specifically chronic lymphocytic leukemia[12]. Future studies required measurement of TLR4 and it's 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).

Marini, Thomas

Preceptors: Kevin Fiscella, MD
Mechelle Sanders, BA
University of Rochester
Department of Family Medicine

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).

Ankit Medhekar

Preceptor:
Michael Stoner, MD
Institution: University of Rochester
Departments: Department of Vascular Surgery, Surgical Health Outcomes & Research Enterprise (SHORE)

Outcomes for Critical Limb Ischemia are Driven by Vascular Procedure Volume, Not Access to Care

Introduction

Critical limb ischemia (CLI) is defined as chronic ischemic rest pain, ulceration, or gangrene that can be proven to be attributed to occlusive artery disease1. A diagnosis of CLI may result in lower limb amputation or mortality. However, revascularization procedures have been shown to be effective in allowing limb salvage in CLI patients2. In addition, those who receive early revascularization are less likely to undergo an amputation3. Prior studies show that distance to a healthcare facility predicts utilization, which in CLI would presumably lead to better outcomes4-8. However, there is a paucity of data relating distance and health outcomes in CLI patients.

Objective

To identify relationships among geographic access to care, vascular procedure volume, limb preservation, and survival in patients diagnosed with CLI.

Background

Distance to a healthcare facility has been shown in many different areas to be a predictor of healthcare utilization. Prior research has found that distance can have impacts on interventions as varied as depression treatment and radiation therapy for breast cancer8,9. In all of the studies cited, a shorter distance to the treatment facility is associated with improved outcomes. We believed that a similar phenomenon would be observed in CLI care.

Methods

Using New York State administrative data from 2000-2013, we identified a patient's first presentation with CLI defined by ICD-9 diagnosis and procedure codes. Distance from the patient's home to the index hospital was calculated using the centroids of the respective zip codes. A multivariable regression model was employed to estimate the impact of distance or hospital vascular procedure volume on the risk of amputation and death while controlling for age, gender, zip code median income, population density, reimbursement type, and Elixhauser comorbidity score. Procedures and distances were analyzed in quintiles. The farthest distance quintile and the highest procedure volume quintile were used as references for generating odds ratios.

Results

49,576 patients were identified with an initial presentation of CLI. The median age was 72, 36,393 (73.4%) had Medicare as a primary insurer, and 32,746 (66.1%) had a diagnosis of diabetes. 11,395 (23.0%) had a major amputation and 4,249 (8.57%) died within 30 days of admission. Patients in the closest distance quintile were more likely to suffer 30-day mortality (odds ratio [OR] = 1.53, $p<.0001$) and undergo amputation (OR = 2.33, $p<.0001$). Patients who visited hospitals in the lowest procedure quintile faced higher 30-day mortality rates (OR = 1.77, $p<.0001$) and greater odds of amputation (OR = 3.15, $p<.0001$). Patients in the farthest distance quintile visited hospitals that performed 2.33 times ($p<.0001$) as many vascular procedures as patients in the closest distance quintile.

Conclusion

Rates of amputation and death are inversely associated with distance from the index hospital and vascular procedure volume. We believe that unless otherwise contraindicated, these data support selective referral of CLI patients to higher-volume centers regardless of distance. Within the context of value-based healthcare delivery, policy supporting regionalization of CLI care into centers of excellence may improve outcomes for these patients.

References

1. Schanzer A, Conte MS. Critical limb ischemia. Curr Treat Options Cardiovasc Med. 2010;12(3):214-229.
2. Henry AJ, Hevelone ND, Belkin M, Nguyen LL. Socioeconomic and hospital-related predictors of amputation for critical limb ischemia. J Vasc Surg. 2011;53(2):330-339 e331.
3. Faglia E, Clerici G, Clerissi J, et al. Early and five-year amputation and survival rate of diabetic patients with critical limb ischemia: data of a cohort study of 564 patients. Eur J Vasc Endovasc Surg. 2006;32(5):484-490.
4. Nemet GF, Bailey AJ. Distance and health care utilization among the rural elderly. Soc Sci Med. 2000;50(9):1197-1208.
5. Burgess JF, Jr., DeFiore DA. The effect of distance to VA facilities on the choice and level of utilization of VA outpatient services. Soc Sci Med. 1994;39(1):95-104.
6. Fortney JC, Booth BM, Blow FC, Bunn JY. The effects of travel barriers and age on the utilization of alcoholism treatment aftercare. Am J Drug Alcohol Abuse. 1995;21(3):391-406.
7. Schmitt SK, Phibbs CS, Piette JD. The influence of distance on utilization of outpatient mental health aftercare following inpatient substance abuse treatment. Addict Behav. 2003;28(6):1183-1192.
8. Nattinger AB, Kneusel RT, Hoffmann RG, Gilligan MA. Relationship of distance from a radiotherapy facility and initial breast cancer treatment. J Natl Cancer Inst. 2001;93(17):1344-1346.
9. Fortney J, Rost K, Zhang M, Warren J. The impact of geographic accessibility on the intensity and quality of depression treatment. Med Care. 1999;37(9):884-893.

Meng, Yifan

Marc Schermerhorn, MD
Beth Israel Deaconess Medical Center
Vascular Surgery

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)

Lalita Movva, MS2

Preceptors:
Jingbing Xue, M.D.
Assistant Professor
University of Rochester Medical Center
Department of Imaging Sciences

Adam Fang, M.D.
Radiology Resident, PGY-5
University of Rochester Medical Center
Department of Imaging Sciences

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:

5. 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.
6. 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.
7. Grieve RJ. Day surgery preoperative anxiety reduction and coping strategies. Br J Nurs 2002; 11(10):670–678.
8. 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.
9. 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.
10. Spaulding NJ. Reducing anxiety by pre-operative education: make the future familiar. Occup Ther Int 2003; 10(4):278–293.
11. 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.

12. 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.
13. 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.
14. Harned RK 2nd, Strain JD. MRI-compatible audio/visual system: impact on pediatric sedation. Pediatr Radiol 2001; 31(4):247-50.

Lam-Anh (Lamie) Nguyen

Preceptor Name: Maria Fagnano, MPH
Title: Associate Director of Clinical Research, Senior Health Project Coordinator
Institution: University of Rochester
Department: General Pediatrics

Preceptor Name: Jill S. Halterman, MD, MPH
Title: Division Chief, Co-Vice Chair for Research, Professor of Pediatrics
Institution: University of Rochester
Department: General Pediatrics

Caregiver Depression, Child Asthma Severity, and Preventive Care among Urban Children with Persistent Asthma

Background: Depression is prevalent among caregivers of urban children with asthma. There is evidence that caregiver depression affects communication with providers and self-efficacy in healthcare visits. It is unclear how depressive symptoms influence asthma severity and preventive care delivery at the time of an office visit for urban children with persistent asthma.

Objective: To compare asthma severity and the delivery of preventive asthma care at the time of an office visit for children of caregivers with and without depression, and assess persistence of symptoms in longitudinal follow-up.

Methods: We analyzed data from caregivers of children (2-12 years) with persistent asthma in the 6 control primary care practices of the PAIR-UP trial in urban Rochester, NY. Caregiver depression was measured using the Kessler Psychological Distress scale within 14 days of the index visit. We assessed asthma severity, asthma care actions occurring at an office visit, and symptoms and healthcare utilization at 2 month follow-up. Bivariate and multivariate analyses assessed associations for caregivers with and without depression.

Results: Overall, 297 caregivers were enrolled (participation rate 80%; 77% Minority race, 67% Medicaid insurance); 32% were depressed. Significantly more children of caregivers with depression had moderate/severe persistent asthma (70% vs 55%, p=.022) and had a caregiver who smoked (4% vs 27%, p=.001) compared to children of caregivers without depression. At the time of an office visit, providers were no more likely to ask about symptoms (58% vs 60%, p=.90), prescribe preventive medications (27% vs 22%, p=.386), or ask about triggers (42% vs 34%, p=.25) for children with vs. without depressed caregivers. These findings persisted in multivariate analyses controlling for baseline symptoms, reason for visit, and demographics. At 2 months, children of depressed caregivers continued to have on average fewer symptom-free

days/2 weeks (8.5 vs 10.1, p=.004), more days needing rescue medication (3.8 vs 2.5, p=.019), and more healthcare visits (.80 vs .48, p=.012).

Conclusions: Children of depressed caregivers clearly experience greater asthma severity and more smoke exposure than children of caregivers without depression. However, they are no more likely to receive guideline-based preventive asthma care at a healthcare visit. At follow-up, these children remained more symptomatic and had more healthcare utilization, highlighting missed opportunities for care and a critical need to reform practice to promote health equity in this urban population.

References

1. Akinbami LJ, Moorman JE, Liu X. Asthma prevalence, health care use and, mortality: United States, 2005–2009. Centers for Disease Control and Prevention National Health Statistics Reports. 2011 Jan 12.32:1–15. 2011.
2. Haselkorn T, Fish JE, Zeiger RS, et al. Consistently very poorly controlled asthma, as defined by the impairment domain of the Expert Panel Report 3 guidelines, increases risk for future severe asthma exacerbations in The Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens (TENOR) study. J Allergy Clin Immunol. 2009; 124(5):895–902. e1–e4.
3. Schmier JK, Manjunath R, Halpern MT, Jones ML, Thompson K, Diette GB. The impact of inadequately controlled asthma in urban children on quality of life and productivity. Ann Allergy Asthma Immunol. 2007; 98(3):245–251.
4. Moonie SA, Sterling DA, Figgs L, Castro M. Asthma status and severity affects missed school days. J Sch Health. 2006; 76(1):18–24.
5. Akinbami LJ, Moorman JE, Garbe PL, Sondik EJ. Status of Childhood Asthma in the United States, 1980–2007. Pediatrics. 2009; 123:S131–S145.
6. National Asthma Education and Prevention Program. Expert Panel report III: guidelines for the diagnosis and mangagment of asthma. Bethesda (MD): National Institutes of Health, National Heart, Lung, and Blood Institute; 2007. Publication No. 07-4051
7. Akinbami, L.J., LaFleur, B.J., Schoendorf, K.C. (2002). Racial and income disparities in childhood asthma in the United States. *Ambulatory Pediatrics, 2,* 382-387.
8. Bartlett SJ, Krishnan JA, Riekert KA, Butz AM, Malveaux FJ, Rand CS. Maternal depressive symptoms and adherence to therapy in inner-city children with asthma. Pediatrics. 2004; 113(2): 229–237.
9. Weil CM, Wade SL, Bauman LJ, Lynn H, Mitchell H, Lavigne J. The Relationship Between Psychosocial Factors and Asthma Morbidity in Inner-City Children With Asthma. Pediatrics. 1999; 104(6):1274–1280.
10. Silver EJ, Warman KL, Stein RE. The Relationship of Caretaker Anxiety to Children's Asthma Morbidity and Acute Care Utilization. J Asthma. 2005; 42(5):379–383.
11. Shalowitz MU, Berry CA, Quinn KA, Wolf RL. The Relationship of Life Stressors and Maternal Depression to Pediatric Asthma Morbidity in a Subspecialty Practice. Ambul Pediatr. 2001; 1(4): 185–193.
12. Davis JB. Neurotic illness in families of children with asthma and wheezy bronchitis: a general practice population study. Psychol Med. 1977; 7:305–310.
13. Kessler RC, Barker PR, Colpe LJ, et al. Screening for serious mental illness in the general population. Arch Gen Psychiatry. 2003; 60(2):184–189.
14. Andrews G, Slade T. Interpreting scores on the Kessler Psychological Distress Scale (K10). Aust N Z J Public Health. 2001; 25(6):494–497.

Jinhee K. Oh

Preceptors Names:
Peter A. Soden, MD
General Surgery Resident, PGY-3
Vascular Surgery Research Fellow
Beth Israel Deaconess Medical Center
Boston, MA

Marc L. Schermerhorn MD, FACS
Chief, Division of Vascular and Endovascular Surgery
Beth Israel Deaconess Medical Center
Associate Professor of Surgery
Harvard Medical School
Boston, MA

Comparison of Dorsalis Pedis Bypass and Percutaneous Transluminal Angioplasty as a durable, long-term repair for Critical Limb Ischemia

Introduction:

Critical limb ischemia (CLI) marks the latter stages of peripheral artery disease, presenting as lower extremity ischemic rest pain that is recurrent and persistent for at least two weeks, along with other clinical features of significantly reduced tissue perfusion1,2. These include gangrenous feet or toes, non-healing ulcers, and decreased systolic pressure at the ankle or toe, and pose a threat of limb loss1,2. The etiology is thought to largely be due to atherosclerosis at infrapopliteal vessels3. This condition is of particular concern for diabetic patients, and is often treated with dorsalis pedis bypass in this patient population as it often presents with the pattern of significant atherosclerosis at the tibial and peroneal arteries while leaving the dorsalis pedis relatively healthy3-5. Current interventions include medications to address risk factors, life-style management, bypass graft surgery, and percutaneous transluminal angioplasty with or without stenting (PTA/S) in favor of amputation, which is the last resort1,6. With its high morbidity and mortality rates and fairly significant prevalence, it is important to better understand the efficacy of current treatments, particularly in exploring which option might be best per anatomical region1.

Advancing technology has helped to make substantial strides in perfecting both endovascular and open procedures. A recent randomized study has compared FUSION BIOLINE heparin-coated vascular grafts with the standard expanded polytetrafluroethylene (ePTFE) grafts, illustrating efforts to improve synthetic grafts and stents with better long-term patency as well as decreased risk of causing clotting6. In the setting of bypass graft surgery, improvement of synthetic conduits is particularly important, as atherosclerosis is a systemic disease, thus decreasing the likelihood that the host veins are of adequate quality to be used. In addition, many of these patients undergo re-intervention that may potentially require a new or additional conduit in the setting of their only appropriate vein having already been used in the previous procedure. Despite this progress in technology, the great saphenous vein has still proven to be the more durable conduit when compared to other vein grafts, the standard PTFE, as well as the heparin-bonded PTFE, for below-knee lower extremity bypass surgeries, particularly in DP- and tibial-bypasses5,7.

In addition, there has been an increasing trend toward the minimally invasive endovascular procedures to correct obstructed arterial flow. However, there is still disagreement between those who favor endovascular procedures over those who favor open surgeries. Those in favor of the endovascular approach stress its faster recovery time, decreased hospital stay, speed of procedure, lowered costs, preservation of collateral vessels, and decreased surgical complications8. In contrast, proponents of open procedures stress that angioplasty of severely diseased or stenotic vessels may be a short-term solution, eliciting a need for an alternative, more durable solution provided by open surgery6,8. The BASIL trial indicates that due to the trade-off between the benefits and risks of both treatments, it is critical to take in factors such as local expertise as well as overall life-expectancy of the patient in determining which treatment (i.e. angioplasty first or bypass graft first) is most appropriate for each case8.

Objective:

We aim to analyze the long-term outcomes of bypass surgeries (open surgery) and percutaneous transluninal angioplasty (endovascular procedure), and compare these treatments to see if one may be better indicated for patients with critical limb ischemia where the dorsalis pedis would be the distal anastomotic target.

Methods:

The charts for all patients who underwent surgery for dorsalis pedis bypass (DPB) or tibial percutaneous transluminal angioplasty (PTA/S) at Beth Israel Deaconess Medical Center to address their CLI were reviewed. DPB procedures captured were from 2000 – 2014 and the tibial PTA/S procedures occurred within the timespan of 2004 – 2014. In order to make the two groups more physiologically comparable, the following inclusion criteria had to be met for patients within the PTA/S cohort: presence of an appropriate and useable DP or distal AT target for bypass as determined by angiography, TASC C or D disease, and meeting bypass surgery criteria. Outcomes of interest include: survival, limb salvage, amputation-free survival (AFS), wound healing, and RAS events ("Reintervention, Amputation, or Stenosis" with stenosis defined as a >3.5x step-up as read by Duplex Scan). Cox proportional hazard models and Kaplan-Meier survival estimates were used to identify predictors.

Results:

Among patients with CLI, 228 limbs underwent DPB. 135 limbs that underwent tibial PTA/S fit inclusion criteria. However, it should be noted that there were some significant differences between the two groups at the time of intervention. There was a higher prevalence of male gender (75% vs. 49%; $p<0.001$), younger age (67 vs. 72 years old; $p<0.01$), diabetes (89% vs. 79%; $p=0.02$), presentation of rest pain (19% vs. 7%; $p<0.001$), and coronary artery disease (61% vs. 50%; $p=0.04$) in the DPB cohort. After adjusting for these differences, it was found that patients who underwent DPB had better long-term outcomes, with significantly increased rates of AFS (61% vs. 46%; HR 1.5, 95% CI 1.1 – 2.2) and 3-year survival (68% vs. 55%; HR 1.8, 95% CI 1.2 - 2.7), as well as reduced RAS events (58% vs. 39%; HR 1.7, 95% CI 1.2 – 2.4).

Conclusion:

Despite recent trends towards minimally invasive procedures in efforts to reduce recovery time and minimize surgical complications, it may be that certain anatomical locations may respond more favorably to endoscopic versus open repair procedures. Our findings indicate that DPB should continue to be practiced as a treatment for CLI as it is proving to be a more durable solution with better survival and limb preservation statistics when compared to the outcomes of endovascular PTA/S treatment.

Data-collection: JKO, JDD; Analysis: JDD, PAS, SZ, KU, MLS

Funding: Robert L. Caldwell Vascular Research Summer Internship at Beth Israel Deaconess Medical Center

References:

1. Abu Dabrh AM, Steffen MW, Undavalli C, et al. The natural history of untreated severe or critical limb ischemia. J Vasc Surg. 2015.
2. Fu X, Zhang Z, Liang K, et al. Angioplasty versus bypass surgery in patients with critical limb ischemia-a meta-analysis. Int J Clin Exp Med. 2015;8(7):10595-10602.
3. Kawarada O, Yokoi Y. Dorsalis pedis artery stenting for limb salvage. Catheter Cardiovasc Interv. 2008;71(7):976-982.
4. Domenig CM, Hamdan AD, Holzenbein TJ, et al. Timing of pedal bypass failure and its impact on the need for amputation. Ann Vasc Surg. 2005;19(1):56-62.
5. 5.Pomposelli FB, Kansal N, Hamdan AD, et al. A decade of experience with dorsalis pedis artery bypass: analysis of outcome in more than 1000 cases. J Vasc Surg. 2003;37(2):307-315.
6. Lumsden AB, Morrissey NJ, Comparison of S, Primary Patency Between the FBH-CVG, Co-investigators ESeT. Randomized controlled trial comparing the safety and efficacy between the FUSION BIOLINE heparin-coated vascular graft and the standard expanded polytetrafluoroethylene graft for femoropopliteal bypass. J Vasc Surg. 2015;61(3):703-712 e701.
7. Neville RF, Capone A, Amdur R, Lidsky M, Babrowicz J, Sidawy AN. A comparison of tibial artery bypass performed with heparin-bonded expanded polytetrafluoroethylene and great saphenous vein to treat critical limb ischemia. J Vasc Surg. 2012;56(4):1008-1014.
8. Adam DJ, Beard JD, Cleveland T, et al. Bypass versus angioplasty in severe ischaemia of the leg (BASIL): multicentre, randomised controlled trial. Lancet. 2005;366(9501):1925-1934.

Ria Pal, B.S.

Preceptor Name: Sanjiv B. Amin, M.B.B.S.
Title: Associate Professor
Institution: University of Rochester Medical Center
Department: Pediatrics, Division of Neonatology

Autism Spectrum Disorder Symptom Stability and Social Communication Questionnaire Validity in Children Born Preterm

Introduction: Autism Spectrum Disorder (ASD) is characterized by persistent, early onset deficits in social communication and restricted or repetitive patterns of behavior, interests, or activities. Premature infants are at increased risk for neurodevelopmental conditions including ASD, language disorders, intellectual disability, and behavioral problems. However, the timing of screening for autism using a commonly used screening tool, the Social Communication Questionnaire (SCQ), for premature infants is unknown. This is critical, considering that autism symptoms may be mutable, and earlier intervention can lead to greater gains in adaptive functional behavior. The SCQ is a widely used caregiver response form which can be used as early as 3 years of age in children.

Objective: Our study seeks to examine the stability of ASD symptoms in a population born preterm over time and to examine the utility of the SCQ (Social Communication Questionnaire) as a screening tool at 3 years of age in infants born at < 33 weeks gestational age.

Background: The SCQ has been demonstrated in an extremely preterm population to have 82% sensitivity and 88% specificity for identifying ASD. Because the utility of SCQ was based on a study conducted on 11 year old former premature infants, further research must be done to inform optimal screening guidelines for a younger preterm population. As current findings challenge the assumption that ASD symptoms are stable over time, the utility of the SCQ as a metric for ASD symptoms must be verified.

Methods: In an ongoing NIH-funded longitudinal study, 380 preterm infants who were born between February 2006 and October 2014 and admitted to the Neonatal Intensive Care Unit were consented for autism study. Of these, 54 infants were administered the SCQ and Modified Checklist for Autism in Toddlers at 3 years of age. Between 4-9 years of age, the same participants were administered the SCQ again to evaluate the stability of score. The scores at 3 years and at > 4 years were correlated.

Correlation
Results: Preliminary data from the ongoing study is provided below. The mean gestational age of participants was 29.2 weeks. Infants with score of 12 (out of 40) or higher were deemed to

have an abnormal SCQ screen. 6 participants had abnormal screen at 3 years while 8 participants had an abnormal screen at > 4 years of age. Of the 6 participants who were identified to have abnormal screen at 3 years, 2 continued to have an abnormal screen at > 4 years while 4 had a normal screen at > 4 years of age. There was non-significant but positive correlation between two time periods (p=0.15, r=0.49). There was no significant difference in the proportion of infants who failed SCQ screen at two time periods (p = 0.23). The calculated difference between the tests was 0.037, with OR 3.5.

Conclusions: Our findings suggest that SCQ scores are stable in preterm infants during early childhood and premature infants can be screened at 3 years of age. A larger study is warranted to confirm our findings.

References:

1. Baio, J. (0400). "Prevalence of Autism Spectrum Disorder Among Children Aged 8 Years — Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2010." Surveillance Summaries **63**(2).
2. Hedvall, Å., J. Westerlund, E. Fernell, F. Norrelgen, L. Kjellmer, M. B. Olsson, L. H. Carlsson, M. A. Eriksson, E. Billstedt and C. Gillberg (2015). "Preschoolers with Autism Spectrum Disorder Followed for 2 Years: Those Who Gained and Those Who Lost the Most in Terms of Adaptive Functioning Outcome." Journal of autism and developmental disorders.
3. Johnson, S., C. Hollis, E. Hennessy, P. Kochhar, D. Wolke and N. Marlow (2011). "Screening for autism in preterm children: diagnostic utility of the Social Communication Questionnaire." Archives of disease in childhood **96**(1): 73-77.
4. Johnson, S., C. Hollis, P. Kochhar, E. Hennessy, D. Wolke and N. Marlow (2010). "Autism spectrum disorders in extremely preterm children." The Journal of pediatrics **156**(4): 525-3100.
5. King, M. and P. Bearman (2009). "Diagnostic change and the increased prevalence of autism." International journal of epidemiology.
6. Limperopoulos, C., H. Bassan, N. R. Sullivan and J. S. Soul (2008). "Positive screening for autism in ex-preterm infants: prevalence and risk factors." Pediatrics.
7. Paul, T. S., D. Maureen, M. Matthew, N. Craig, S. M. David, W. Lisa, L. Li-Ching, R. Catherine, G. Ellen, K. Russell, B. Jon, P.-M. Jennifer and C. Christopher (2009). "Timing of Identification Among Children With an Autism Spectrum Disorder: Findings From a Population-Based Surveillance Study." Journal of the American Academy of Child & Adolescent Psychiatry.
8. Pellicano, E. (2012). "Do autistic symptoms persist across time? Evidence of substantial change in symptomatology over a 3-year period in cognitively able children with autism." American journal on intellectual and developmental disabilities **117**(2): 156-166.

Deborah Paul

Preceptor(s) Name: Wakenda K. Tyler, MD, MPH; Edward M. Schwartz, Ph.D; Chao Xie, MD
Title: Associate Professor, Department of Orthopaedics; Director, Center for Musculoskeletal Research; Assistant Professor, Department of Orthopaedics
Institution: University of Rochester School of Medicine and Dentistry
Department: Orthopaedics

A Histological Comparison of Vascularity in Renal Cell Carcinoma with IMP3 Gene Knockout

Introduction: Renal cell carcinoma (RCC) is the most common type of kidney cancer and is among a group of localized cancers that tend to metastasize to the bone due to its high vascularity, resulting in a poor prognosis for the patient. When compared to prostate cancer, which expresses significantly less vascularity and has a better prognosis for the patient, RCC has a much higher mortality and bone morbidity.

Objective: This study examined the efficiency of CRISPR/Cas9 targeted IMP3 knockdown in the RCC cell line (786-O/Luc) that was introduced into a well-established tibia injection murine model in our lab. The immunohistochemical (IHC) staining was performed on tissue sections that were obtained from day 35 sacrifices in the following experimental groups, as (1) RCC, (2) Scramble (empty vector), (3) IMP3 knockdown, and (4) PC3 (prostate cancer).

Background: Based on our previous studies, an oncofetal protein, Insulin-like growth factor II mRNA binding protein 3 (IMP3) has been identified through gene array testing as an independent marker for identifying patients that have an increased risk of developing metastasis of RCC due to its over expression in patients with metastatic RCC. Thus, we hypothesized that knocking down this critical protein in localized RCC can increase patient survival rates and prevent or delay metastasis to the bone.

Methods: After 35 days of tumor growth, RCC samples were isolated from the four groups of mouse models and were analyzed through IHC staining. Following antigen retrieval with Tris EDTA buffer, the slides were stained with DAKO reagents. The non-specific binding sites were blocked with Vectastain universal blocking serum and incubated overnight with the IMP3 primary antibody (Abcam company, 1:200) in serum. The following day, the slides were incubated with the secondary antibody (Vector company, 1:500), Vectastain ABC reagent and underwent a positive color reaction with Vector impact DAB. The slides were then counterstained with hematoxylin and analyzed using the Visiopharm software to detect IMP3 positive cells and tumor vascularity percentages.

Results: Vascularity analysis using Visiopharm software showed average IMP3 positive cells that related vascularity percentages of the four groups as 17.61% (RCC), 16.06% (Scramble), 10.98 (RCC-IMP3 knockdown) and 1.66% (PC3), showing a significant decrease in tumor vascularity from 17.61% in the RCC cell line to 10.98% vascularity in the IMP3 knockdown cell line.

Conclusion: Results from this study further confirm IMP3 knockdown's efficiency in decreasing vascularity in RCC. Future studies will aim to further decrease tumor vascularity in RCC to resemble percentages seen in prostate cancer to improve patient survival rates and delay metastasis to the bone.

References:

1. Bell JL, Wachter K, Muhleck B, Pazaitis N, Kohn M, Lederer M, Huttelmaier S. Insulin-like growth factor 2 mRNA-binding proteins (IGF2BPs): post transcriptional drivers of cancer progression? Cellular and Molecular Life Sciences 2013; 70:2657-2675.
2. Cohen HT, McGovern FJ. Renal-cell carcinoma. New England Journal of Medicine 2005; 353:2477-2490.
3. Jiang Z, Chu PG, Woda BA, et al. Analysis of RNA-binding protein IMP3 to predict metastasis and prognosis of renal-cell carcinoma: a retrospective study. Lancet Oncology 2006; 7:556-564.
4. Jiang Z, Chu PG, Woda BA, et al. Combination of quantitative IMP3 and Tumor Stage: A new system to predict metastasis for patients with localized Renal Cell Carcinomas. Clinical Cancer Research 2008; 14:5579-5584.
5. Xie C, Schwarz EM, Sampson ER, Dhillon RS, Li D, O'Keefe RJ, Tyler W. Unique angiogenic and vasculogenic properties of renal cell carcinoma in a xenograft model of bone metastasis are associated with high levels of vegf-a and decreased ang-1 expression. Journal of orthopaedic research. 2012;30:325-33.

Piazza, Nina

Preceptors:
Andrew Aligne, MD
University of Rochester Medical Center
Department of Pediatrics, Hoekelman Center

Katherine Greenberg, MD
University of Rochester Medical Center
Department of Pediatrics, Adolescent Medicine Division

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 URMC 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.

Pitch, Michelle

Preceptors:
Muriel Laine, Ph.D.
University of Chicago
Ben May Department for Cancer Research

Geoffrey Greene, Ph.D.
University of Chicago
Ben May Department for Cancer Research

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 (ERα) 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, ERα 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 ERα 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 ERα 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 ERα in therapies and treatment.[5]

Objectives: We aim to study the effect of a mixed ERα 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 ERα 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 ERα-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 ERα target genes TFF1, GREB1, PTGS2, PDZK1.

Results: By co-immunoprecipitation, it is evident that the mutated ERα 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 ERα dimer complex is sufficient to impact substantial differences in the protein-protein interactions and downstream target gene expression in the ERα 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.

Vishaal Prabhu, MS2

Preceptor:
Theodore H. Schwartz, M.D.
Professor of Neurosurgery, Neurology, and Otolaryngology
Weill Cornell Medicine, NewYork-Presbyterian Hospital
Department of Neurological Surgery

Endoscopic Endonasal Versus Open Transcranial Resection of Craniopharyngiomas: A Single Institution Analysis of Outcomes

Introduction

Craniopharyngiomas are histologically benign epithelial tumors that arise along the path of the craniopharyngeal duct and are derived from the epithelial remnants of Rathke's pouch.[1] Comprising approximately 3% of all intracranial tumors, craniopharyngiomas may be cystic, solid, or both and have two major pathological subtypes, namely, the adamantinomatous and squamous-papillary varieties.[2-4] Common presenting symptoms include hypopituitarism, cognitive dysfunction, and visual impairment due to mass effect.[3]

Treatment of craniopharyngiomas is traditionally centered on gross total resection (GTR), although recent evidence suggests that subtotal resection and adjuvant therapy may provide comparable control of the tumor.[5] Given the anatomical location of these tumors in the anterior skull base and close relation to vital structures, including the pituitary gland, optic chiasm, hypothalamus, and anterior cerebral artery, surgical resection is a significant challenge.[6]

While craniopharyngiomas have traditionally been resected via the open transcranial approach, the endoscopic endonasal approach has been recently developed as an alternative. This emerging technique eliminates the need for brain retraction and minimizes the manipulation of neurovascular structures by providing a more direct trajectory to the tumor, but is limited in its lateral reach.[6] Early experience with the endoscopic endonasal approach has yielded positive results in terms extent of resection, visual outcomes, and rates of diabetes insipidus and hypopituitarism but has also been associated with greater rates of cerebrospinal fluid leakage.[7] Further analysis of outcomes in treated patients is thus necessary to gain a more comprehensive assessment of both approaches.

Objective

To compare the clinical outcomes between the endoscopic endonasal approach and open transcranial approach to resection of craniopharyngiomas at a single institution.

Methods

A retrospective review of a prospective database containing records of all patients with craniopharyngiomas that were treated at Weill Cornell Medical Center, New York Presbyterian Hospital between 2000 and June 2015 was performed. After blinded review of the preoperative images by the senior author (T.H.S.), patients with craniopharyngiomas that were amenable for gross total resection and could be resected by either surgical approach (endoscopic endonasal or open transcranial) were selected for extensive review. The 32 selected cases were separated into 2 groups based on the surgical approach. The endoscopic endonasal approach was taken in 24 cases and the open transcranial approach in 8 cases. Patient demographics, surgical outcomes, and clinical data including pathologic, ophthalmologic, and endocrine assessments were collected and analyzed. Ophthalmologic assessment consisted of neurosurgical evaluation as well as neuro-ophthalmologic evaluation and formal visual field testing when possible. Endocrine assessment consisted of neuro-endocrine evaluation as well as pre- and post-operative studies of cortisol, adrenocorticotropic hormone, thyroid function, growth hormone, insulin-like growth factor-1, and prolactin.

Results

Preliminary analysis was completed for 32 cases: 24 endoscopic endonasal, 8 open transcranial. GTR was achieved in 23 surgeries in the endoscopic endonasal cohort (95.8%) and in 3 surgeries in the open transcranial cohort (37.5%). The mean length of hospital stay was 9.0 days in the endoscopic endonasal cohort and 15.7 days in the open transcranial cohort. Among 20 patients with a preoperative visual deficit in the endoscopic endonasal group, vision improved in 16 patients (80%), declined in 2 patients (10%), and remained stable in 2 patients (10%). Among 7 patients with a preoperative visual deficit in the open transcranial group, vision improved in 2 patients (28.6%), declined in 2 patients (28.6%), and remained stable in 3 patients (42.9%). New onset diabetes insipidus developed postoperatively in 72.2% of patients in the endoscopic endonasal group and in 85.7% of patients in the open transcranial group. In the endoscopic endonasal cohort, new ACTH deficiency developed in 72.2%, new thyroid insufficiency developed in 66.6%, and new growth hormone deficiency developed in 40.9% of patients. In the open transcranial cohort, new ACTH deficiency developed in 100%, new thyroid insufficiency developed in 100%, and new growth hormone deficiency developed in 66.7% of patients. The postoperative CSF leak rate was 4.2% (1 patient) in the endoscopic endonasal group and 0% in the open transcranial group. Postoperative cognitive loss was reported in 0 patients of the endoscopic endonasal group and in 5 patients (62.5%) of the open transcranial group.

Conclusion

Preliminary results of this study indicate that endoscopic endonasal surgery can be an effective approach to gross total resection of craniopharyngiomas and may result in more favorable clinical outcomes compared to the open transcranial approach. Further analysis must be completed to compare the outcomes of the approaches and assess the significance of the data.

References

1. Karavitaki N, Cudlip S, Adams BT, Wass JAH. Craniopharyngiomas. *Endocrine Rev*. 2006; 27:371–97.

2. Bunin GR, Surawicz TS, Witman PA, Preston-Martin S, Davis F, Bruner JM. The descriptive epidemiology of craniopharyngioma. *J Neurosurg*. 1998; 89:547–51.
3. Jane JA Jr, Laws ER. Craniopharyngioma. *Pituitary*. 2006; 9:323–26.

4. Zada G, Lin N, Ojerholm E, Ramkissoon S, Laws ER. Craniopharyngioma and other cystic epithelial lesions of the sellar region: a review of clinical, imaging, and histopathological relationships. *Neurosurg Focus*. 2010; 28:E4.

5. Yang I, Sughrue ME, Rutkowski MJ, Kaur R, Ivan ME, Aranda D, Barani IJ, Parsa AT. Craniopharyngioma: a comparison of tumor control with various treatment strategies. *Neurosurg Focus*. 2010; 28:E5.

6. Leng LZ, Anand VK, Schwartz TH. Endoscopic management of craniopharyngiomas. *Operative Techniques in Otolaryngology*. 2011; 22:215–22.

7. Komotar RJ, Starke RM, Raper DM, Anand VK, Schwartz TH. Endoscopic endonasal compared with microscopic transsphenoidal and open transcranial resection of craniopharyngiomas. *World Neurosurg*. 2012; 77:329–41.

Kyle E. Rodenbach

Preceptor Name: George J. Schwartz, MD
Title: Renal Reserve: Development of a Kidney Stress Test
Institution: University of Rochester Medical Center
Department: Pediatrics

Renal Reserve: Development of a Kidney Stress Test

Introduction: Protein loading is an effective, non-invasive method for assessing renal reserve (RR, difference between stimulated and baseline glomerular filtration rate) and is conceptually similar to other stress testing modalities including cardiac stress testing and glucose tolerance testing. Lack of RR in the setting of a normal GFR suggests glomerular hyper-filtration exists at baseline. Normal values for creatinine and BUN are maintained by hyper-filtration despite the loss of functional renal mass in this pre-clinical state [1]. Over time, hyper-filtration likely causes progressive decline in renal function, as in diabetic nephropathy [2].

Objective: The purpose of this study was to compare a meat versus liquid protein load in a cystatin-C-based (Cys-C) RR test using cimetidine-inhibited creatinine clearance (Cr Cl) and iohexol infusion clearance (Io Cl) for validation.

Background: Cystatin C-estimated RR was previously developed in a population of healthy, young adults [3]. Individuals consumed a beef burger containing 60 grams of protein following a baseline blood draw for serum Cystatin C (Cys-C). A second Cys-C sample was obtained 125-141 minutes after the protein load. Subjects showed a mean increase in Cys-C estimated GFR (eGFR) of 12.0 +/- 5.2 (P=0.0003) following the protein load, which represented 12.2% of the mean baseline eGFR (98.1 +/- 9.1 mL/min/1.73m2).

Methods: Participants (N=18) were screened for health status, blood pressure, and proteinuria. They followed a low protein diet and took cimetidine (20 mg/kg) for two days prior to the study. Water loading was used to maintain urine flow, and two hours were allotted for iohexol steady state equilibration. Participants 1-10 received a hamburger (1 g/kg protein); 11-15 received a ProCel® shake (1 g/kg protein); and 16-18 received a high dose ProCel® shake (1.5 g/kg protein). Data were analyzed for significance of RR. Cystatin-C estimated GFR (Cys-C eGFR) was calculated using the CKD-EPI Cys-C formula following IFCC calibration using ERM-DA471/IFCC.

Results: Participants (N=18) had a mean (SD) age of 22 (2) years and were 39% male and 72% white. Baseline GFR (SD) in mL/min/1.73m^2 averaged 103.4 (14.7) for Cr Cl; 108.9 (9.0) for Io Cl (N=8); and 117.4 (6.1) for Cys-C eGFR. For the hamburger group (N=10), mean RR (SD) in mL/min/1.73m^2 was 17.1 (11.6) for Cr Cl (P=0.001); 8.4 (4.3) for Io Cl (P<0.001); and 4.7 (2.4) for Cys-C eGFR (P<0.001). For 1.0-1.5 g/kg shakes (N=8), mean RR (SD) in mL/min/1.73m^2 was 15.8

(5.8) for Cr Cl (P<0.001), 11.7 (9.0) for Io Cl (P=0.008), and 2.4 (2.9) for Cys-C eGFR (P=0.05). The hamburger and shake groups did not differ significantly in RR determined by Cr Cl, Io Cl, or Cys-C but Cys-C-based RR was significantly less than Io-based RR for both groups. There were no differences in post-load versus pre-load Cr/Io clearance ratios.

Conclusion: Cys-C-based RR following a hamburger provides a simple stress test of kidney function which was validated by classical renal clearances and can be applied to those who recover from acute kidney injury. Why Cys-C-based RR was smaller than Io RR, the reference standard, is a topic for future investigation. This might be due, in part, to the dilutional effect of water loading on biomarker estimates of GFR.

References:

1. Thomas DM, Coles GA, Williams JD. What does the renal reserve mean? Kidney Int. 1994;45:411-16.
2. Ruggenenti P, Porrini EL, Gaspari F, et al. Glomerular hyperfiltration and renal disease progression in type 2 diabetes. Diabetes Care. 2012 Oct;35(10):2061-8.
3. Fuhrman DY, Maier PS, Schwartz GJ. Rapid assessment of renal reserve in young adults by cystatin C. Scandinavian journal of clinical and laboratory investigation. 2013:10.3109/00365513.2013.765964. doi:10.3109/00365513.2013.765964

Nichole Roxas

Preceptors: Clara Lampi, MD and Alicia Lieberman, MD
University of Rochester School of Medicine and Dentistry
Department of Pediatrics

Drug-induced Reactive Eosinophilia with Systemic Symptoms (DRESS) Syndrome associated with Minocycline Exposure and HHV6 Reactivation: A Case Report

Introduction: DRESS is a life-threatening condition, with mortality rates ranging from 10-20% (1). Its defining clinical triad is the development of fever, skin rash, and internal organ involvement. Its pathophysiology is thought to involve drug metabolism enzyme defects, viral reactivation (2,3), and genetic predisposition. Minocycline, aromatic antiepileptic medications (carbamazepine, phenytoin, phenobarbital, lamotrigine), sulfones, sulfonamides, allopurinol, azathioprine, and terbinafine are the most common culprits associated with DRESS Syndrome. Disease onset occurs 3-8 weeks after exposure to the offending agent. Presenting symptoms include fever and a generalized maculopapular rash, sometimes associated with lymphadenopathy. Other skin findings include facial edema, exfoliation, and bullae. Internal organ involvement most commonly involves the liver, kidneys, and hematologic system (4). Treatment includes immediate discontinuation of suspected causal agent, systemic corticosteroids in severe cases and supportive care including antipyretic and antipruritic medications.

Case: A 17-year-old previously healthy, fully immunized, sexually active black adolescent female presented to the emergency department with five days of fever, sore throat, cervical and submandibular lymphadenopathy, a single buccal ulceration and a head-to-toe, (palm-and-sole sparing), pruritic, maculopapular confluent skin eruption with blanching erythema that had been progressing over the preceding 2 weeks. History was notable for recent completion of a month-long course of minocycline and topical retinoid for acne vulgaris. She also had a Mirena IUD placed and new right upper extremity tattoo within the past month.

Admission labs were notable for a leukocytosis (14,000μL; ref. range: 4,000-10,000μL [to convert to × 10^9/L, multiply by 0.001]) without peripheral eosinophilia (0.0%; ref. range: 0.7-5.8%) and reactive lymphocytosis (20%, 7,200/μL; ref. range: 1,200-3,700/μL). She also had elevated transaminase levels (330 ALT; ref. range: 0-35 U/L), (84 AST; ref. range: 0-35U/L); (215 Alk Phos; ref. range: 50-130U/L).

During her hospitalization, hepatitis progressed with max. ALT of 1504 U/L, max. AST of 762 U/L, max alkaline phosphatase 244 U/L, associated with hypoalbuminemia (nadir of 2.2g/dL [ref. range 3.5-5.2 g/dL]), and coagulopathy (INR 2.0 [ref. range 1.0-1.2]) without DIC. She developed non-oliguric acute renal failure with serum creatinine peaking at 3.52mg/dL [ref. range: 0.50-

1.00mg/dL], and hypoxia (O_2 sat <82%) associated with pulmonary edema with small effusions and JVD. Hematologic abnormalities included thrombocytopenia (nadir level, 37,000/uL [ref. range: 160,000-370,000/uL]) and anemia (Hemoglobin nadir level, 9.2g/dL [ref. range: 11.2-15.7g/dL] and elevated ferritin (max. 2727ng/mL [ref. range: 10-120ng/mL]). CRP was elevated at 118 (ref. range: 0-10mg/L), ESR was normal. ANA screen was positive at 1:160, all extractable nuclear antigen antibody titers were negative. Smooth muscle, F-actin and liver-kidney microsomal antibody titers were negative. C3 was mildly depressed at 62 [ref range 90 - 180 mg/dL], C4 was normal. Her skin biopsy showed a non-specific lymphocytic infiltrate with eosinophils. Kidney biopsy revealed tubulointerstitial nephritis (TIN). Hepatic eosinophils were visualized via liver biopsy.
Infectious evaluation included a negative HIV screen, negative CMV viral load, CMV viral load, EBV serology, measles IgM, Hepatitis A IgM, Hepatitis B and C serology, Parvovirus B19 Antibody IgM, and Rapid Viral Panel were negative. Anaerobic, aerobic, Rapid Strep, Strep pyogenes, and urine cultures were negative. Serum HHV6 PCR was positive with 76,300 copies/mL.

She was treated with 1g of solumedrol x 3 days followed by 1mg/kg Prednisone with prompt clinical improvement. Renal insufficiency gradually returned to baseline with corticosteroid treatment over the subsequent 2 months. She has also developed seronegative, insulin-dependent diabetes mellitus attributed to steroid treatment.

Discussion:
Main differential diagnostic categories in this case were hypersensitivity (DRESS), autoimmune (SLE, Autoimmune Hepatitis, Macrophage Activation Syndrome), and infection with systemic response. Our patient met diagnostic criteria for DRESS with her clinical triad of fever, generalized maculopapular rash, and internal organ involvement of her liver and kidneys. Her lymphadenopathy is also characteristic as are her laboratory findings of leukocytosis with atypical lymphocytes, elevated transaminases, and positive HHV6 serology (5). Eosinophilia is not required for the diagnosis, but the presence of eosinophils in her skin and liver biopsy findings are suggestive of DRESS as well.

At 17 years old, our patient was younger than those included in the available literature, but her presentation fits the general trend reported in the literature. Her acute liver injury is consistent with a reported incidence of liver involvement in up to 75% of cases (6). Other organs at risk of injury in DRESS include the kidneys (also seen in our patient) and lung. Among the adult population, there is a documented propensity for extremely high AST or ALT to be associated with a younger age at presentation and fewer eosinophils on skin biopsy (7). This is also consistent with our patient's presentation. Fortunately, the majority of patients eventually recover normal organ function, although this can take months. Major causes of morbidity and mortality include the acute organ injury, including occasional need for organ transplant, and the immunosuppressive risks associated with long term corticosteroid use during the convalescent period (7, 8).

There is growing recognition of HHV6 and other viral reactivation in association with severe cases of DRESS (9,10).

References:

1. E. Lopez-Rocha, L. Blancas, K. Rodriguez-Mireles, *et al.* (2014). Prevalence of DRESS syndrome. *Rev Alerg Mex,* 61: 14-23.
2. Shiohara, T., Inaoka, M., Kano, Y. (2006). Drug-induced hypersensitivity syndrome (DIHS): a reaction induced by a complex interplay among herpesviruses and antiviral and antidrug immune responses. *Allergol Int,* 55:1-8.
3. Hamm, R. (2011). Drug-hypersensitivity syndrome: diagnosis and treatment. *J Am Coll Clin Wound Spec,* 3:77-81.
4. Sullivan J, Shear N. (2001). The drug hypersensitivity syndrome: what is the pathogenesis?*Arch Dermatol*, 137: 357. [PubMed: 11255340]
5. Darlenski, R., Kazandjieva, J., Tsankov, N. (2015). Systemic Drug Reactions with Skin Involvement: Stevens-Johnson syndrome, toxic epidermal necrolysis, and DRESS. 33(5): 538-541. doi:10.1016/j.clindermatol.2015.05.005
6. Kardaun, S., Sekula, P., Valeyrie-Allanore, L., Liss, Y., Chu, C., Creamer, D., ... Roujeau, J. (2013). Drug reaction with eosinophilia and systemic symptoms (DRESS): An original multisystem adverse drug reaction. Results from the prospective RegiSCAR study. *Br J Dermatol,* 1071-1080. doi: 10.1111/bjd.12501
7. Lin, I., Yang, H., Strong, C., Yang, C., Cho, Y., Chen, K., Chu, C. (2015). Liver injury in patients with DRESS: A clinical study of 72 cases. *J Am Acad Dermatol*, 72(6):984-91. doi: 10.1016/j.jaad.2015.02.1130.
8. Um, S., Lee, S., Kim, Y., Kim, K., Son, C., Roh, M., Lee, M. (2010). Clinical Features of Drug-induced Hypersensitivity Syndrome in 38 patients. *J Investig Allergol Clin Immunol*, 20(7): 556-562. Retrieved from http://www.jiaci.org/issues/vol20issue7/3.pdf
9. Pritchett, J., Nanau, R., Neuman, M. (2012). The Link Between Hypersensitivity Syndrome Reactivation Development and Human Herpes Virus 6 Reactivation. *Int J Hepatol,* 723062. doi: 10.1155/2012/723062
10. Seishima, M., Yamanaka, S., Fujisawa, T., Tohyama, M., Hashimoto, K. (2006). Reactivation of Human Herpesvirus (HHV) family members other than HHV-6 in drug-induced hypersensitivity syndrome. *Br J Dermatol*, 155(2):344-349.
11. Brown, R., Rother, K., Artman, H., Mercurio, M., Wang, R., Looney, R., Cowen, E. (2009). Minocycline-induced Drug Hypersensitivity Syndrome Followed by Multiple Autoimmune Sequelae. 145(1): 63-66. doi: 10.1001/archdermatol.2008.521
12. Thomas J, Perron A., Brady W. (2011). Chapter 245. Serious Generalized Skin Disorders. In Tintinalli J.E., Stapczynski J, Ma O, Cline D.M., Cydulka R.K., Meckler G.D., T (Eds), *Tintinalli's Emergency Medicine: A Comprehensive Study Guide, 7e*. Retrieved September 27, 2015 from http://accessmedicine.mhmedical.com/content.aspx?bookid=348&Sectionid=40381732.

Rudofker, Eric

Preceptors:
Jeffrey D. Alexis, MD, FAAC, Saadia Sherazi, MD, MS
University of Rochester School of Medicine & Dentistry, Rochester, NY
Division of Cardiology

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.

Adam Russak

Preceptor: Dr. G. Edward Vates
University of Rochester, Department of Neurosurgery

Angiotensin II Increases Glymphatic Flow Through a Norepinephrine-Dependent Mechanism

Introduction, Background, and Objective: The CNS possesses the astrocyte-dependent perivascular glymphatic pathway to facilitate CSF-ISF exchange and clearance of interstitial wastes. Cerebral arterial pulsations drive glymphatic flow, and cerebrovascular pulsatility is dependent, at least in part, on systemic blood pressure. Renin-angiotensin-aldosterone axis dysregulation is responsible for hypertension, a condition that affects nearly 30% of the US population and 40% of individuals globally. Here, we investigate how manipulation of the RAA axis, both with angiotensin and common anti-hypertensive pharmacotherapy, influences glymphatic flow.

Methods: All drugs were administered to the cisterna magna via cannulation at a rate of 1 µL/min for a total volume of 5 µL. Immediately after, 1% AlexaFluor-555 conjugated bovine serum albumin (BSA-555) was delivered intracisternally at a rate of 2 µL/min for a total volume of 10 µL. 30 minutes following tracer injection, cerebral tissues were collected and processed for ex vivo conventional fluorescence microscopy. Tissue area occupied by fluorophore was quantified, with greater percent areas indicating increased glymphatic influx.

Results: Pre-treatment with Angiotensin II (ATII, 1 µM) increased glymphatic influx relative to vehicle-injected controls. Losartan (1 µM), an AT1 receptor inhibitor, was found to decrease glymphatic CSF influx, indicating that ATII acts through the AT1 receptor to increase glymphatic flow. Systemic administration of DSP-4 (50 mg/kg), a neurotoxin known to deplete locus coeruleus norepinephrine, resulted in suppressed glymphatic influx. Co-administration of ATII in DSP-4 treated mice or in mice receiving a norepinephrine inhibitory cocktail (1 µM) resulted in decreased glymphatic influx, suggesting that ATII regulates glymphatic pathway function through a NE-dependent mechanism.

Conclusions: Angiotensin II acts via the AT1 receptor to increase glymphatic influx in a norepinephrine-dependent manner. Further study on hemodynamic regulation of glymphatic flow may reveal mechanisms of hypertension-related brain pathology.

References:

1. Nedergaard, M. "Garbage Truck of the Brain." *Science* 340.6140 (2013): 1529-530.

2. Iliff, J. J., and M. Nedergaard. "Is There a Cerebral Lymphatic System?" *Stroke* 44.6, Supplement 1 (2013): S93-95.

3. Iliff, J. J., M. Wang, Y. Liao, B. A. Plog, W. Peng, G. A. Gundersen, H. Benveniste, G. E. Vates, R. Deane, S. A. Goldman, E. A. Nagelhus, and M. Nedergaard. "A Paravascular Pathway Facilitates CSF Flow Through the Brain Parenchyma and the Clearance of Interstitial Solutes, Including Amyloid Beta." *Science Translational Medicine*
4.147 (2012): 147ra111.

4. Yang, Lijun, Benjamin T. Kress, Harris J. Weber, Meenakshisundaram Thiyagarajan, Baozhi Wang, Rashid Deane, Helene Benveniste, Jeffrey J. Iliff, and Maiken Nedergaard. "Evaluating Glymphatic Pathway Function Utilizing Clinically Relevant Intrathecal Infusion of CSF Tracer." *Journal of Translational Medicine* 11.1 (2013): 107.

5. Thrane, Vinita Rangroo, Alexander S. Thrane, Benjamin A. Plog, Meenakshisundaram Thiyagarajan, Jeffrey J. Iliff, Rashid Deane, Erlend A. Nagelhus, and Maiken Nedergaard. "Paravascular Microcirculation Facilitates Rapid Lipid Transport and Astrocyte Signaling in the Brain." *Scientific Reports* 3 (2013): n. pag.

6. Kress, Benjamin T., Jeffrey J. Iliff, Maosheng Xia, Minghuan Wang, Helen S. Wei, Douglas Zeppenfeld, Lulu Xie, Hongyi Kang, Qiwu Xu, Jason A. Liew, Benjamin A. Plog, Fengfei Ding, Rashid Deane, and Maiken Nedergaard. "Impairment of Paravascular Clearance Pathways in the Aging Brain." *Annals of Neurology* 76.6 (2014): 845-61.

7. Mendelsohn, Andrew R., and James W. Larrick. "Sleep Facilitates Clearance of Metabolites from the Brain: Glymphatic Function in Aging and Neurodegenerative Diseases." *Rejuvenation Research* 16.6 (2013): 518-23.

8. Weller, Roy O., Malavika Subash, Stephen D. Preston, Ingrid Mazanti, and Roxana O. Carare. "SYMPOSIUM: Clearance of Aβ from the Brain in Alzheimer's Disease: Perivascular Drainage of Amyloid-β Peptides from the Brain and Its Failure in Cerebral Amyloid Angiopathy and Alzheimer's Disease." *Brain Pathology* 18.2 (2008): 253-66.

9. Iliff, J. J., M. Wang, D. M. Zeppenfeld, A. Venkataraman, B. A. Plog, Y. Liao, R. Deane, and M. Nedergaard. "Cerebral Arterial Pulsation Drives Paravascular CSF-Interstitial Fluid Exchange in the Murine Brain." *Journal of Neuroscience* 33.46 (2013): 18190-8199.

10. Iliff, J.J., Chen, M.J., Plog, B.A., Zeppenfield, D.M., Soltero, M., Yang, L., Singh, I., Deane, R., Nedergaard, M.: "Impairment of Glymphatic Pathway Function Promotes Tau Pathology after Traumatic Brain Injury." *The Journal of Neuroscience* 34.49 (2014): 16180-6193.

Gabrielle Santangelo

Preceptor(s) Name:
Edward Vates, Jonathan Stone, Doran Mix, Michael Richards, Michael Stoner
Institution: University of Rochester School of Medicine and Dentistry
Department: Neurosurgery

Simulated Inanimate Model for Physical Learning Experience (SIMPLE) of Carotid Endarterectomy Using a 3-D Printing Technology

Introduction: Surgical education relies heavily on operative exposure with live patients. The carotid endarterectomy (CEA) is a procedure that vascular and neurosurgeons learn during residency. However, this procedure demands an experienced surgeon with a <2% complication rate. The high-risk nature of this procedure and the decline in number of CEAs performed annually result in training gaps for residents. Surgical skill simulators in their current state do not provide a complete operative experience.

Objective: The SIMPLE-CEA is a comprehensive and realistic operative exercise that replicates all vital steps in a CEA and permits measurement of clinically significant metrics.

Background: The rate of CAEs in the United States is steadily decreasing. This decline, along with new restrictions on training time, leaves many new vascular and neurosurgeons under exposed to technically difficult procedures. Obtaining this surgical expertise is often at the expense of patient care (1).

Methods: Using a novel method, anatomically accurate models of the human neck and carotid artery were created using poly-vinyl alcohol hydrogels. Relevant structures were also fabricated including the vagus and hypoglossal nerves, internal jugular and facial veins, sternocleidomastoid and omohyoid muscles, and carotid sheath. 3D models were created based on an amalgamation of patient data using CAD software. Injection molds of the modeled organs were 3D printed. Graded polymerization of the hydrogel is achieved by inducing crosslinks during freeze/thaw cycles, which stiffen the phantom organs to realistic tactile properties.

Results: Realistic models were produced using 3D printed injection models and polymer hydrogels. Preliminary findings show an average of 4/5 for face validity surveys according to the experts who performed preliminary testing. Comparison of surgeon performance is feasible using construct metrics such as: carotid clamp time, estimated blood loss, and nerve injury.

Conclusion: SIMPLE-CEA is a realistic, inexpensive model of high fidelity, offering comprehensive training for CEA allowing residents to master required skills prior to operating on a live patient. Next steps include testing content and construct validity of the model

References:

Kamamru, H., Jalbert, J.J., Nguygen, L.L., Gerhard-Herman, M.D., Williams, L.A., Chen, CY., et al. Surgeon case volume and 30-day mortality after carotid endarterectomy among contemporary medicare beneficiaries: before and after national coverage determination for carotid artery stenting. Stroke, 2015; 46 (5): 1288-94

Catherine Sheils, MS2

Mentors:
Karl Bilimoria, MD, MS
Director of the Surgical Outcomes and Quality Improvement Center
Department of Surgery
Northwestern University

Anthony Yang, MD, MS
Assistant Professor of Surgery-Surgical Oncology
Northwestern University

Allison Renee Dahlke, MPH
Program Manager, Surgical Outcomes and Quality Improvement Center
Department of Surgery
Northwestern University

Are ACS-NSQIP Hospitals Unique? A Description of Hospitals Participating in the American College of Surgeons National Surgical Quality Improvement Program.

Introduction: The American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) is a well-recognized program for surgical quality measurement. NSQIP began in the Department of Veterans Affairs Health System and, once adopted by the American College of Surgeons, rapidly expanded to enroll nearly 500 U.S. hospitals in the academic and private sectors.[1-4] Hospitals participating in ACS NSQIP have demonstrated reductions in morbidity and mortality, and benefited from the cost savings associated with improved quality.[2] State and regional NSQIP collaboratives have also emerged to manage quality improvement efforts on a local level,[5] many with notable successes.[6,7]

Given the widespread use of ACS NSQIP in research and recent calls for it to become a platform for national public reporting and pay-for-performance initiatives, it is important to understand which types of hospitals elect to participate in the program. Participation is both costly and resource intensive due to the required data collection by a skilled nurse reviewer or health information expert.[8,9] Others have suggested that smaller community hospitals in particular may lack the infrastructure and resources necessary to enroll in the ACS NSQIP.[10]

Thus, despite a preponderance of research studies utilizing ACS NSQIP data, the scope and reach of the program has not been meaningfully defined. A detailed description of ACS NSQIP-participating hospitals will provide insight into the generalizability of the program's results and indicate opportunities for program expansion; thus improving surgical quality at the national level. Our objective was to compare the characteristics of ACS NSQIP-participating hospitals to non-participating hospitals in the United States.

Methods: Using the 2013 American Hospital Association data on hospital characteristics, hospitals participating in ACS NSQIP were compared to non-participating hospitals. The 2013 Healthcare Cost Report Information System (HCRIS) dataset was used to calculate hospital operating margin as a measure of financial health. The Center for Medicare and Medicaid Services 2013 Inpatient Prospective Payment System (IPPS) Final Rule Impact File was used to abstract the Medicare and Medicaid Services Value Based Purchasing and Disproportionate Share adjustment scores, which were used as proxies for hospital quality and patient population, respectively.

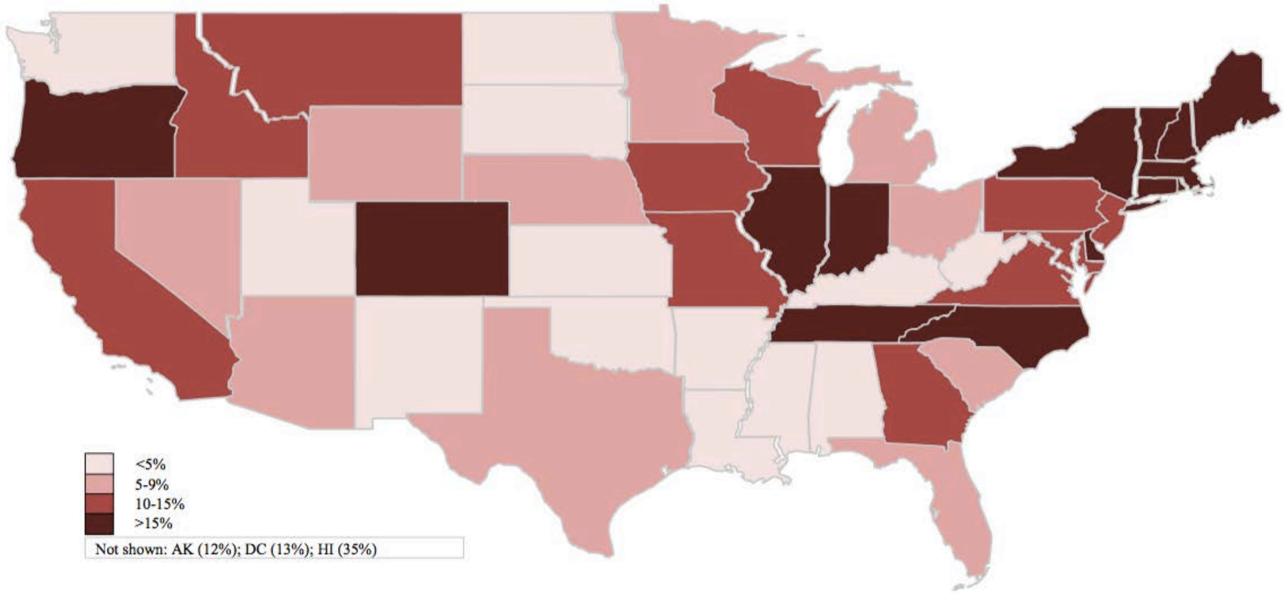
Results: Of 3,872 total U.S. general medical and surgical hospitals, 475 (12.3%) participated in ACS NSQIP. Participating hospitals performed 29.0% of operations in the U.S, with a slightly greater share of inpatient operations (32.4%) and a smaller share of outpatient operations (27.1%; Table 1). Compared to non-participating hospitals, ACS NSQIP hospitals had a higher mean annual inpatient surgical case volume (6,426 vs 1,874; $p<0.001$), a larger number of hospital beds (420 vs 167; $p<0.001$), were more often academic affiliates (35.2% vs 4.1%; $p<0.001$), were more often accredited by the Joint Commission (JCAHO) and American College of Surgeons Commission on Cancer ($p<0.001$), and had higher mean operating margins ($p<0.05$). ACS NSQIP hospitals were also less likely to be designated as critical access hospitals ($p<0.001$). No significant differences in Value Based Purchasing or Disproportionate Share adjustment scores were found. States with the highest percentage of hospitals participating in ACS NSQIP were states with established surgical quality improvement collaboratives (Figure 1).

Conclusions: Hospitals that participate in ACS NSQIP represent 12% of all U.S. hospitals performing inpatient surgery, yet they perform nearly 30% of all surgeries done in the U.S. ACS NSQIP disproportionately includes larger, accredited, and academic-affiliated hospitals with more financial resources. These findings should be taken into account in research studies using ACS NSQIP, and more importantly, indicate that additional efforts are needed to address barriers to enrollment in order to facilitate participation in surgical quality improvement programs by all hospitals.

Table 1.

	Total Number done in the U.S (n=3872)	Total Number done at NSQIP Hospitals (n=475)	% U.S. operations done at NSQIP hospitals
Total Surgical Operations	26,980,736	7,817,673	29.0%
Total Inpatient Operations	9,419,715	3,052,538	32.4%
Total Outpatient Procedures	17,561,021	4,765,324	27.1%

Figure 1.



References

1. Cohen ME, Ko CY, Bilimoria KY, et al. Optimizing ACS NSQIP modeling for evaluation of surgical quality and risk: patient risk adjustment, procedure mix adjustment, shrinkage adjustment, and surgical focus. *J Am Coll Surg.* 2013;217(2):336-346 e331.
2. Hall BL, Hamilton BH, Richards K, Bilimoria KY, Cohen ME, Ko CY. Does surgical quality improve in the American College of Surgeons National Surgical Quality Improvement Program: an evaluation of all participating hospitals. *Ann Surg.* 2009;250(3):363-376.
3. Khuri SF, Henderson WG, Daley J, et al. Successful implementation of the Department of Veterans Affairs' National Surgical Quality Improvement Program in the private sector: the Patient Safety in Surgery study. *Ann Surg.* 2008;248(2):329-336.
4. Merkow RP, Ju MH, Chung JW, et al. Underlying reasons associated with hospital readmission following surgery in the United States. *JAMA.* 2015;313(5):483-495.
5. Ingraham AM, Richards KE, Hall BL, Ko CY. Quality improvement in surgery: the American College of Surgeons National Surgical Quality Improvement Program approach. *Adv Surg.* 2010;44:251-267.
6. Campbell DA, Jr., Kubus JJ, Henke PK, Hutton M, Englesbe MJ. The Michigan Surgical Quality Collaborative: a legacy of Shukri Khuri. *Am J Surg.* 2009;198(5 Suppl):S49-55.
7. Guillamondegui OD, Gunter OL, Hines L, et al. Using the National Surgical Quality Improvement Program and the Tennessee Surgical Quality Collaborative to improve surgical outcomes. *J Am Coll Surg.* 2012;214(4):709-714; discussion 714-706.
8. Birkmeyer JD, Shahian DM, Dimick JB, et al. Blueprint for a new American College of Surgeons: National Surgical Quality Improvement Program. *J Am Coll Surg.* 2008;207(5):777-782.
9. Hammermeister K. The National Surgical Quality Improvement Program: learning from the past and moving to the future. *The American Journal of Surgery.* 2009;198(5):S69-S73.
10. Finlayson SR. Surgery in rural America. *Surg Innov.* 2005;12(4):299-305.

Steiner, Jack

Preceptor:
Craig A. Mullen, MD, PhD
Department of Pediatric Hematology/Oncology
University of Rochester Medical Center

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-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 25µg 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±9.77% reduction in ALL cell viability when measured by flow cytometry, and a 50.01±15.65% reduction when measured by ATP-luminescence assay (p=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.

St.John, Matthew

Preceptor
Dr. John C. Elfar, MD
Associate Professor
Department of Orthopedics
University of Rochester Medical Center

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 evidence[2]. 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 results[4]. One meta-analysis did demonstrate a significant difference in symptom relief between corticosteroid injections and placebo at the two-week mark[1]. 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 year[3]. 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 option[3].

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 Mondern 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

Kriti Thapa, MPH

Preceptor:
Elizabeth Kelvin, PhD, MPH
Assistant Professor
Epidemiology & Biostatistics
CUNY School of Public Health, Hunter College
2180 Third Avenue
New York, NY 10035

The effect of albendazole treatment on non-seizure outcomes in patients with symptomatic neurocysticercosis

Background: Neurocysticercosis (NC) results from infection of the central nervous system (CNS) by the larval stage of the tapeworm *Taenia solium* and is the most frequently occurring parasitic disease affecting the CNS.[1] NC is a serious public health problem in many low- and middle-income nations as well as in high-income nations with substantial immigration from endemic countries in Latin America, Asia, and Africa.[2] Designated as an emerging infection by the US Centers for Disease Control and Prevention (CDC),[3] NC accounts for more than 1000 cases per year in the US. [4] However, there is little information about the effect of antihelminthic treatment on non-seizure outcomes in patients with neurocysticercosis (NC).

Objective: We aimed to explore the effect of albendazole treatment on non-seizure symptoms experienced by NC patients over 24 months follow-up, compared to placebo.

Methods: We used negative binomial regression, logistic regression, and Cox proportional hazards models to explore the effect of albendazole treatment on any non-seizure symptoms as well as six common specific symptoms experienced by NC patients (headaches, limb weakness or gait problem, anxiety and/or depression, vision problems (double vision and/or other vision difficulties), stomach problems (vomiting, nausea and/or stomach pain), and memory loss and/or confusion over 24 months follow-up. The data for this study come from a randomized controlled trial comparing albendazole plus prednisone to placebo plus prednisone for treatment of NC among 178 patients with active and/or transitional NC cysts and new-onset symptoms.

Results:
Overall, albendazole was not associated with the odds of experiencing any non-seizure symptoms nor the number of months symptoms were experienced or the time symptom free. When looking at specific symptoms, there were a few significant associations. Those treated with albendazole had significantly lower odds of memory loss and/or confusion during 13-24

months and months 1-24 (odds ratio [OR]=0.20, 95% confidence interval [CI]=0.04, 0.95 and OR= 0.43; 95% CI= 0.21, 0.88, respectively) and fewer months during which memory loss and/or confusion were experienced during months 13-24 (Rate Ratio=0.51; 95% CI= 0.27, 0.97, respectively). Additionally, albendazole was associated with a significantly reduced odds of anxiety and/or depression during 13-24 months (OR=0.11; 95% CI=0.02, 0.51) and an increased odds of vomiting, nausea and/or stomach pain over 24 months follow-up (OR=5.00; 95% CI=1.32, 19.02). There was no difference by treatment in headaches, limb weakness or gait problems, or vision problems.

Conclusion: While the prevalence of non-seizure symptoms was extremely high in this cohort of patients both before and after treatment, there was little difference in the non-seizure symptoms experienced by NC patients over 24 months between those treated with albendazole compared to those treated with placebo. Albendazole treatment was associated with a decrease in the probability and frequency of memory loss and/or confusion, a decrease in the probability of anxiety and/or depression, and an increase in the probability of stomach problem and limb weakness and/or gait problems in certain models, but there was no clear pattern for these associations over time or across different ways of looking at the outcome (presence of symptom, time to symptom or number of times symptom was reported). While antihelminthic treatment is the standard of care in treating patients with NC, the clinical benefits of this treatment are not clear and further research is needed to identify more effective treatment and management of NC to reduce the burden of clinical symptoms.

Keywords: *Taenia solium*, cysticercosis, neurocysticercosis, parasitic diseases, helminths, cestode infections, albendazole

References:

1. White A. Neurocysticercosis. *Current Treatment Options in Infectious Diseases.* 2000;2:78-87.
2. Carpio A, Hauser WA. Prognosis for seizure recurrence in patients with newly diagnosed neurocysticercosis. *Neurology.* Dec 10 2002;59(11):1730-1734.
3. Wallin MT, Kurtzke JF. Neurocysticercosis in the United States: review of an important emerging infection. *Neurology.* Nov 9 2004;63(9):1559-1564.
4. Carpio A. Neurocysticercosis: an update. *The Lancet. Infectious diseases.* Dec 2002;2(12):751-762.

Seth Tobolsky, MS-2

Preceptors:
Dean Schillinger, M.D.
Chief of General Internal Medicine/Professor of Medicine, San Francisco General Hospital
University of California, San Francisco

Courtney Lyles, Ph. D.
Assistant Professor, Division of General Internal Medicine, San Francisco General Hospital
University of California, San Francisco

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.

Walia, Ritika, MS2

Preceptor:
Robert Sackstein, MD.,Ph.D.
Brigham and Women's Hospital, Department of Dermatology
Harvard Skin Disease Research Center, Harvard Medical School
Program of Excellence in Glycosciences

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 year[1]. The danger lies in its virulent capacity to metastasize[2]. 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 α(1,3) or α(1,4) linkage, respectively, to the GlcNAc residues[4]. Previous studies have suggested that O-sialofucosylated variant isoforms of the ubiquitous protein CD44, termed hematopoietic cell E-/L- selectin ligand (HCELLv), 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 cells[7], 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 jeman 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.

Hannah Ward

Sarah Hallen, M.D.
Physician, Geriatrics
Maine Medical Center
Center for Outcomes Research

Evaluation of a "surprise" question for fall risk assessment in skilled nursing facilities: a pilot study

Introduction: Falls are a frequent cause of morbidity and mortality among older adults living in an institutional setting.[1] While one-third of community-dwelling people over the age of 65 fall each year, it is estimated that half of all nursing home residents fall each year.[2,3] Patients in skilled nursing facilities (SNF) are likely to be at an even greater increased risk for several reasons. SNF patients are often recovering from an acute illness or injury; this increases the likelihood of polypharmacy and delirium. These conditions are associated with increased fall risk.[4,5] Additionally, patients who are in SNF often have high degrees of debility and variable mobility. High patient to staff ratios in SNF also limit the amount direct patient supervision possible. Given the high risk of this population and the limitations of the setting, determining which patients are at highest risk of falls would be of significant benefit.

Objective: To assess the predictive value and inter-rater reliability of a surprise question for falls (SQ-F), "Would you be surprised if this patient fell within the next 7 days?" when used by physicians and registered nurses in a skilled nursing facility setting.

Background: Many risk factors for falls have been proposed, and it is often assumed that the risk of falling is proportional to the number of risk factors an individual patient has.[6-11] Mortality prognostication is similar in this regard. The Surprise Question (SQ), "Would you be surprised if this patient died within the next 12 months?" was originally developed as a screening tool for use in a primary care setting to identify patients who might benefit from an end-of-life supportive services program.[12] Subsequent research has shown the SQ to be a simple and effective screening tool for mortality over various time frames (1 week, 6 months, and 1 year) and among various patient groups, including dialysis patients with ESRD and patients with cancer.[13-16] To our knowledge, a surprise question screening tool has never been developed for any outcome besides mortality. We hypothesized that a surprise question would be a useful screening tool for falls because of the multifactorial nature of both falls and death. A fall, like mortality, is an outcome that has been associated with many clinical factors and can have multiple, interacting proximate causes.

Methods: A prospective observational study was completed at three skilled nursing facilities in the Portland, Maine, area. All patients admitted to the study facilities during the study period were eligible to enroll. The SQ-F was completed by both registered nurses and physicians at the time of admission. Data on subjects' presenting diagnoses, prescribed medications, and history of delirium and dementia was collected. The outcome measured was a fall with or without injuries. Subjects were followed until discharge or conversion to long-term care.

Results: All patients admitted to the study facilities (n=71) were enrolled; admitting registered nurses and physicians (n=4) completed the SQ-F. Four subjects (6%) fell at least once. When completed by physicians, the SQ-F had a sensitivity of 75% (95% CI = 19 – 99%), a specificity of 47% (95% CI = 39-66%), a positive predictive value (PPV) of 9% (95% CI = 2-24%) and a negative predictive value (NPV) of 97% (95% CI = 82 – 100%). When completed by nurses, the SQ-F had a sensitivity of 100% (95% CI = 40 – 100%), a specificity of 50% (95% CI = 33 – 67%), a PPV of 17% (95% CI = 0 – 39%) and a NPV of 100% (82 – 100%). The inter-rater reliability between physicians and nurses, measured by kappa, was 0.29.

Conclusion: The SQ-F is a brief instrument that relies on clinician judgment to predict fall risk among patients in the skilled nursing facility setting. The sensitivity, specificity, and negative predictive value of the SQ-F are comparable to that of other fall risk assessment tools used in various settings. This result is supported by previous studies that have found clinician judgment to be at least as accurate as formal fall risk assessment tools. The poor PPV and good NPV of the SQ-F emphasizes the importance of universal fall prevention practices, with exceptions made only for those patients for whom the clinician “would be surprised” if they fell.

References:

1. Rubenstein L, Josephson K, Robbins A. Falls in the Nursing Home. Ann of Intern Med 1994.
2. Hausdorff JM, Rios DA, Edelberg HK. Gait variability and fall risk in community-living older adults: a 1-year prospective study. Arch Phys Med Rehabil 2001;82:1050-6.
3. Hirsch CH, Sommers L, Olsen A, Mullen L, Winograd CH. The natural history of functional morbidity in hospitalized older patients. Journal of the American Geriatrics Society 1990;38:1296-303.
4. Woolcott J, Richardson K, Wiens M, et al. Meta-analysis of the Impact of 9 Medication Classes on Falls in Elderly Persons. Archives of Internal Medicine 2009;169.
5. Wolff M, Hassett M. Falls in Skilled Nursing Facilities Associated with Opioid Use. Journal of American Geriatrics Society 2012;60.
6. Tinetti ME, Speechley M, Ginter SF. Risk factors for falls among elderly persons living in the community. N Engl J Med 1988;319:1701-7.
7. Tinetti ME, Williams TF, Mayewski R. Fall risk index for elderly patients based on number of chronic disabilities. Am J Med 1986;80:429-34.
8. Vassallo M, Poynter L, Sharma JC, Kwan J, Allen SC. Fall risk-assessment tools compared with clinical judgment: an evaluation in a rehabilitation ward. Age Ageing 2008;37:277-81.
9. Oliver D, Britton M, Seed P, Martin FC, Hopper AH. Development and evaluation of evidence based risk assessment tool (STRATIFY) to predict which elderly inpatients will fall: case-control and cohort studies. BMJ 1997;315:1049-53.
10. Downton JH, Andrews K. Prevalence, characteristics and factors associated with falls among the elderly living at home. Aging (Milano) 1991;3:219-28.
11. Morse JM. The modified Morse Fall Scale. Int J Nurs Pract 2006;12:174-5.
12. Pattison M, Romer AL. Improving Care Through the End of Life: launching a primary care clinic-based program. J Palliat Med 2001;4:249-54.
13. Moss AH, Ganjoo J, Sharma S, et al. Utility of the "surprise" question to identify dialysis patients with high mortality. Clin J Am Soc Nephrol 2008;3:1379-84.
14. Moss AH, Lunney JR, Culp S, et al. Prognostic significance of the "surprise" question in cancer patients. J Palliat Med 2010;13:837-40.
15. Cohen LM, Ruthazer R, Moss AH, Germain MJ. Predicting six-month mortality for patients who are on maintenance hemodialysis. Clin J Am Soc Nephrol 2010;5:72-9.
16. Hamano J, Morita T, Inoue S, et al. Surprise Questions for Survival Prediction in Patients With Advanced Cancer: A Multicenter Prospective Cohort Study. Oncologist 2015.

Waroich, Jozal

Holly Hindman, MD
University of Rochester
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.
14. 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.
15. Zhang M., et al., Altered corneal nerves in aqueous tear deficiency viewed by in vivo confocal microscopy. Cornea, 2005. 24(7): p. 818–824.

Sam Weisenthal

Preceptor(s) Name: Vincent Silenzio, MD, MPH (LINCS), David R. Lambert, MD (URSMD)
Institution: URMC
Department: OME

Text mining medical education course material

Background: There is increasing interest in using big data and analytics to improve higher education (1). In medical education, data-driven course material analysis is already an area of active research. For example, for concept identification within a medical education corpus, researchers at Vanderbilt University leveraged the National Library of Medicine's Unified Medical Language System to create KnowledgeMap (2). The interplay between national licensing and competency standards and institutional curricula is an important concept in medical education (3); in order to compare a curriculum to national standards, researchers at the University of Arizona developed a computer-based tool that used Medical Subject Headings (MeSH) terms to map the University of Arizona curriculum to the United States Medical Licensing Examination (USMLE) Step 1 Exam content outline (4). In particular for medical education, these computational tools are beneficial for their objectivity (5).

Objective: In this study, we aimed to devise a data-driven method for determining the emphasis put on a particular topic within the course material and to use the method on the syllabus data from our own institution.

Methods: Python natural language toolkit (NLTK) (6) was used for pre-processing procedures. To determine the emphasis, or "coverage," on a topic, we used the Gensim (7) implementation of a well-known probabilistic topic model (8), Latent Dirichlet Allocation (LDA) (9). Under LDA, the probability of a corpus D with K topics and M documents each of length N is

$$p(D|\alpha,\beta) = \prod_{j=1}^{K} \int p\left(\beta_j|\eta\right) \prod_{d=1}^{M} \int p\left(\Theta_d|\alpha\right) \left(\prod_{n=1}^{N_d} \sum_{z_{dn}} p(z_{dn}|\Theta_d)\, p\left(w_{dn}|z_{dn},\beta_j\right) \right) d\Theta_d d\beta_j$$

where the multinomial Θ_d is sampled for document *d* from a Dirichlet distribution parameterized by α. The topic z_{dn} is then sampled for word *n* of document *d* from Θ_d. Each word w_{dn} is then sampled from the multinomial $p\left(w_{dn}|z_{dn},\beta_j\right)$. The V-dimensional vector β_j ~ Dirichlet(η) and each β_j is a V-dimensional vector whose entry $\beta_{vj} = p(w = v|z = j)$ for $v \in V$. So that the topics in our model would correspond to conventional topics, a common USMLE Step 1 exam review book (10) split into documents corresponding to each of the 17 topics from a step 1 score report and then transformed according to term frequency-inverse document frequency (tf-idf) was smoothed and used as a prior η on β. We used the Gensim version of variational Bayes (9, 11) to determine the topics β and a K-dimensional vector γ_d whose entry γ_{di} for $i \in K$ represents the weight of topic i in document *d* given the topics β. γ_d was caculated for a concatenation of all the documents in USMLE and a concatenation of all the documents in URSMD, providing approximations to the corpus-level posterior topic distributions. We compared the URSMD coverages to the coverages of topics in a USMLE review book (RB). The ratio of coverages for each topic was compared to the average URSMD scores from the 2011-2013.

Results: The length of USMLE was 92,629 words and the length of URSMD was 1,128,235 words. There were 44,920 unique words in URSMD and 13,190 unique words in USMLE. There were 46,565 unique words in the both USMLE and URSMD combined and 11,545 unique words shared by URSMD and USMLE. There were 33,375 unique words in URSMD but not USMLE and 1,645 unique words in USMLE but not URSMD.

As shown in Figure 1, our work suggests that USMLE emphasizes microbiology, reproductive and endocrine systems, and the nervous system; URSMD emphasizes microbiology and the nervous system. Relative to USMLE, URSMD emphasizes biostatistics, behavioral sciences, genetics, the immune system, and the respiratory system; relative to URSMD, USMLE emphasizes microbiology, reproductive and endocrine systems, and the renal/urinary system.

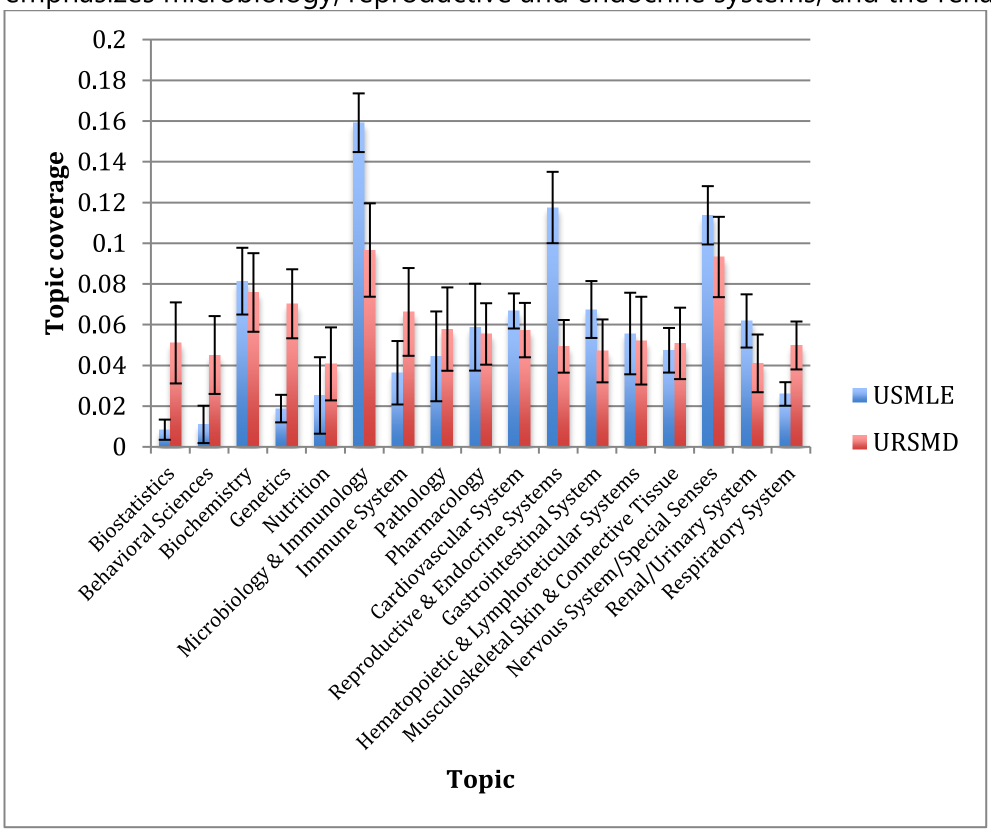


Figure 2. Topic coverages for USMLE and URSMD for the topics in the USMLE score report. The error bars show standard deviation over 1000 trials.

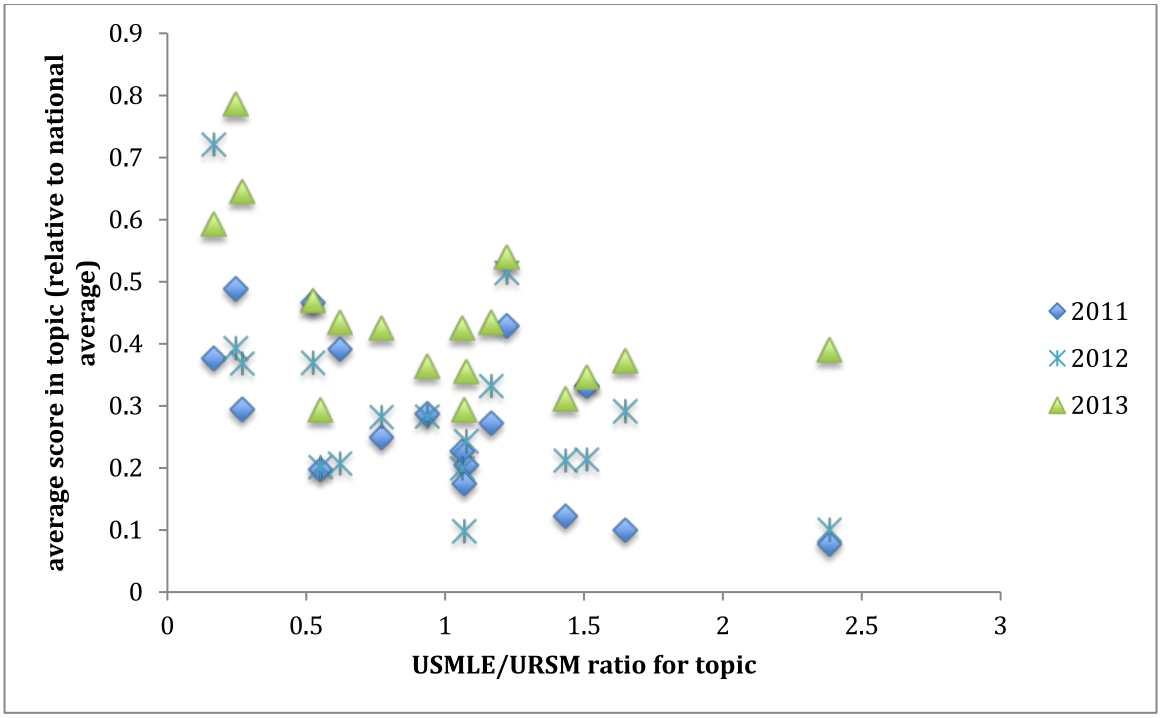


Figure 3. The ratio of the coverage of a topic in USMLE versus URSMD plotted against the average score in that topic during 3 years.

As shown in Figure 2, behavioral science, biostatistics, genetics, and the respiratory system, subjects in which URSMD students generally score highly, are also shown by LDA to have high coverage at URSMD relative to USMLE.

Conclusion: Our study suggests that LDA can be used to determine the emphasis put on a topic in the course material. Since the output is a purely text-based metric, these coverages can then be compared to the coverages from another corpus, such as the USMLE review book. Our method might apply to curriculum development and assessment.

References:

1. van Barneveld A, Arnold KE, Campbell JP. Analytics in higher education: Establishing a common language. EDUCAUSE learning initiative. 2012;1:1-11.
2. Denny JC, Smithers JD, Armstrong B, Spickard A. Where do we teach what? Journal of general internal medicine. 2005;20(10):943-6.
3. Lambert DR, Lurie SJ, Lyness JM, Ward DS. Standardizing and personalizing science in medical education. Academic Medicine. 2010;85(2):356-62.
4. Dexter J, Koshland G, Waer A, Anderson D. Mapping a curriculum database to the USMLE Step 1 content outline. Medical teacher. 2012;34(10):e666-e75.
5. Denny JC, Irani PR, Wehbe FH, Smithers JD, Spickard III A, editors. The KnowledgeMap project: development of a concept-based medical school curriculum database. AMIA Annual Symposium Proceedings; 2003: American Medical Informatics Association.

6. Bird S, editor NLTK: the natural language toolkit. Proceedings of the COLING/ACL on Interactive presentation sessions; 2006: Association for Computational Linguistics.
7. Řehůřek R, Sojka P. Gensim—Statistical Semantics in Python. 2011.
8. Blei DM. Probabilistic topic models. Communications of the ACM. 2012;55(4):77-84.
9. Blei DM, Ng AY, Jordan MI. Latent dirichlet allocation. the Journal of machine Learning research. 2003;3:993-1022.
10. Le T, Bhushan V, Sochat M. First aid for the USMLE step 1 2015. 25 ed: McGraw-Hill Education; 2015.
11. Hoffman M, Bach FR, Blei DM, editors. Online learning for latent dirichlet allocation. advances in neural information processing systems; 2010.

William Archibald, URSMD MS2, Ryan Gamlin, Katia Johnston, Daniel Ayala, Khloe Frank, Alazar Haregu, Natalie Hartman, Kelly O'Connor

Preceptor Names: Emily Gottenborg MD, Read Pierce MD
Institution: University of Colorado Anschutz Medical Campus – Aurora, CO
Department: Institute for Healthcare Quality, Safety and Efficiency

FORMALIZING COMMUNICATION IN DISCHARGE PLANNING: A STUDENT-LED, TARGETED QUALITY IMPROVEMENT EFFORT

Introduction:

Discharge from the hospital is a complex process, requiring effective and timely communication between patients, families and caregivers, and multiple inpatient providers and staff. Suboptimal communication may contribute to delays in discharge, in turn causing patient dissatisfaction, provider care team frustration, increased potential for iatrogenic harm, and inefficient use of resources. Checklists and standardization of roles and responsibilities are tools commonly employed in health care quality improvement efforts, and may also improve care team communication in the discharge process.

Objective:

The intervention sought to create clear, standardized roles, processes, and tools to enhance care team communication regarding the discharge planning process for an inpatient medical service at a large academic medical center.

Background and Methods:

A team of 8 medical students participating in the Health Innovations Scholars Program at the University of Colorado developed a focused quality improvement project to improve the patient discharge process. Over five weeks, the team performed a detailed needs assessment and current state analysis (via stakeholder interviews, process mapping and measurement, and literature-based research regarding discharge best practices). Multiple communication failure modes were identified. During three PDSA cycles, the QI team introduced communication tools and systems intended to address the most common failure modes and enhance care-team collaboration.

Specific interventions focused on rigorous definition of roles and responsibilities in soliciting and articulating the estimated date of patient discharge (EDD) during discharge rounds, recording the current EDD within the patient's Electronic Health Record (EHR), and using a visual indicator of EDD (VID) within patients' rooms to help foster structured conversations regarding potential barriers to discharge. Key metrics included adherence to prescribed roles during discharge rounds, correct usage of tools (EHR and VID), the number of weekly unanticipated discharges, average length of stay (LOS), percentage of discharges by 2pm, and HCAPHS scores relevant to discharge communication

Results:

The project achieved substantial success across all chosen metrics. Audits of adherence (n = 53) to prescribed roles during discharge rounds were 96% (soliciting and articulating EDD), 92% (EDD entered in EHR), and 77% (use of of VID). Additionally, unanticipated discharges decreased from a baseline median of four per week to two per week. Over the month-long project, average LOS decreased by 0.4 days (8% compared to an equivalent non-intervention cohort) and percentage of discharges by 2pm increased from 20% to 35%. The PDSA cycles did not increase length of discharge rounds. HCAPHS scores from the project period are pending.

Conclusion:

Formalizing roles and responsibilities in the discharge planning process is an effective method of standardizing communication between providers, staff, and patients, and can improve the efficiency and effectiveness of discharge planning.

Burzynski, Caitlin

Preceptors:
Mary Tantillo, PhD, PMHCNS-BC
University of Rochester School of Nursing
Director, Western New York Comprehensive Care Center for Eating Disorders

Richard E. Kreipe, MD
Golisano Children's Hospital
Division of Adolescent Medicine, Department of Pediatrics
Medical Director, Western New York Comprehensive Care Center for Eating Disorders

Raising Eating Disorder Awareness and Education Within Local College Communities

Background:

Though college students represent a large group of at-risk individuals for the development or exacerbation of an eating disorder, adequate education and prevention resources for students, parents, and staff are greatly lacking on college campuses. Current estimates of eating disorder prevalence among college students ranges from 8-17%, with only a small percentage of those with eating disorders receiving the proper diagnosis and treatment[1]. Recent studies have shown that students with symptoms of eating disorders are more likely to experience other mental health pathologies, including depression, anxiety, suicidal ideation, and self-injury[1]. Given that eating disorders having the highest mortality rate of any mental illness, prevention, early detection, and treatment are vitally important in ensuring the safety and wellness of college populations[2].

A recent survey from the National Eating Disorders Association (NEDA) on the services and programs available on college campuses for students struggling with, recovering from, or at risk of developing an eating disorder highlights the need for greater resources for prevention, education, and treatment[3]. In particular, the survey showed that screenings of athletes were especially lacking as well as the need for education and training for individuals on campus who could identify and refer at risk students to the proper treatment options[3]. Overall, the results indicate that greater funding and resources are needed to educate, identify, and provide services for college students struggling with eating disorders.

Objective:

We held a focus group to assess the eating disorder education and outreach needs of university and college personnel in the greater Rochester-area. We also provided educational materials and will provide training to meet the needs of faculty, staff, students, and parents on college campuses. We also hoped to initiate and encourage dialogue between college staff in various departments who are in a position to identify students with eating disorders and provide the appropriate resources or referral.

Methods:

Representatives from the Athletic Departments, Residential Life, Health Centers, and Counseling Centers from 12 colleges in upstate New York were invited to a focus group in order to gather input on their current eating disorder outreach and education needs as well as the challenges and barriers they face in relation to eating disorder identification and care. A panel of eating disorder experts was present to answer attendees' questions and share information regarding the prevalence of eating disorders in the college population. We also provided information on identifying warning signs of an eating disorder, debunking myths relating to eating disorders, and approaching students with a suspected eating disorder.

Results:

Staff from the Athletic Departments, Residential Life offices, Health Centers, and Counseling Centers of seven area colleges and universities were represented at the focus group, held at the Healing Connection, a partial-hospitalization treatment center for adolescents and adults with eating disorders. Common challenges and barriers identified by attendees included not knowing how to approach an individual with a suspected eating disorder, a lack of education related to identifying eating disorders, especially early warning signs, not knowing what resources are available, including resources in the community, and difficulty navigating the continuum of care from on-campus treatment to hospital or community treatment.

In assessing the needs of colleges, many attendees wanted training on how to approach and motivate students to seek help as well as how to involve parents in the students' care. Many staff also reiterated that a collaborative approach to supporting students with disordered eating issues would be beneficial to ensure consistent policy and procedure across departments and provide additional support. When asked about future goals, common answers included training for RA staff, collaborating with other campus departments to plan outreach events and raise awareness campus-wide, and providing more educational programming for students, staff, parents, and faculty.

Conclusion:

From the responses gathered at the focus group, we concluded that there is a need to form a collaborative team of representatives from Health Services, Counseling, Athletics and Residential Life to ensure the safety and health of students. We also assigned an eating disorder expert from the Western New York Comprehensive Care Center for Eating Disorders to each college or university to consult this team as needed. Future eating disorder training should emphasize why transitions like attending college can create risk and outline early and later warning signs of eating disorders. Training and informational materials should also outline the steps to take when a student is suspected of having an eating disorder and eating disorder treatment options within the community.

In the long-term, we propose that colleges should emphasize caring for the whole student by sending the message at the start of the college experience that a student's academic, emotional, and physical health are important to them and that they will provide resources to support wellness. Colleges should also normalize that students are undergoing a big transition when they go to college. While this is an exciting time, it can also be very stressful and some students may be extra vulnerable to mental health or substance abuse disorders. This highlights the importance of paying attention to not only academic success but also wellness during this time. Having programming that bolsters common underlying protective factors like self-esteem and body-esteem and that decreases the influence of risk factors is essential.

References:

1. Eisenberg, D., Nicklett, E. J., Roeder, K., & Kirz, N. E. (2011). Eating disorder symptoms among college students: prevalence, persistence, correlates, and treatment-seeking. Journal of American College Health: J of ACH, 59(8), 700–7.
2. Arcelus, J., Mitchell, A. J., Wales, J., & Nielsen, S. (2011). Mortality rates in patients with anorexia nervosa and other eating disorders. A meta-analysis of 36 studies. Archives of General Psychiatry, 68(7), 724–31.
3. "Eating Disorders on the College Campus: A National Survey of Programs and Resources". (2013). National Eating Disorders Association. http://www.nationaleatingdisorders.org/sites/default/files/CollegeSurvey/eatingdisordersonthecollegecampus/index.html

Carafone, Lindsay

Preceptor:
Suzanne Piotrowski, MD
Clinical Associate Professor
University of Rochester School of Medicine and Dentistry
Department of Family Medicine
Director, Teen Health and Success Partnerships, Center for Community Health

Sexual Education in Rochester Adolescents

Background and Introduction:

Teenage pregnancy is associated with higher risk of adverse birth outcomes (1), including preterm births and low birth weight babies (2), as well as long-term negative effects for the children including higher incidences of behavioral problems, chronic medical conditions, and unemployment later in life. Teen pregnancy and childbirth contribute to higher drop-out rates among high school girls: approximately 50% of teen mothers receive a high school diploma by age 22, compared with nearly 90% of teenage girls who did not give birth (3). Most adolescents begin to be sexually active during their teenage years, and as a result, contraception counseling is a crucial part of adolescent health care and should include a discussion of various methods, their efficacy, the patient's preferences, barriers to use, methods for preventing sexually transmitted infection (STI) and preparation in case of contraceptive failure (4).

Research has shown that there is still a need for primary care professionals to increase discussion of pregnancy risk with adolescents and review sexual health behaviors. A recent study of pregnant adolescents showed that 57% did not have documentation of sexual activity in their medical records and 47% did not have documentation of reproductive health counseling (5), and only 35% had contraception prescribed within 12 months of becoming pregnant. Discussion and education are essential for reducing pregnancy and STI risk. With regards to condom use, studies have demonstrated proper condom application is necessary to prevent errors (6). Primary care settings provide an opportunity for sexual health discussion, and evidence has shown that brief counseling interventions reduce the incidence of STIs, HIV and pregnancy (7).

Rochester, in particular, struggles with high rates of teen pregnancy and STIs. Rochester has the highest number of teen pregnancies in the state outside of New York City, and STI rates are higher in Rochester compared to all other cities in New York including New York City. A Monroe County Youth Risk Survey from 2011 showed that between 2001 and 2011 there were significant increases in the proportions of high school students who reported that they had ever had sex, were currently sexually active and had four or more sexual partners in their lifetime (8). Improved interventions and discussions, through primary care visits, hospital, school and community initiatives, are necessary to address these alarming rates of pregnancy and STIs in Rochester teens.

Objectives:

This project aimed to identify effective methods for discussion and education about sexual health with Rochester adolescents, particularly with regards to pregnancy and STI prevention. We sought to examine the level of knowledge regarding sexual health in Rochester adolescents and attitudes towards sexual health education by surveying youths enrolled in the Teen Health and Success Partnership. We aimed to determine what methods of sexual health education worked well in the past and what approaches are most effective in Rochester adolescents currently. Additionally, we hoped to identify newer approaches to sexual education, including the use of texting, social media, YouTube videos and other online materials, that might be well-received by Rochester adolescents. We anticipate that information from these surveys will help inform us about why the rates of pregnancy and STIs in Rochester are higher than other cities and how we can successfully intervene. This data could potentially be used in the future to train health educators, shape sexual health seminars and curricula, or be incorporated into primary care visits.

Methods:

Two surveys were designed to evaluate knowledge level regarding pregnancy and STI prevention, and attitudes towards different approaches to sexual health education among adolescents. These included questions about their preferences for having sexual health questions answered in traditional settings such as a doctor's office versus online forums, texts, YouTube videos, Facebook and other social media platforms. The project was conducted as part of an established program at the University of Rochester Center for Community Health called the Teen Health and Success Partnerships (THSP). A key part of THSP is the social and academic support services, long-term advocacy, career and life skills development, job training, health education and wellness programs offered to adolescents from the Rochester City School District. THSP has demonstrated enormous success since its initiation. So far, 100% of the THSP students have graduated from high school (compared to overall <50% high school graduation rate of Rochester City School District teens) and 89% are enrolled in college or trade school. We anticipated that by starting this project within an established program that has demonstrated success with teens in Rochester, we would have higher compliance with the study than otherwise expected.

Adolescents in THSP attend a three day conference called "Your Vision, Your Future" (YVYF) each summer. A 45 minute presentation regarding sexual health resources was provided during this year's YVYF conference , which included an introduction to online sexual health resources, such as those provided by Highland Family Planning and Planned Parenthood. The second questionnaire in our study, which will be administered starting in January 2016, will evaluate which of these resources were used by THSP adolescents and which ones they found most helpful, as well as their level of knowledge answering questions about pregnancy and STI prevention after having the opportunity to utilize these resources.

Results:

Forty participants, ranging in age from 16-23 years old, completed the first survey. 78% were female and 23% were male. 98% indicated that they had received sexual health education at their school previously. 80% indicated their healthcare provider had spoken to them about birth control and 90% indicated their healthcare provider had spoken to them about STIs.

The questions aimed at evaluating participants' level of knowledge regarding sexual health revealed that 70% of participants correctly answered that condoms can help protect against sexually transmitted infections like chlamydia or HIV. 78% responded correctly that intrauterine devices (IUDs) do not protect against STIs, however 10% incorrectly responded that IUDs do protect against STIs and the remaining responded that they did not know the answer. 88% correctly responded that condoms or dental dams are necessary to use while engaging in oral sex to protect against STIs. However, only 23% correctly responded that condoms are 82% effective at preventing pregnancy with *typical* use, while the majority of participants (68%) incorrectly responded that condoms are 95% effective with *typical* use. When asked to compare different types of birth control, only 33% correctly answered that IUDs are most effective at preventing pregnancy, 33% incorrectly responded that condoms are most effective and 28% incorrectly responded that birth control pills are most effective. Regarding knowledge of the HPV vaccine, only 33% responded that the vaccine should be delivered to all preteens aged 11 or 12 years (both male and female), while 30% responded incorrectly that the vaccine should be delivered to only females.

Finally, with regards to questions evaluating participants' preferences for different approaches to sexual health education, 86% of participants indicated that they "agreed" or "strongly agreed" that they would find it helpful to have a private discussion with their doctor or trusted adult about their sexual health. 38% "agreed" or "strongly agreed" that they would find it helpful to have a lecture-style presentation, while 30% "agreed" or "strongly agreed" that role playing would be helpful. Even fewer (21%) "agreed" or "strongly agreed" that they would find it helpful to use Facebook to have their sexual health questions answered. Only 25% "agreed" or "strongly agreed" that other forms of social media like Twitter, Tumblr or Instagram would be helpful, and only 35% "agreed" or "strongly agreed" that YouTube videos such as those provided by Planned Parenthood would be helpful.

Conclusions:

So far, conclusions can only be drawn from the results of the first survey. Administration of the second survey will take place in January 2016 and will be offered to participants who completed the first survey. Overall, the majority of participants answered many of the questions evaluating sexual health knowledge correctly. However, only 33% of participants correctly answered that IUDs are most effective at preventing pregnancy compared to birth control pills, condoms and spermicide foams. It is noteworthy that 33% responded that condoms are the most effective form of birth control to prevent pregnancy. Regarding HPV vaccine delivery, the majority of participants did not respond correctly that the vaccine should be delivered to all preteens aged 11 or 12 years old (both male and female). These results suggest that despite 98% of participants receiving sexual education in the Rochester City School District, there are areas where education needs to be substantially improved or supplemented.

Our results regarding preferences for different approaches to sexual health education were somewhat surprising, as we anticipated many teens would welcome the use of social media (YouTube, Facebook, Twitter, online forums) compared to private discussions with healthcare providers. These unexpected results might stem from the population we used in this study - adolescents in the Teen Health and Success program. Adolescents in THSP tend to have greater access to support, including one-on-one mentoring and enrichment programs offered through THSP, compared to many of their peers. This could explain the greater percentage of participants preferring private discussion with doctors compared to the use of social media and other online forums for accessing information about sexual health.

Further conclusions will be made in 2016 when the second survey is administered. Future directions will also include trying to expand the survey to include adolescents in the Rochester City School District who are not part of THSP so that we can compare responses from adolescents who are members of a supportive teen program like THSP to those who do not have access to such resources.

References:

15. Chen XK, Wen SW, Fleming N, Demissie K, Rhoads GG, Walker M. Teenage pregnancy and adverse birth outcomes: a large population based retrospective cohort study. Int J Epidemiol. 2007 Apr;36(2): 368-73.
16. Yadav S, Choudhary D, Agrawal P. Adverse Reproductive Outcomes Associated with Teenage Pregnancy. McGill Journal of Medicine. 2008 Nov; 11(2):141-144.
17. Centers for Disease Control and Prevention. Teen Pregnancy: Improving the Lives of Young People and Strengthening Communities by Reducing Teen Pregnancy. 2011.
18. Potter J and Santelli J. Adolescent contraception: review and guidance for pediatric clinicians. Minerva Pediatrica. 2014 Oct 31.
19. Kharbanda EO, Stuck L, Molitor B, Nordin JD. Missed opportunities for pregnancy prevention among insured adolescents. JAMA Peditr. 2014 Dec1;168(12).
20. Crosby R, Graham C, Milhausen R, Sanders S, Yarber W, Shrier LA. Associations between rushed condom application and condom use errors and problems. Sex Trans Infect. 2013 Nov 12.
21. Cooper B, Toskin I, Kulier R, Allen T, Hawkes S. Brief sexuality communication --a behavioural intervention to advance sexually transmitted infection/HIV prevention: a systematic review.
22. Monroe County Adolescent Health Report Card, November 2012 http://www2.monroecounty.gov/files/health/DataReports/adolescent%20report%20card%20final.pdf.

Jennifer Corcoran

Preceptors:
David Adler, MD, MPH
Associate Professor of Emergency Medicine
University of Rochester Medical Center

Flavia Nobay, MD
Associate Professor of Emergency Medicine
University of Rochester Medical Center

A Mixed-Methods Analysis of Emergency Healthcare Utilization by the Homeless Population of Rochester, NY

Introduction:
Homelessness and health interact in complex ways; mental and physical illness can put one at risk for homelessness, and homelessness itself is a risk factor for poor health and mortality. Homelessness is a significant problem in Rochester, NY. The homeless population in Rochester includes 640 families with dependent children, 1,161 single men aged 25 or older, 693 single women aged 25 or older, and 206 single young adults between the ages of 18 and 24.[1]

Homelessness increases all-cause mortality risk.[2] Substance abuse, cardiovascular disease, and cancer have been identified as major causes of mortality in one study.[3] These are chronic disease best managed with consistent care, yet the homeless are likely to lack primary care access.[4] Lacking access to primary and preventive care, the homeless are more likely to use the emergency department (ED) as a major or only source of care[5]. The inability of Rochester's clinicians to provide longitudinal preventive care to this high-risk population is problematic for hospitals, health care providers, local communities, and the homeless themselves. Hospitals may lose money due to the high cost of ED care and low rates of health insurance among the homeless. Providers may feel frustrated and unable to

---

[1] Homeless Resolution Strategy: Rochester and Monroe County, Final Report. September 2012, revised 19 November 2012.
[2] Morrison, DS. Homelessness as an independent risk factor for mortality: results from a retrospective cohort study. *International Journal of Epidemiology.* 2009;38:877-883.
[3] Baggett, T.P., et al. Mortality among homeless adults in Boston: Shifts in Causes of Death over a 15-Year Period. *JAMA Intern Med.* 2013 Feb 11;173(3):189-95.
[4] White, B.M., and Newman, S.D. Access to Primary Care Services Among the Homeless: A Synthesis of the Literature Using the Equity of Access to Medical Care Framework. *J Prim Care Community Health.* 11 Nov 2014. Accessed 19 Jan 2015.
[5] Kushel, M.B., et al. ED Use Among the Homeless and Marginally House: Results from a Community-Based Study. *Am J Public Health.* 2002;92:778-784.

effect real change for their patients through emergency medical interventions.[6] Communities shoulder the costs through higher insurance premiums. Most importantly, the homeless suffer because the ED is not designed for provide longitudinal holistic care.

Objective:
This study seeks to build on previous research in Rochester that has identified the health needs, barriers to care, and existing resources in the city for the chronically homeless. The qualitative arm of the present study seeks to understand emergency care for homeless individuals in Rochester from the perspectives of both homeless patients and ED staff through semi-structured interviews. The quantitative arm seeks to describe characteristics, burden of disease, and emergency health care utilization of homeless adults compared to low-income, non-homeless adults in Rochester, NY, via retrospective chart review of Strong Memorial Hospital ED visits over a two-year period.

Methods:
For the qualitative arm of the study, semi-structured interviews were conducted with currently homeless patients who had been treated at a Rochester ED, and with ED staff, including residents, attending physicians, nurses and social workers. To be eligible for inclusion in the study, staff members were required to be at least 18 years old and have at least one year of hospital experience. Recruitment was done via e-mail, and verbal consent obtained in person after the staff member expressed interest in participation via e-mail. Homeless subjects were recruited in person during the course of University of Rochester street outreach. To be eligible for inclusion in the study, homeless individuals must self-identify as homeless, have received care in a Rochester ED while homeless, be at least 18 years old, and be able to answer questions coherently in English. The interviews were audio recorded for accurate transcription of the subjects' answers. No names were recorded in order to ensure subjects' privacy.

For the quantitative arm of the study, potential charts to abstract were identified by a search for keywords indicating homelessness in ED physician and social work notes for Strong Memorial Hospital ED visits between March 2013 and March 2015. Medicaid-enrolled patients who were not identified as homeless were used as a control group. Data points extracted include patient demographics, diagnoses, health care utilization, ED discharge plans, and dispositions.

Results and Conclusion: Interviews of ED staff and homeless individuals are ongoing. Chart extraction has been completed, but analysis has not yet been completed.

[6] Doran, K.M., et al. "Rewarding and Challenging at the Same Time": Emergency Medicine Residents' Experiences Caring for Patients Who Are Homeless. *Acad Emerg Med.* 2014 Jun:21(6):673-679.

Beatriz Malibiran

Katherine Greenberg, MD; Sara Jenks MPH; Andy Aligne, MD, MPH
Strong Memorial Hospital
Pediatrics Department
The Hoekelman Center

Decoding Adolescent Perspectives to Inform the LARC Initiative

Introduction:

The LARC Initiative is an outreach program that promotes the use of long-acting reversible contraceptives (LARCs, an umbrella term that includes both IUDs and contraceptive implants) in adolescents by educating Rochesterian healthcare providers and clinics about the efficacy, safety, and benefits of use in the pediatric population. With increased effectiveness in pregnancy prevention relative to other birth control methods, the AAP recently recommended LARC as first line contraceptive methods for the adolescent population (1).

This initiative was a reaction to both the AAP recommendations as well as the Family Benefits Planning Program (FPBP), a NYS Medicaid program that provides birth control options to young women for little to no cost based upon the individual's income. With FPBP, accessible and affordable LARC is available to all adolescents throughout the state. In response to this, the LARC Initiative is working to raise awareness about LARC and its availability in the Rochester community.

Objective:

The objective of my project was to qualitatively assess the pre-existing knowledge and misconceptions that Rochester teens have with regards to LARC. Other members of the LARC Initiative, including a number of other medical students, moderated a series of focus groups on this topic. My work this summer was dedicated to analyzing and categorizing the transcripts of these groups. By identifying prevalent themes in these discussions, we hoped to inform the Initiative of widespread deficits in adolescent knowledge of general contraception, including LARC. With this knowledge, we hoped to understand the baseline knowledge of our target population and perhaps better target the work of the LARC Initiative to the community's needs.

Background:

Both teenage mothers and their children suffer from a greater incidence of health problems that include, but are not limited to, preterm birth, low birth weight, developmental delay, and neonatal mortality (2). Within the United States, the rate of teenage pregnancy is estimated to be about 29.5 births per 1000 females ages 15-19 years old (3). Relative to other developed nations, this rate is abnormally high. Compounding this issue, the rate of teenage pregnancy in Rochester, NY is estimated to be as high as 93.7 births per 1000 females ages 15-19 years (4). As such, the United States federal government has declared that the reduction of teen pregnancy is a major public health initiative in the United States. In New York state, Medicaid has implemented a program called the Family Planning Benefits Program, granting young women from the ages of 12 to 26 ready and affordable access to various forms of birth control, including LARC. Despite this option, however, LARC uptake in NYS remains low with about 6.1% of the population currently utilizing either an IUD or a Nexplanon implant (5). As such, the LARC Initiative is a response to this under-utilization. By educating healthcare professionals and community service centers about LARC and its availability, adolescents will have more informants and better access to the most effective types of birth control, likely bringing the teenage pregnancy rate down.

Methods

Participant Qualifications

All participants were adolescent females aged 15-19 years old. Eligibility for this study required prior written consent from a parent or guardian, as well as oral and written consent from the participants themselves.

Sample and Data Collection

We recruited adolescent females from Rochester, Monroe County, NY through various teen empowerment programs known through our network of positive teen development agencies.

Data were collected from seven focus group discussions conducted with a semi-structured and open-ended interview guide. During the discussion, participants were invited to discuss their knowledge and opinions on any of the contraceptive methods presented on an illustrated sheet. After the open-ended portion of the discussion was concluded, participants were asked: “How likely would you be to recommend this method to a friend?”. For each method, participants verbally rated their recommendation for each method on a scale from 1 to 10. They were free to elaborate upon their reasoning for each rating. The focus groups included 2 to 6 participants and were each moderated by 2 members of the LARC Initiative at the Hoekelman Center. Discussions lasted between 30 to 90 minutes.

Every session was audio recorded and transcribed verbatim.

The transcripts were read by the analysis team and emergent themes identified as a series of initial codes. Two team members then coded the transcripts individually but were each blinded to the other’s work. They later verified their codes and settled any discrepancies through discussion and consensus.

Analysis

Initial analysis was performed between three different coders—Dr. Katherine Greenberg, Sara Jenks, and myself. All transcripts were coded using Microsoft Word and Apple Pages software. Using two transcripts to inform the process, each coder independently identified prominent themes in the discussions. A finalized set of themes were arrived at through unanimous consensus among the coders.

With the thematic codes established, each coder individually coded all of the transcripts, meeting periodically to establish unanimous consensus of the coding for each transcript.

The codes were then quantified using Apple Numbers software and reviewed by the analysis team for relevant trends.

Results
Reported here are the results of the thematic coding process. Any participants who did not meet eligibility criteria were excluded from analysis post-discussion.

1) Ratings and Comments
Participants were asked to rate each contraception method on a scale from 0 to 10 based on their likelihood of recommending the method to a friend.
The average rating for each method is reported here, along with the range.

Method	Average Rating	Range	Standard Deviation
Condom	8.7	2-10	2.3
Emergency Contraception	6.5	0-10	3.4
Depo Provera	5.9	0-10	2.9
Implant (Nexplanon)	7.8	0-10	2.5
IUD	6.3	0-10	3.7
OCP	5.0	0-10	3.3
Patch	3.8	0-8	2.8
Ring	3.4	0-10	2.4

Table 1: Average rating of each contraceptive method across all focus groups conducted. Also reported at the range and standard deviation of ratings for each.

Participants were also asked to explain their reasons for these ratings. Overall, the popularity of the condom was related to its protection against STDs. It is important to note that many participants also cited the need for a second method of contraception because of the relatively lower efficacy of condoms when protecting against pregnancy. The contraceptive implant and IUD were both noted to have high efficacy rates, but were often devalued because of perceived health risks from having a “foreign object” in the body.

2) Sources
Additionally, participants spontaneously disclosed their sources of information for contraception. The majority of these disclosures was attributed to personal anecdotes (32 of 62) and self disclosures (14 of 62). Outreach education programs, medical professionals, and school were only a minority of these reported sources (5, 6, and 5 of 62, respectively).

Conclusion:
The results of this coding were used to assemble a "snapshot" of adolescent perspectives on contraceptive methods, particularly on LARC. Presented in this paper are the ideas generated during the focus group discussions. Given that the sample is biased towards adolescents with greater exposure to sexual health education, it must be understood that this analysis is not broadly representative of all high school age groups.

It appears that there is a rising awareness of LARC methods among teenagers. The implant was the second-highest rated method of contraception among participants. Often cited as a good method for its efficacy, the implant was better rated than the IUD because of a perception of a less invasive localization of the device. As noted, these participants have better access to sexual education than the general public. Their knowledge of LARC efficacy is technical knowledge that likely results from participation in their specific extracurricular programs that offer such formal education.

The mostly highly rated method of contraception amongst our participants was actually the condom. Interestingly enough, the condoms was always mentioned as the primary means of preventing STD rates, thus warranting its high rating. Regardless, each group also mentioned that condoms do not provide sufficient protection against pregnancy to be used as the primary method of birth control. A sophisticated answer provided by many of these groups was to use multiple methods in conjunction. These teenagers are educated in the methods of birth control, but they have not yet surmounted the mythology of danger surrounding the IUD and the implant. This is a more instinctive reaction, that may be mitigated with more personal exposure to LARC.

It is also important to address the sources that the adolescent community relies upon to gain their knowledge of contraception. According to participant responses, personal anecdotes—that is, stories from friends and family—were their most common and salient sources of information. This is understandable; adolescents look to peers and family for advice in many fields. It is also exciting. Many of the adolescents who participated in our conversations noted the increasing prevalence of the implant among their peers. Even though the participants who did not have the implant were generally averse to the idea of a "foreign object" as their means of contraception, they also noted its efficacy (as discussed earlier) and the positive experiences of their friends with this method.

More concerning, however, was the absence of medical providers and educational programs in this discussion. While these sources can provide the most up to date and accurate information, it appears that they do not yet have that role in the adolescent community. On the other hand, many providers are hesitant when offering expensive forms of birth control to teenagers. It is hard to encourage the distribution of LARC when common perception is that adolescents are poorly motivated to maintain contraception use. However, when young women are well-informed and granted wide access to all the methods of birth control, they overwhelmingly choose LARC for themselves (6).

With this in mind, the work of the LARC Initiative is put into perspective. By promoting LARC to providers and social services for adolescents, the LARC Initiative is broadly promoting appropriate contraceptive education at appropriate sources. Crucial to expanding the contraceptive knowledge base of Rochester, the doctors, nurses, and caseworkers who work with young women should be kept abreast of the advantages of LARC. Knowing that adolescents are starting to see LARC—the implant especially—as an effective contraceptive means in their own community means that adolescents now need unbiased facts about LARC. Providers that we reach can provide further encouragement to teenagers considering LARC, normalizing a method that hopefully can come to prominence soon.

References:

1**-** AAP Updates Recommendations on Teen Pregnancy Prevention. October 2014. https://www.aap.org/en-us/about-the-aap/aap-press-room/pages/AAP-Updates-Recommendations-on-Teen-Pregnancy-Prevention.aspx

2- Chen, XK; Wen, SW; Fleming, N; Demissie, K; Rhoads, GG; Walker, M. Teenage pregnancy and adverse birth outcomes: a large population based retrospective cohort study. International Journal of Epidemiology. 36 (2):368-73. April 2007.

3-About Teen Pregnancy. *CDC Fact Sheet*. June 2014. http://www.cdc.gov/teenpregnancy/aboutteenpreg.htm

4-County/ZIP Code Perinatal Data Profile. *New York State Vital Statistics Data.* March 2014.

5-Contraceptive use in the United States. The Guttmacher Institute.

6- Ricketts, S; Klinger, G; Schwalberg, R. Game change in Colorado: Widespread use of long-acting reversible contraceptives and rapid decline in birthed among young, low-income women. Perspectives on Sexual and Reproductive Health. 46 (3):125-202. September 2014.

Jackie Murtha, Liz Levy, Michelle Nessen

Student Run Clinics: Patient Recruitment and an Analysis of Common Problems

Introduction:
Despite the rollout of the Affordable Care Act, 8.9% of people in New York State remain uninsured [1]. UR Well, a network of three student run clinics run by students at University of Rochester School of Medicine and Dentistry, is designed to serve as a safety night, providing high-quality and affordable healthcare to individuals in need. The UR Well clinics at Asbury First United Methodist Church and St. Luke's provide acute care and physical exams. The clinic at St. Joseph's Neighborhood Center provides longitudinal primary care and uses the resources of the clinic that operates at that location during the day to provide additional services such as counselors, physical therapy, dietitians, socials workers, and other medical sub-specialities. Apart from serving as a safety net in the Rochester community, the clinics also provide students a chance to practice clinical skills and be exposed to urban healthcare and issues of social justice.

Each summer three students remain in Rochester to do an internship with the three clinics. The internship gives the students a more in-depth experience with with inner workings of the clinics and prepares them to be clinic directors. It also allows them to conduct multiple projects to help assess the clinics and improve their functioning. This summer the projects (1) expanded community awareness of the new clinic, St. Luke's, (2) assessed a project started the previous summer that refers patients from Asbury and St. Luke's to St. Joe's for more longitudinal care, and (3) digitizing charts at St. Joe's in preparation for the shift to electronic medical records and to begin data analysis of the clinic clientele.

Patient Recruitment:
The efficiency and efficacy of UR Well at Asbury depend largely on the number of patients seen per night and the causes of their visits. While Physical Exam nights at Asbury, held the first Tuesday of every month, tend to draw large crowds, we see significantly fewer patients on the remaining Thursday nights, and a number of these patients include those who were unable to receive physicals on the allotted night. Thus, increasing awareness of the services provided by UR Well will increase our patient load on a given night and help better serve the Rochester community.

<u>Methods:</u>
Efforts to increase awareness of the clinic were specifically targeted towards sites with particularly in-need individuals. The RochesterWorks website provided comprehensive lists of support services in the Rochester area. From the lists of consignment stores and food pantries, locations were chosen within about a 5-mile radius of the Asbury clinic. At these sites, information was disseminated that included descriptions of the clinic services as well as the clinic's business cards. Intake forms at Asbury now include a question about how each patient originally heard about the clinic.

Future Directions:
Patient recruitment is an ongoing process, and will continue be so as UR Well grows. Expanding the patient population at the Asbury clinic, as well as at St. Luke's and St. Joe's, is a priority moving forward. We will direct our efforts towards more locations where we can find members of the community who would most benefit from our services. Furthermore, as more information about how patients find out about the clinic is collected, a systematic analysis of how to best recruit patients can be performed. As we gain a better sense of who our patients are, and how they end up with us, we can even better target our intended patient population.

Clinic Referrals:

Background:
Lack of patient follow-up and continued care pose significant barriers in prevention of disease and managing patients' health. This is true in all areas of healthcare and most especially in populations with under insured, uninsured or financially troubled individuals. Access to healthcare for low to no income individuals and families proves to be very difficult. At Asbury Clinic, we see patients on a walk-in basis for any acute care needs they may have. Our St. Joseph's clinic allows for long-term follow-up for established clinic patients who do not have insurance. Over the past year, we implemented a new strategy to link our acute care patients from Asbury with potential long-term follow-up at St. Joseph's. Anyone that was referred from Asbury to St. Joseph's is contacted by the St. Joseph's Access department for financial assessment and to determine eligibility for St. Joseph's services.

Objective:
To assess the effectiveness and utility of our 'Asbury to St. Joseph's referral system.'

Methods:
Assess the referral system based on utilization and follow-up. Reviewed referral logs, Asbury clinic EMR and St. Joseph's scheduling system to determine what patients had been seen at Asbury and referred, and what patients had been contacted successfully by the St. Joseph's access team. From these records, it could be determined how many patients had had an Access appointment and who was established as long term patients at St. Joseph's.

Results:
119 patients were referred from Asbury to St. Joseph's. Of these 119 patients, 88 were seen for physicals and 31 were seen for an acute care need. Of these 119 referrals, 40 patients were successfully contacted by the St. Joseph's access department. Of the 40 that were contacted, 9 patients were established as patients at St. Joseph's. 7 of these 9 were seen for acute needs and 2 were seen for physicals. The other 31 patients were either not interested, did not qualify for the services based on financial assessment or did not show up to their appointment with the access department.

Conclusion and Future Directions:

Our referral system has been limited in its success to connect patients from Asbury with St. Joseph's. We now know that those patients seen for acute care needs are more likely to follow-up with St. Joseph's than those seen for physicals. This is not surprising in that those seen for acute care visits may be in need of immediate additional healthcare whereas those seen for physicals likely have no immediate need for the services available at St. Joseph's. There is a high chance of loss to follow-up in this system because it involves many transfers of information between people for successful contact by the Access department to be made. Future plans will involve decreasing the chance for loss to follow-up by exploring the possibility of a more direct referral system that could link the patient directly with the Access team instead of relying on phone contact.

Chart Digitalization:

Objective:

St. Joseph's Neighborhood Center is currently transitioning to electronic medical records. The project is designed to streamline the transition by coding the problem lists to ICD-9 and creating an electronic patient database. The patient's PMP numbers will function as reference allowing the merging of multiple different electronic databases so future studies can combine the financial, demographic, appointment history, and medical history. These studies will allow us to assess for the first time who uses the clinic services, how frequently they are used, and for what reasons. The services provided at the clinic can then be tailored to better suit the needs of the patients. Furthermore, patients can be tracked to see if they are utilizing services such as dietitians, foot care, social work, counseling, and eye care to manage all aspects of their health.

Methods:

Table 1. Clinic Demographics by Ethnicity and Gender

Ethnicity	Female	Male
Asian	9	12
Black	115	84
Hispanic	32	31
White	125	115
Other	49	41

Medical students performed chart reviews of 650 patients at St. Joseph's Neighborhood Center. Problem lists were updated and consolidated by consulting provider notes, medication lists, and laboratory results. Only longterm medical issues were included on the lists. Patients solely utilizing dental and counselor services were excluded from the project. Finalized problem lists were entered into an Access file that included age, ethnicity, general provider, specialists, medical problems, and surgeries. Individual patients were tracked using PMP numbers as an identifier. To combine multiple patient databases, the problem list data was transferred into MySequel. Using the PMP number as a reference, the problem list data will be linked to their financial, demographic and household information. Tableau was used to graph the data. 37 of the patients had blank problem lists and their data was not initially transferred into MySequel and Tableau. Going forward that problem will be corrected. The results reflected below represent the 613 patients with chronic medical problems. Also 5 patients had incorrectly entered date of birth so their age did not calculate in the database. This problem will also be corrected in the future.

Results:

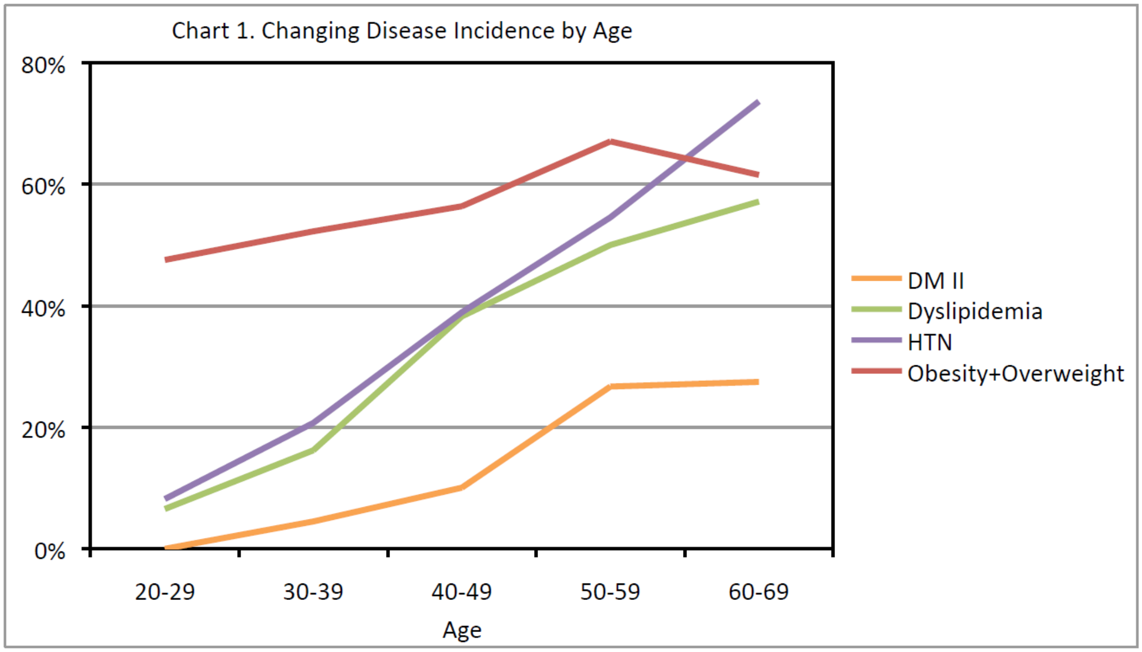
Of the 613 patients analyzed the majority classified themselves as Black (32%) or White (39%) (Table 1). Hispanic (10%) and Asian (3%) represent the next two biggest categories. The remainder of patients either did not declare an ethnicity or marked other. Patients range in age from less than 20 to over 80. Due to Medicare and Medicaid, the majority of patients range in age from 20-69 with 24% aged 40-49 and 29% aged 50-59
(Table 2).

The top 4 medical problems be all patients are obesity, HTN, tobacco abuse, and dyslipidemia. The frequency of tobacco abuse changes by age group, peaking at 50% of patients in the 30-39 age group and then declining to 31% in the 60-69 age group. These rates, regardless of age group, are significantly than the New York state average of 17.1% (2). To patients that attend URWell evening clinic, another student run group called Smoking Cessation will talk to all patients that use tobacco products about quitting.
Promoting their services to the patients that attend St. Joe's during the day may help reduce the above average smoking rate.

Table 2. Clinic Demographics: Age

Age	Male	Female	Total Male + Female	Percent Patients
<20	2	1	3	0%
20-29	23	38	61	10%
30-39	57	54	111	18%
40-49	80	68	148	24%
50-59	72	104	176	29%
60-69	42	49	91	15%
70-79	5	5	10	2%

The other top three medical problems, obesity, HTN, and dyslipidemia, along with DM Type II, increase in frequency by age group. Obesity rates remain the most stable, increasing from 36% in patients aged 20-29 to 47% of patients aged 60-69. These rates are higher but follow a similar trend as the national numbers reported by CDC: age 20- 39 (30.3%), 40-59 years old (39.5%), or adults over 60 or above (35.4%) (3). HTN, dyslipidemia and DM Type II display much more drastic increases by age (Chart 1). Obesity is a risk factor for all three of the conditions. Early prevention and weight management could help reduce the incidence in the St. Joe's patient population. There are a couple of different dietitian-run programs offered through the clinic whose use and effectiveness should be evaluated. If they prove effective, then they should be expanded to help more patients. A shortcoming of the above data at this point is that the incidence of the problems has not been correlated with the medication lists and lab values in the database yet. Afterwards it will be possible to see how patients are managing their dyslipidemia, HTN and DM II.



There was also variation in chronic medical problem incidence by gender and ethnicity, although the top 4 problems remain the same for all groups except White females where Depressive Disorder has displaced HTN (Charts 2-4). The higher rates of obesity among Blacks and Hispanics than Whites correlates with the national trend, although the rates are higher (3). Obesity has been shown to correlate with socioeconomic status so it is not surprising that patients at St. Joe's will have higher rates.

Regardless of ethnicity, rates of dyslipidemia and HTN are higher among males than females.

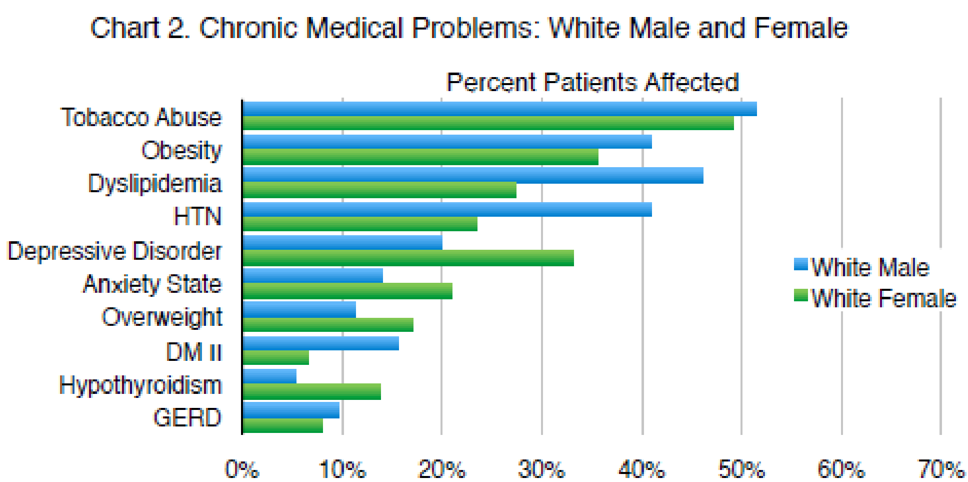


Chart 3. Chronic Medical Problems: Black Male and Female

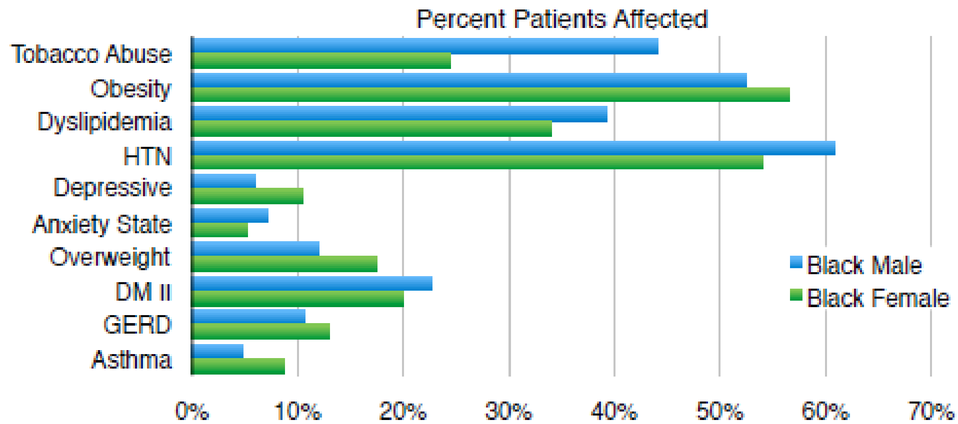
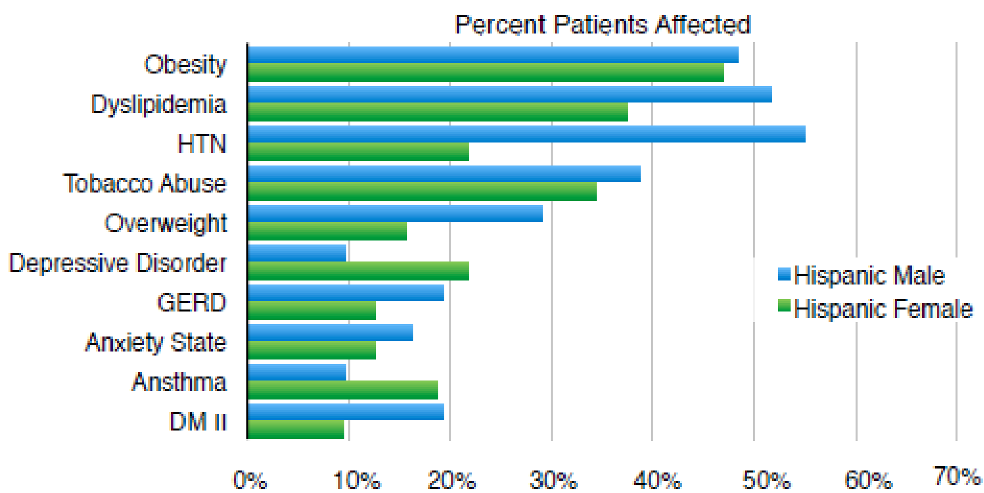


Chart 4. Chronic Medical Problems: Hispanic Male and Female



<u>Conclusion:</u>

At this stage, the problem list project has shown the common problems at St. Joe's along with a breakdown by age, gender and ethnicity. Going forward the information will be further supplemented with household information, frequency of visits to the clinic, medications, finances, use of counselors and social workers, and use of other services through the clinic and community referrals. This will allow for more in-depth analysis of the data to better target services at the clinic going forward.

From a student perspective, it will allow us to give more infromaton to our medical student volunteers so they can more accurately screen patients and provide them with the necessary services. It can also be used to increase the involvement of axillary student groups such as smoking cessation.

References:

Kaiser Family Foundation analysis of the 2015 ASEC Supplement to the CPS.
Map of Current Cigarette Use Among Adults (Centers for Disease Control and Prevention). 2013. http://www.cdc.gov/statesystem/cigaretteuseadult.html
Adult Obesity Facts (Centers for Disease Control and Prevention). 2015. http://www.cdc.gov/obesity/data/adult.html

Clayton Buback
Tina Wu

Dr. Yeates Conwell
Professor of Psychiatry
Director, Geriatric Psychiatry Program
Director, URMC Office for Aging Research and Health Services
University of Rochester Medical Center

Dr. Shulin Chen
Associate Professor
Zhejiang University
Department of Psychology

Evaluating Volunteer Activities and Social Connectedness in Older Adults of Hangzhou, China

Introduction:

Suicide is major concern within the geriatric population around the world. In the US, the Diagnostic and Statistical Manual of Mental Disorders IV (DSM IV) axis system identifies psychopathology, personality, physical health, social context, and level of functioning as key in considering suicide risk[1]. Within these axes, social context can be a broad and difficult category to quantify in relation to suicide risk. The Medical Outcomes Study-Social Support Survey, or MOS-SSS, is a widely accepted tool for quantification of social connectedness, an aspect of social context[2]. This survey contains subscales that further detail a person's social supports, including emotional support (the expression of positive affect, empathetic understanding, and the encouragement of expressions or feelings), tangible support (the provision of material aid or behavioral assistance), positive social interaction (the availability of other persons to enjoy activities), and affectionate support (the expressions of love and affection)[2]. Previous studies have shown that higher levels of social connectedness are correlated to better health outcomes in older adults, especially related to depression and mental health[3]. Increasing social connectedness may therefore serve as an avenue for suicide prevention. A Chinese-language version of this tool (denoted MOS-SSS-C) has been validated and used in the Chinese population[4].

One proposed method of achieving an increase in social connectedness is through the promotion of volunteer activities. Previous work in Australia has shown that volunteers have higher rates of social connectedness[5], but we cannot simply generalize this conclusion to a different culture such as China. With the largest population of older adults and third highest suicide rate in older adults[6-7], China boasts unique cultural differences that warrant detailed investigation. Affirming the link between volunteerism and social connectedness within the cultural context of China would be useful in guiding policies to reach the greatest number of at-risk older adults. For this reason, we sought to evaluate the correlation between volunteerism and social connectedness in our study population of older adults in Hangzhou, China. Through this study, we hope to illuminate some of the demographic features and health characteristics of older adult volunteers in Hangzhou to better assist us in creating mental wellness programs.

Objective:

This study investigated the link between volunteer activities and social connectedness in older adults in Hangzhou, China. Specifically, the following research questions were addressed: 1) Do high levels of volunteer activity correlate to high levels of social connectedness? 2) Are there demographic trends in volunteer activities and/or social connectedness levels? 3) How does ableness correlate to volunteer activities and/or social connectedness levels? Surveys were administered to visitors identified as willing volunteers at the Xiao Ying Community Center in Hangzhou. The survey collected demographic information, assessed physical and mental health, quantified the subject's social connectedness, and evaluated the subject's volunteer activities.

We expected that subjects who reported high levels of volunteer activity would report, on average, higher social connectedness than subjects that reported low or no volunteer activities. We also expected that high levels of ableness would correspond to increased volunteer activities. This information would be helpful in identifying ways to increase social connectedness in this population, which is well-established to be correlated with better overall health outcomes.

Background:

Facing mental illness, the older adult population encounters challenges ubiquitous in the context of aging. However the study of mental illness in this population has been largely overlooked in favor of other aged populations, which limits our ability to create effective treatments and therapies targeted at the individual and societal level. This is evident when we talk about suicide, the tenth leading cause of death in the world[8-9]. The resulting societal and economic burden is a significant public health concern. This is especially true in China, a country with the largest population of older adults and third highest suicide rate in older adults[6-7]. Suicidal ideation has also been found to be present in over ten percent of the Chinese older adult population[10]. It becomes important then to identify and develop effective suicide prevention programs. Exploring social connectedness in later life for suicide prevention has been proposed as an area of high priority research to meet this goal[11].

The viability of this suggestion is supported by studies done such as one in neighboring Japan, where it was found that home visits from welfare volunteers were associated with significantly lower risk of suicidal ideation in older adults[12]. Indeed a meta-analysis of 148 studies also supported that stronger social connections were associated with a 50% increase in survival[13]. This was accompanied by the assertion that social connectedness was as strong of a risk factor for death as other well-known risk factors such as smoking[14]. All of this creates compelling evidence for why social connectedness should be an active area of research in promoting elderly health and well-being.

In our study, we explored the efficacy of volunteerism as a way to create social connectedness. There is already evidence to suggest that volunteering for “other-oriented reasons” creates a protective effect on the older adult’s overall health[15-16]. Our hope was thus to reaffirm this link in our older adult population in Hangzhou, in an attempt to aid in identifying some possible mechanisms for improving the well-being of Chinese older adults.

Methods:

Visitors to the Xiao Ying Community Center were approached and asked to participate in our study. Subjects who were not older than 55 years old or who were unable to provide consent were excluded. A total of 85 subjects consented to be surveyed, of which 75 completed the survey. These subjects were administered our survey (Appendices A and B) in-person, which has four distinct parts. This survey collects demographic information, measures physical and mental health using the 12-item short-form Medical Outcomes Scale (SF-12)[17], assesses social connectedness using the Medical Outcome Study-Social Support Survey[4], and collects information on volunteer activities using methods adapted from the U.S. Department of Labor[18]. All information was presented to the subjects in written form, and most required oral administration due to illiteracy or poor vision.

Small Stata™ was used to perform univariate and multivariate linear regression analysis to test for statistical significance. Information collected about the age and gender of subjects’ children was not used. Responses regarding hours per month of volunteering were deemed unreliable based on wide variability and lack of confidence of the subjects, and was not used in analysis. A free-entry question inquiring about the number of friends and close relatives on the MOS-SSS-C was not required for scoring and thus also excluded. Questions on the MOS-SSS-C were scored on a 1-5 point scale with increasing frequency of contact. Responses regarding level of education were coded for use in Small Stata by assigning scores for educational norms: 1 for less than nine total years of formal education, 2 for nine to fifteen years of formal education, and 3 for obtaining sixteen or more years of formal education. The SF-12 was scored using US normative data due to availability.

Results:

Table 1: Survey Results of Volunteers and Non-Volunteers with Univariate Analysis Using Linear Regression

	Volunteer		
	Yes	No	P-value
Number	16	59	
% Female	62.5	71.1	0.583
Average Age	69	70	0.510
% Married	87.5	78.0	0.405
Average Education Score	1.75	1.68	0.709
% ≥2 children	56.3	40.7	0.905
Average MOS-SSS-C	64.72	72.40	0.227
Emotional Support	3.39	3.80	0.135
Tangible Support	3.84	4.09	0.452
Affectionate Support	3.85	4.05	0.495
Positive Social Interaction	3.65	3.73	0.815
Additional Item	3.19	3.98	0.029
Physical Composite Score	44.68	43.29	0.571
Mental Composite Score	47.35	50.14	0.316

Demographics

As shown in Table 1, among our 75 participants, 16 (21%) of these individuals identified as volunteers, while 59 (79%) reported no volunteer work which was defined as "activities for which people are not paid, except perhaps expenses… [done] through or for an organization." The average age of volunteers (69 years) and non-volunteers (70 years) was similar. Though not statistically significant, a greater proportion of volunteers were currently married (87.5%), obtained higher educations (Edu Score=1.75), and had more children (56.25% with ≥2 children) than their non-volunteer counterparts. Volunteers also included proportionately fewer females (62.5%) than non-volunteers (71.2%). Most volunteer activities fell within Xiao Ying Community Center. Other volunteer events included political obligations, veteran's affairs, class reunion planning, childcare, and other community events.

Social Support

The overall MOS-SSS-C score was lower for volunteers (64.72) than non-volunteers (72.40), though there was no significant correlation between volunteerism and the overall MOS-SSS-C score. However when broken down into its five components, certain parts of the MOS-SSS-C stood out as having more potential for correlation with volunteerism. The additional item, which asks the person to rank how often they have "someone to do things with to help you get your minds off things" was significantly correlated with volunteer activity (p=0.029). Of interest is that people who volunteered reported on average a lower frequency of support in that category than non-volunteers. It is also important to note that though not statistically significant, emotional support was on average higher among non-volunteers (3.80) than volunteers (3.39). These could suggest that non-volunteers have established social activities and stable supports that occupy their time effectively and do not lead them to want to pursue activities such as volunteering. It could also suggest that volunteers are individuals that are lacking in social supports who proactively seek opportunities to reconnect with those around them.

Physical and Mental Composite Scores

On average, volunteers report higher physical composite scores (44.68) and lower mental composite scores (47.35) than their non-volunteer counterparts (43.29, 50.14 respectively). Neither of these health indicators are significantly correlated with volunteer activity. The observation of higher average physical composite scores among volunteers could support the idea that volunteers are those that are better able to handle the physical demands of volunteering. Lower average mental composite scores among volunteers may comment on the type of person that is attracted or not attracted to volunteering. It is important to note that there is no current Chinese normative data being used to score the SF-12, and this may hinder our ability to accurately interpret the results.

Table 2: Multivariate Analysis Using Linear Regression of Volunteer Activity and Selected Characteristics

	Volunteer			
	Coefficient	P-value	[95% Confidence Interval]	
Age	-0.00148	0.807	-0.0135	0.0105
Gender	-0.0470	0.674	-0.2690	0.175
Marital Status	-0.1079	0.435	-0.382	0.166
Overall MOS-SSS-C Score	-0.0746	0.211	-0.192	0.0433
Physical Composite Score	0.0034	0.576	-0.0087	0.0156
Mental Composite Score	-0.0040	0.461	-0.0148	0.00677

Volunteer Correlates

As shown in Table 1, univariate analysis using linear regression of volunteering was not shown to be correlated with any of the major variables identified (while additional item shows significance, overall MOSS does not). Shown in Table 2, multivariate analysis using linear regression looking at characteristics chosen by potential significance, no statistical significance is shown between volunteering and age, gender, marital status, overall MOSS score, physical composite score, or mental composite score. This is contrary to our expectation that a significant correlation exists between overall MOS-SSS-C score and volunteer activity. This is likely in part due to our small sample size. Other factors to consider may include MOS-SSS-C score as a function of duration of volunteer activity. It is possible that social connectedness scores are correlated with volunteering over longer spans of time, which we did not quantify in our participants.

Table 3: Univariate and Multivariate Analysis Using Linear Regression of Marital Status and MOS-SSS-C Subgroups

	Marital Status (Living partner or Widowed)				
	Univariate	Multivariate			
	P-Value	Coefficient	P-Value	[95% Confidence Interval]	
Emotional Support	0.0180	-0.0514	0.465	-0.191	0.0882
Tangible Support	0.00300	-0.121	0.039	-0.2346	-0.00656
Affectionate Support	0.375	0.0833	0.196	-0.0441	0.211
Positive Social Interaction	0.0460	-0.0215	0.741	-0.151	0.108
Additional Item	0.171	0.00142	0.976	-0.0930	0.0958

Marital Status and Social Support

Interestingly, marital status (non-widowed vs. widowed) was shown to have a series of significant correlations with the overall MOS-SSS-C score (p=0.011), and several subgroup scores including emotional support, tangible support, and positive social interaction (p<.05) shown in Table 3. A multivariate analysis using linear regression to remove confounders was performed between marital status and the MOS-SSS-C subgroup scores, which showed that tangible support was significantly correlated with marital status. It is interesting to note that in this population, the most valued functional support from a partner was reported as provision of aid or material assistance, and not emotional, affectionate, or informational companionship. This may be because self-reporting of these other aspects of support are low in Chinese culture. But it can also provide us with a useful way of thinking about what types of volunteer activity may provide the most fulfillment for the volunteer and recipient.

Discussion:

The results of our study showed that having a currently living spouse correlated with higher scores of tangible support when accounting for confounding, which may be generalizable to higher overall MOS-SSS-C scores in a larger population based on the trend of our data. This is notable because in this population, it is implicit that emotional support, affectionate support, positive social interaction, and additional item are not well identified or verbalized with the spouse. It is possible that this information can be used to implement future social programs that increase self-worth and provide social supports effectively. There were no other demographic trends identified that significantly correlated to higher levels of volunteer activity or social connectedness. This may suggest that volunteering is relatively accessible to a wide range of demographics, and that social connection is not necessarily impeded by existing demographic features. However it is possible that there are broad, underlying demographic trends that our small sample size was unable to capture.

We were unable to find any statistically significant differences between volunteer and non-volunteer MOS-SSS-C scores. However when broken down, the additional item of MOS-SSS-C was reported to be significantly lower in volunteers than non-volunteers. Since volunteers also reported lower average levels of emotional support and overall MOS-SSS-C scores (though statistically insignificant), the entirety of this data may suggest that volunteers on average experience less social support than their non-volunteering counterparts. This is contrary to what we hypothesized entering this study. This data may indicate that volunteers come preferentially from individuals with fewer social connections. Perhaps they seek to enrich their social lives through volunteering, or perhaps those with strong social supports are not seeking to volunteer. It is also possible that social connectedness increases with longer durations of volunteering, and we did not ask for length of volunteer activity so were unable to assess how this affected our data.

Our study was limited by the duration of time we had to interview residents that visited the community center, thus leaving us with a smaller sample size. There were also literacy, language, and cultural barriers that made it difficult to interpret responses at times, which may have affected the objectivity of the data.

For future work, it will be helpful to survey a larger sample size to explore if volunteers truly have lower MOS-SSS-C scores than non-volunteers. It would be useful to identify underlying causes for these lower MOS-SSS-C scores. Ideally older adults would be surveyed at the start of a volunteering experience, and then resurveyed periodically over a long time course. This would allow for better description of volunteering's impact on a person and would control for demographic differences in the types of people who choose to volunteer. Furthermore, focus group discussions with open-ended non-leading questions could provide insight into attitudes towards volunteering, which would help identify the reasons and motivations for volunteering in Chinese older adults.

References:

1. American Psychiatric Association. (2000). Diagnostic and statistical manual of mental disorders (4th ed., text rev.).

2. Sherbourne, Cathy Donald, and Anita L. Stewart. "The MOS Social Support Survey." Social Science & Medicine. 1991;705-14. Print.

3. Vanderhorst, R. K., and S. Mclaren. "Social Relationships as Predictors of Depression and Suicidal Ideation in Older Adults." Aging & Mental Health. 2005;517-25. Print.

4. Yu, Doris S.f., Diana T.f. Lee, and Jean Woo. "Psychometric Testing of the Chinese Version of the Medical Outcomes Study Social Support Survey (MOS-SSS-C)." Res. Nurs. Health Research in Nursing & Health. 2004;135-43. Print.

5. Brown, Kevin M., Russell Hoye, and Matthew Nicholson. "Self-Esteem, Self-Efficacy, and Social Connectedness as Mediators of the Relationship Between Volunteering and Well-Being." Journal of Social Service Research. 2012;468-83. Print.

6. Leng SX, Tian XP, Durso S, Lazarus G, Lu C, Park E, et al. The aging population and development of geriatrics in China. J Am Geriatr Soc 2008;56(3):571-3. [PMID:18315675].

7. Li X, Xiao Z, Xiao S. Suicide among the elderly in mainland China. Psychogeriatrics 2009;9(2):62-6. [PMID:19604327].

8. Hawton K, van Heeringen K. Suicide. Lancet 2009;373(9672):1372-81. [PMID:19376453].

9. Varnik P. Suicide in the world. Int J Environ Res Public Health 2012;9(3):760-71. [PMID:22690161].

10. Dong, Y., et al. The prevalence of suicidal ideation among the elderly in China: A meta-analysis of 11 cross-sectional studies. Comprehensive Psychiatry 2014;55: 1100-1105. http://dx.doi.org/10.1016/j.comppsych.2014.02.010.

11. Conwell, Yeates. Suicide Later in Life Challenges and Priorities for Prevention (2014). American Journal of Preventive Medicine 2014; 47 (3S2): S244-S250. http://dx.doi.org/10.1016/j.amepre.2014.05.040.

12. Noguchi, M., et al. Social support and suicidal ideation in Japan: are home visits by commissioned welfare volunteers associated with a lower risk of suicidal ideation among elderly people in the community?. Social Psychiatry and Psychiatric Epidemiology 2013;49: 619-627. DOI 10.1007/s00127-013-0752-5.

13. Holt-Lunstad J, Smith TB, Layton JB. Social relationships and mortality risk: a meta-analytic review. PLoS Med 2010;7(7):e1000316.

14. Conwell, Y. Van Orden, K., Caine, E.D.. Suicide in Older Adults. Psychiatric Clinics of North America 2011;34: 451-468. doi:10.1016/j.psc.2011.02.002.

15. 10. Konrath, S., Fuhrel-Forbis, A., Lou, A., & Brown, S.. Motives for volunteering are associated with mortality risk in older adults. Health Psychology, 2012;31(1), 87–96. doi:10.1037/a0025226

16. 11. Anderson, N.D., et al. The Benefits Associated With Volunteering Among Seniors: A Critical Review and Recommendations for Future Research . Psychological Bulletin. 2014. http://dx.doi.org/10.1037/a0037610.

17. Gandek, Barbara, John E. Ware, Neil K. Aaronson, Giovanni Apolone, Jakob B. Bjorner, John E. Brazier, Monika Bullinger, Stein Kaasa, Alain Leplege, Luis Prieto, and Marianne Sullivan. "Cross-Validation of Item Selection and Scoring for the SF-12 Health Survey in Nine Countries." Journal of Clinical Epidemiology. 2004;1171-178. Print.

18. News Release. Volunteering In the United States—2009. Bureau of Labor Statistics, U.S. Department of Labor. 2010, USDL-10-0097.

Rohini Bhatia, MS2

Preceptors:
Surbhi Grover, M.D., MPH
University of Pennsylvania
Assistant Professor of Radiation Oncology

David H. Adler, M.D., MPH
University of Rochester
Associate Professor of Emergency Medicine
Associate Professor of Public Health Sciences

Observations and Analysis of Cervical Cancer Presentation and Treatment Among Women in Gaborone, Botswana

Background:

Invasive cervical cancer is the third most common cancer among women worldwide, and the most common cancer diagnosed in women in Sub Saharan Africa (SSA). In 2008, there were over 75,000 women diagnosed and over 50,000 who died from the disease in the region.[7] Cervical cancer is also characterized as an AIDS-defining illness, along with other malignancies such as Kaposi's sarcoma and lymphoma. Sixty percent of the world's HIV cases are found SSA, and Botswana has the second highest prevalence of HIV in the continent (18%). With increased use of HIV/AIDS Antiretroviral Therapy (HAART), patients are living longer, widening the vulnerability window for development of malignancies. A 2015 study looked at over 8000 incident cancer cases from the Botswana National Cancer Registry during a period of significant ART expansion. They found that though ART expansion decreased age specific cancer risk, an aging population yielded a higher incidence of cancers in the HIV population. .[8] This study further underscores the imminent need for early detection and treatment of HIV-associated cancers in Africa. The incidence of cervical cancer in particular still remains a significant cause of morbidity for HIV-positive women.[9] Globocan 2008 data reports cervical cancer incidence in the United States at 6.6 per 100,000 while incidence in Botswana is 22.2 per 100,000 women.

Most patients in the developing world present with locally advanced disease at diagnosis, in part due to lack of widespread screening. In the US, greater than half of all cervical

---

[7] De Vuyst H, Alemany L, Lacey C, et al. "The Burden of Human Papillomavirus Infections and Related Diseases in Sub-Saharan Africa." *Vaccine*. 31S(2013)F32-46.
[8] Dryden-Peterson S, Medhin H, Kebabonye-Pusoentsi M, et al. "Cancer Incidence following Expansion of HIV Treatment in Botswana." *PLoS One.* 12 Aug 2015.
[9] Shiels MS, Pfeiffer RM, Hall HI, et al. "Proportions of Kaposi sarcoma, selected non-Hodgkin lymphomas, and cervical cancer in the United Staets occurring in persons with AIDS, 1980-2007. JAMA. 2011;305(14):1450-9

carcinomas were diagnosed at the localized stage, in part due to widespread screening. [10]The primary treatment for advanced cervical cancer is radiation therapy (RT), with additional chemotherapy if necessary. A recent review highlighted that only 20 countries in Africa have brachytherapy services; 75% of which are centered in North Africa and in South Africa.[11] [12] There is only one radiation therapy treatment center for Botswana, located in the capital, Gaborone. It began brachytherapy treatment program in 2012.

Even after arriving at Gaborone Private Hospital that houses the only linear accelerator in the country, many patients are not able to complete treatment as prescribed due to increased hematologic or gastrointestinal toxicity when given chemotherapy and radiation treatments concurrently compared to radiation alone.[13] Furthermore, recent data from South Africa suggests that HIV infected patients are significantly less likely to complete the prescribed course of chemotherapy and radiation. The study showed that only 50% of HIV positive patients completed chemotherapy and 79% of the HIV positive patients completed their radiation treatment. Inability to complete treatment was a significant predictor for poor outcomes.[14] For an estimated population of 2 million, there is a single radiation oncology facility in Botswana with one linear accelerator, located at the Gaborone Private Hospital (GPH), which although private sees and treats 95% of the patients diagnosed with cancer from public hospitals in the entire country. The goals of this study are to assess the late presentation of cervical cancers to Princess Marina Hospital and identify perceived barriers to both catching cancer earlier and completing treatment as prescribed.

Methods

Objective 1: Cancer Survey

Anecdotal observations prompted the formation of a focus group composed of Batswana women in which discussion surrounding the perceptions towards cancer and treatment in the hospital. Five women and two researchers participated in this focus group and the group was video-recorded to be analyzed for qualitative themes.

Upon analysis of focus group themes, the researchers consulted a baseline survey of analyzing cervical cancer presentation delay from India. In partnership with Batswana researchers, the survey was edited to reflect cultural compatibility (i.e. education, living

---

[10] Watson M, Saraiya M, Benard V, et al. “Burden of Cervical Cancer in the United States, 1998-2003.” *Cancer* Supplement: Assessing the Burden of HPV-Associated Cancers in the United States. 2008;113(10 suppl):2855–64.

[11] Abde-Wahab M, Bourque JM, Pynda Y et al. Status of radiotherapy resources in Africa: An International Atomic Energy Agency analysis. Lancet Oncol 2013; 14:e168-e175.

[12] Bvochara-Nsingo M, Grover S, GIegra DP, et al. “Cervical Brachytherapy Exchange: Steps Toward Oncology Capacity Building in Botswana.” *The Oncologist.* Letters to the Editor. TheOncologist2014;19:e1–e2

[13] Keys Hm Fau - Bundy, B.N., et al., *Cisplatin, radiation, and adjuvant hysterectomy compared with radiation and adjuvant hysterectomy for bulky stage IB cervical carcinoma.* (0028-4793 (Print)).

[14] Simonds, H.M., et al., *Completion of and early response to chemoradiation among human immunodeficiency virus (HIV)-positive and HIV-negative patients with locally advanced cervical carcinoma in South Africa. LID - 10.1002/cncr.26639 [doi]*. (1097-0142 (Electronic)).

situations, use of "traditional healers" were added). The survey is currently undergoing edits before being utilized in Princess Marina Hospital.

Objective 2: Assessing Toxicity and Completion of Therapy

Patients who presented to Princess Marina Hospital with confirmed cervical cancer who received radiation treatment were eligible to participate in the study. Length of treatment lasted about 2.5 months, and in total 180 women were recruited and followed for 11 months. Information on demographics, HIV status, HIV history, ART regimen, CBC, and creatinine were collected at initial visit. During treatment, weekly information on toxicity data (i.e. performance status, weight, gynecological and urinary toxicities and neuropathy), and labs were also collected. Each woman was followed from initial visit to end of treatment, with the recoding of up to 8 "on treatment visits" in between.

Additionally, adherence to treatment schedules and reasons for missed appointments were monitored. The primary endpoint for this objective was to identify whether or not the individual completed the therapy. The criteria for completion of therapy included 1) completion of chemotherapy as prescribed 2) no missed chemotherapy appointments 3) completion of radiation as prescribed and 4) no missed radiotherapy appointments. The secondary endpoint for this objective was the collection of toxicity data, collecting heme and GI toxicity information while the patient was on treatment to analyze any potential barrier toxicity posed.

Results:

Table 1: Demographics

	Completed Treatment	**Did Not Complete Treatment**
Age	52.8	45.9
Stage of Cancer		
Localized (<iib)	3 (9.6)	21 (15.1)
Regional (iib-iiib)	27 (87.1)	115 (82.7)
Distant (iv)	1 (3.2)	3 (2.2)
HIV Positive	35 (32.11)	74 (67.9)
On HAART	17 (54.8)	86 (61.4)
History of TB	10 (62.5)	6 (37.5)
Smoker	2 (40)	3 (60)
Distance		
<350km	21 (70)	103 (73.6)
>350km	9 (30)	37 (26.4)

We collected data from 180 women at the Princess Marina Hospital in Gaborone, Botswana. The average age of our population was 48.5 (range: 25-81). Most women who presented to the hospital, presented with at least a regionally spread cancer (84.3%). About half presented with stage iib, and just under a third presented with iiib. About one third of the women we followed completed chemotherapy according to the previous criteria (i.e. completing chemotherapy dose as initially prescribed and not missing any appointments). Almost three quarters of the patients (72.7%) completed radiation therapy as prescribed by similar criteria. Diarrhea was the number one medical reason for missing previous radiation therapy appointments and neutropenia was the number one reason for missing previous chemotherapy visits.

Conclusions

Researchers followed 180 women with cervical cancer to assess factors that related to their presentation at the hospital and treatment course. Initial analyses point towards a majority of cancers presented after they have spread regionally. This is a stark contrast to the stage of presentation in the United States where a majority presented at a localized stage. It further underscores the need for well-established and widespread screening programs throughout Botswana. Additionally, by quantifying the reasons for missing previous appointments for radiation and chemotherapy, we are able to gain insight into potential barriers for not completing treatment. Next steps for this project include assessing individual toxicities (GI, pelvic pain, etc.) and conducting a multivariate analysis to highlight factors that influence the completion of treatment.

References:

[1] De Vuyst H, Alemany L, Lacey C, et al. "The Burden of Human Papillomavirus Infections and Related Diseases in Sub-Saharan Africa." *Vaccine.* 31S(2013)F32-46.
[1] Dryden-Peterson S, Medhin H, Kebabonye-Pusoentsi M, et al. "Cancer Incidence following Expansion of HIV Treatment in Botswana." *PLoS One.* 12 Aug 2015.
[1] Shiels MS, Pfeiffer RM, Hall HI, et al. "Proportions of Kaposi sarcoma, selected non-Hodgkin lymphomas, and cervical cancer in the United Staets occurring in persons with AIDS, 1980-2007. JAMA. 2011;305(14):1450-9
[1] Watson M, Saraiya M, Benard V, et al. "Burden of Cervical Cancer in the United States, 1998-2003." *Cancer* Supplement: Assessing the Burden of HPV-Associated Cancers in the United States. 2008;113(10 suppl):2855–64.
[1] Abde-Wahab M, Bourque JM, Pynda Y et al. Status of radiotherapy resources in Africa: An International Atomic Energy Agency analysis. Lancet Oncol 2013; 14:e168-e175.
[1] Bvochara-Nsingo M, Grover S, GIegra DP, et al. "Cervical Brachytherapy Exchange: Steps Toward Oncology Capacity Building in Botswana." *The Oncologist.* Letters to the Editor. TheOncologist2014;19:e1–e2
[1] Keys Hm Fau - Bundy, B.N., et al., *Cisplatin, radiation, and adjuvant hysterectomy compared with radiation and adjuvant hysterectomy for bulky stage IB cervical carcinoma.* (0028-4793 (Print)).
[1] Simonds, H.M., et al., *Completion of and early response to chemoradiation among human immunodeficiency virus (HIV)-positive and HIV-negative patients with locally advanced cervical carcinoma in South Africa. LID - 10.1002/cncr.26639 [doi]*. (1097-0142 (Electronic)).

Karen Chong and Victoria Zhou

Dr. Luis Fernando Zavalaga Llanos
Universidad Peruana Cayetano Heredia
Ministry of Development and Social Inclusion

Dr. Rokhsanna Sadeghi
University of Rochester Medical Center
Emergency Medicine

Relationship between Age and ASQ-3 Scores per Screening Interval in Peruvian Infants

Introduction: The Ages and Stages Questionnaires (ASQ-3) play a vital role in diagnosing developmental delays in children under 5 years old, and are currently being used in many countries in several different languages. The ASQ-3 collects information about five dimensions of development: communication, gross motor, fine motor, resolution of problems, and social-individual. Although the ASQ-3 has been used in various large scale evaluations, there is frequently great variation in scores between children eligible to take the same ASQ-3 interval based on a 2-month age screening window.

Cuna Más, a national program implemented by the Ministry of Development and Social Inclusion in Perú to improve childhood development, has implemented the ASQ-3 as a method of evaluating early development in Peruvian infants living in rural and impoverished areas. Its subject population provides a useful source to study the possibility of an association between age and ASQ-3 score within an ASQ-3 screening interval from the large quantity of collected scores and the wide geographical span of Peru involved of the program.

Objective: The objectives of this study were to determine whether a relationship exists between age and ASQ-3 score for each ASQ-3 screening interval, and its impact on clinical decision-making and on population data.

Background: The first years of life are an important window of opportunity for early infant development, which is heavily influenced by the environment and experiences one accumulates since birth. Studies have shown that children demonstrating delays in physical, cognitive or social-emotional development before the age of six not only have poorer performance in school, but also eventually earn lower incomes as adults.

The ASQ-3 plays a vital role in screening for developmental delays in children younger than 5 and a half years old. The ASQ-3 collects information about five areas of development: communication, gross motor, fine motor, problem solving, and personal-social. The ASQ-3 test has been used in various large scale impact evaluations, including evaluations in Perú.

While this test has been used in several large scale evaluations in many countries, there is frequently great variation in scores between children eligible for the same ASQ-3 screening interval, based on a two month flexibility window. Janson et al. 2008 found that in a sample of 2,633 children with ASQ (second edition) scores, 10% of children with the appropriate age for a given screening interval received a positive screening in comparison to 22% of children 1-2 months too young and 5% too old for a given screening interval. The increase in false positives in the children below the age window and the false negatives in the children over the age window indicate a dependence of ASQ sensitivity on age. However, whether or not this relationship exists within the appropriate age window for each screening interval has not been established.

An age-dependent fluctuation in ASQ-3 scores can have important implications in clinical decisions concerning developmental delays, as well as a psychosocial impact on both the parents and the child. Glascoe 2001 discusses how variability in screening results and the possibility of false positives may cause persistent anxiety in parents of these children. Therefore, it is important to determine whether there is a tendency towards false positive results associated with age variation in a given ASQ-3 screening interval.

Methods: This was a cross-sectional study of infants under 2 years old enrolled in Cuna Más, a national program implemented by the Ministry of Development and Social Inclusion in Perú. Age was adjusted in the case of premature birth according to the standardized ASQ-3 Age calculator. This adjusted age determined the appropriate ASQ-3 screening interval (2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, or 24 month) administered. For analysis purposes, the infants were divided into four 2-week chronological subgroups based on age within each 2 month screening window, then aggregated across all 12 screening intervals (age subgroup). Linear regression was performed to assess the relationship between total and sectional ASQ-3 score and age subgroup.

Results: 5,850 Peruvian infants under 2 years of age were evaluated from April 2013 to August 2013. Mean age was 13 months and there was a nearly equal gender distribution (50.7% males). 20.0% shared their home with 1 or more nuclear families outside of their own. Mothers had been educated for a mean of 6.6 ± 4.0 years and 29.3% did not have health insurance. 48.1% of the infants had a medical issue in the last month, 34.8% were stunted (length for age < -2 SD T_c), 7.8% were underweight (weight for age < -2 SD T_c), and 0.9% were wasted weight for length < -2 SD T_c). Mean total ASQ-3 was 42.2 ± 8.2. The ASQ-3 allocated 49.6% of the infants as having a suspected developmental delay in one or more areas of development.
The age subgroups were nearly evenly distributed (24.5%, 25.9%, 25.7%, 23.9%). The difference in mean total ASQ-3 scores between the lowest and highest age subgroups ranged from 2.3 up to 12.2, with a mean of 6.0 points across the ASQ-3 screening intervals. Linear regression showed a significant association between age subgroup and both total (β=1.8, CI: 1.7-2.0, $p<0.001$) and sectional ASQ-3 score (all $p<0.001$). Age subgroup was also inversely associated with scores reflecting a developmental delay in at least one section ($p<0.001$). After multivariable regression adjusting for wealth quintile, education level of the mother, and stunted and underweight measures of malnutrition, age subgroup remained significantly associated with both total ASQ-3 score (β=1.8, CI: 1.7-2.0, $p<0.001$), sectional ASQ-3 score (all $p<0.001$) and inversely associated with 1 or more scores indicating suspected developmental delay ($p<0.001$).

Conclusion: Peruvian infants in the lower age range for an ASQ-3 screening interval may generate a false positive score reflecting developmental delays. Therefore, clinicians and parents need to be properly informed about the possibility of false positives or overscreening if the infant's age is at the younger end of the appropriate screening interval age.

References:

1) Barnett, W. (1995): "Long-term effects of early childhood programs on cognitive and school outcomes", *Future of Children*, Vol. 5, N° 3, pp. 25-50.

2) Feinstein, L. y K. Duckworth (2006): "Development in the early years: its importance for school performance and adult outcomes", Wider Benefits of Learning Research Report N° 20.

3) Fernald, L.C., P.K. Kariger, M. Hidrobo, y P. Gertler (2012): "Socio-economic gradients in child development in very young children: Evidence from India, Indonesia, Peru and Senegal", *Proceedings of the National Academy of Science* (PNAS), Oct 16; 109 Suppl 2:17273-80.

4) Galiani, S. y A. Orsola-Vidal (2010): "Scaling up Hand Washing Behavior: Findings from the Impact Evaluation Baseline Survey in Peru", Water and Sanitation Program, Technical Paper.

5) Glascoe, F. (2001): "Are Overreferrals on Developmental Screening Tests Really a Problem?", *Archives of Pediatrics & Adolescent Medicine*, 155(1), pp. 54-59.

6) Grantham-McGregor, S.M., Y.B. Cheung, S. Cueto, P. Glewwe, L. Richter, y B. Strupp (2007): "Developmental potential in the first 5 years in developing countries", *Lancet*, 369:60-70.

7) Heckman, J. (2000): "Policies to foster human capital", *Research in Economics*, vol. 54, N° 1, pp. 3-56.

8) Janson, H. (2008): "Effect of Violating the Indicated Age Window For a Parent-Completed Child Development Screening Questionnaire", *Australian Journal of Education & Developmental Psychology*, vol. 8, pp. 98-102.

9) Leseman, P. (2002): "Early childhood education and care for children for low-income or minority backgrounds", OECD.

10) [Schady, N. (2006): "Early Childhood Development in Latin America and the Caribbean", World Bank Policy Research Working Paper 3869.

Lauren Cowen, MS2

Preceptor and Collaborators:
Daniel Yawman, M.D., M.P.H., F.A.A.P.
Assistant Professor of Pediatrics, Emergency Medicine, Ethics/Humanities
University of Rochester School of Medicine and Dentistry

Dra. Teresa Velásquez
Directora de Hospital Primario El Sauce

Arnold H. Matlin, M.D., F.A.A.P.
Clinical Assistant Professor of Pediatrics
University of Rochester School of Medicine and Dentistry

Rosa Amelia Valle Vargas
Alcaldesa en Alcaldía Municipal El Sauce

Program Evaluation of Casa Materna Arlen Siu and its Impact on Maternal/Child Health Outcomes in El Sauce, Nicaragua

Introduction/Background:
Nicaragua is one of the poorest countries in the Western Hemisphere and as a consequence hosts considerable health concerns. The country's poverty, susceptibility to natural disasters and underfunded healthcare system have been cited as significant contributors to Nicaragua's immense health needs.[1] Despite gains in the last 25 years, the country's maternal mortality ratio remains high at 100 per 100,000 live births accounting for 6.8% of deaths for women of reproductive age, with particular concern among rural and indigenous populations.[2] Infant mortality is also alarmingly high at 20 per 1,000 live births[3] with a portion attributed to neonatal sepsis and congenital malformations. WHO (World Health Organization) indicates that around 55 percent of rural women give birth at home and adolescents account for approximately one-third of maternal deaths.[1] Only 77.5% of births had skilled health personnel in attendance.[2] Thus, successful programs targeting the health of pregnant women and infants in rural communities of Nicaragua is of high public health importance.

The first *Casa Materna* in Matagalpa, Nicaragua was so successful that the Nicaraguan health ministry (*Ministerio de Salud* or MINSA) adopted the model as a national strategy (*Red Nacional de Casas Maternas*) to address the UN's Millennium Development Goals. MINSA provides a portion of medical care and monetary support but additional costs must be covered by the individuals or collaborations with other institutions (i.e. NGO, local government, private investment) hence the diversity of *Casa Maternas* within the country of Nicaragua.[4]

The *Casa Materna* project in El Sauce was developed as a partnership between MINSA, the local government (*la Alcaldia*) and private contributions from the Matlin family (Rochester, NY USA). It opened its doors in December 2009. This joint collaboration differs significantly from the larger highly developed *Casa Materna* in Matagalpa that is completely funded by international supporters and is not affiliated with the Nicaragua's MINSA. To date, no program evaluation or quality assurance research has been completed for the *Casa Materna Arlen Siu* of El Sauce.

Objective:
This project aimed to assess the quality, success and challenges of the *Casa Materna* program in El Sauce, Nicaragua in regard to improving maternal and infant outcomes among rural pregnant Nicaraguans in the surrounding areas. My proposal was to assist the collaborating institutions and staff in analyzing the current situation by evaluating demographics, population and outcomes reached, services received, and challenges confronted. This program evaluation was intended to provide information to guide decision-making in terms of expansion, adjustment, and focusing resources for more efficient services.

Methods:
The program evaluation of *Casa Materna Arlen Siu* was conducted during June and July of 2015 in the town of El Sauce, Department of León, Nicaragua. Data was reviewed onsite from *Libro de Registro*, *Ficha de Ingreso* and *Encuesta de Satisfacción de Usarios* documents. The *Libro de Registro* included 1033 total entries, of which 883 unique pregnancies were determined, from October 2009 to June 2015. *Ficha de Ingreso* is a document filled out by staff members upon admission; these were not fully reviewed for all 883 documented pregnancies due to time constraints and missing information. This data was entered into an Excel spreadsheet for analysis. Qualitative information about the program operation was collected through observation and informal interviews with the *Casa Materna* staff and current resident women. Additionally, interviews were conducted with two nurses who work at Health Posts for a perspective from those involved with the early prenatal care of women in rural communities and the referral process of these remote community members to the *Casa Materna*. In completing this program review, identification of areas of importance considered the national *Casa Materna* program objectives per MINSA's document "*Ministerio del Poder Ciudadano Para Salud Funcionamiento de Las Casas Maternas*."

Findings/Results:
General Infrastructure, Operations and Policies
Casa Materna Arlen Siu has capacity for 12 pregnant and postpartum women. A nurse who works at El Sauce hospital comes to do health checks in varying frequency based on her availability. In line with MINSA regulations, the *Casa Materna* does not permit the women to be accompanied overnight by spouse, children or other relatives, and the premises are used exclusively for housing the women and for use in program related activities.

Women are referred to the *Casa Materna* at 37 weeks gestational age, although it is rare for them to enter this early. On occasion, women ask permission and are granted leave for a period of time to be with their families and return to the *Casa Materna* closer to expected labor. The women are invited to return to the *Casa Materna* for up to 10 days postpartum. Those recovering from a Cesarean delivery do return postpartum but the majority of the women who have uncomplicated pregnancies return home directly from the hospital. While the aforementioned is the standard time guidelines, there can be exceptions. During the study period, there was one woman who spent 6 months at the *Casa Materna* due to her high nutritional deficiency (significant anemia and low weight), high risk for miscarriage/premature delivery, lack of social support and housing. She was a wonderful example of what a *Casa Materna* program can do for high-risk pregnant women. During her stay, she recovered from anemia, showed healthy weight gain, and carried a healthy baby to nearly full term with no delivery complications.

Health Checks
The nurse visits on average 3-4 days a week. During her visit, she provides prenatal check-up including patient vitals with particular attention to preeclampsia risk, pregnancy weight gain, fetal heart rate, fundal height measurement and evaluation of fetal positioning (cephalic, transverse or breech presentation) by physical examination. Ultrasound imaging and lab testing are not available on site, so women are sent to El Sauce hospital for this workup. The nurse educates and evaluates the women for signs of labor and danger, instructs them on breastfeeding, care of newborn and the umbilicus. If she identifies any health concerns or determines early labor, she will coordinate transportation to the El Sauce hospital. She is able to recommend transfer to a higher-level resource hospital in León, but the women are often first sent to El Sauce hospital for further evaluation. If a woman is suspected to go into labor when the nurse is not present, other staff members call the hospital to make transportation arrangements. For women returning post Cesarean surgical delivery, she examines and cleans the wound and removes stitches after the appropriate time period.

Nutrition and Involvement of Women in Cooking and Gardening
The MINSA objectives for *Casa Materna* include involving the pregnant women in food preparation, cleaning and vegetable gardening. One of the major aims is to teach them how to prepare more nutritious meals and incorporate certain vegetables that are rich in nutrients that they and their children have a high demand for (e.g. iron rich spinach, replacing red beans with more nutritious black beans). Currently, the women are not included in the food preparation. The garden provides a decorative environment but there has not been an adequate incorporation of the garden as a source of nutrient rich herbs and vegetables for cooking usage.

Educational Activities, Workshop Skills Training and Recreational Activities
The *Ficha de Ingreso* data forms indicated that residents in past years have received educational talks on health themes ranging from labor warning signs to care of newborn and exclusive breastfeeding to family planning. Educational sessions did not appear to be regularly scheduled; during the 2-month observation period, there was only one session conducted. In the month of July 2015, a European volunteer from Spain started a sewing skills project with the women in the mornings to make baby clothing, handkerchief and diapers that are of immediate utility. Apart from this, there were no other projects or skills training workshops. Recreation predominantly included television and visitation hours.

Age Distribution and Gestational Parity

Of the 883 unique pregnancies: Maternal pregnancy age ranged from 13 to 46, with an average age of 24.25 years. The women's gestational parity values were as follows: 306 were nulliparous, 621 were multiparous and 19 had unknown parity.

"Comarca" distribution of referrals

The rural hospital in El Sauce services urban neighborhoods and surrounding rural communities that form a total population of 31,099. Many rural community members live hours away from the hospital; some of these residences are only accessible by foot or by horseback with significantly more challenges during rainy season. To address this limited health care access, there are 9 Health Posts ("*Puestos de Salud*") that are staffed by nurse and/or doctor during the morning Monday through Friday. Each Health Post has a designated rural region ("*sector*") that is further divided into village communities ("*comarcas*").

El Programa Comunitario de Salud y Nutrición (PROCOSAN), is a project designed for community level maternal and child health interventions through the aid of community health workers or *brigadistas* who provide the human resources for home visit outreach.[5] PROCOSAN is currently operating in 17 *comarcas* pertaining to 8 different rural *sectores*. Notably, the Health Post *sectores* that have the most *comarcas* participating in PROCOSAN are also those sending the largest percentages of women to the *Casa Materna*. In addition, rapport between *Puesto de Salud* nurse and community also appears to increase referral success.

Outcomes (Birth Condition, Hospital Transfers for Complications)

The presumed total number of pregnancies is 883, 10 of which were twin gestations, thus resulting in 893 total births. Of the total 10 sets of twins: 8 sets of twins were healthy, 1 set had a single fetal death, and 1 set was not reported. Birth condition reporting included simple descriptors. Data regarding birth condition for 805 of the total reported births are as follows: healthy not otherwise specified=790; fetal death=4; low birth weight=3; fever=3; heart murmur grade II=1; malformation of the feet=1; kidney infection=1; hemorrhage=1; pneumonia=1. The remaining 88 did not have birth condition information indicated. This number potentially includes miscarriages, loss to follow-up or non-pregnancy hospital visits. It is also possible that additional multiples pregnancies were not documented under these unreported entries.

Prior to 2011, El Sauce had a *Centro Medico Integral* (health center). In 2011, the health facility was upgraded to a *hospital primaria* signifying the most basic level of resources under the category of hospitals. The hospital has no blood bank and limited resources so that complicated cases must be referred to HEODRA (*Hospital Escuela Oscar Danilo Rosales Argüello*) in León. Situations for a transfer to HEODRA include the following: preeclampsia; genital warts; twins; previous Cesarean; expected Cesarean based on transverse or breech fetal presentation; Rh (-) blood type; low weight; premature rupture of membranes; absence of fetal movement; fever; vaginal bleeding; threat of miscarriage 20 weeks; premature labor. Data on Delivery Location: 264 women delivered in El Sauce medical facilities; 573 were transferred to León; 5 were home births (1 with midwife); and the location is unknown for the remaining 41.

Obstacles to Service Referral and Casa Materna Utilization:
The interviews conducted shed light on a number of obstacles to service utilization. The most significant reasons for women not wanting to go to the *Casa Materna* are the following: 1) Leaving behind and not being able to take care of their children and spouse; 2) Concern of home burglary and theft, if they leave their residence unattended. The nurse working at El Guacucal indicated in additional to the aforementioned concerns, most women in El Guacucal have better transportation access to the center of El Sauce and its hospital. The majority of the residences surround a major road with motor vehicle transportation and the commute is 40 minutes or less. As a result, more prefer to stay at home instead of using the *Casa Materna* as they felt they have adequate means to get to the hospital when they begin labor. Results of the Patient Satisfaction survey also indicated that the women's main concern while staying at the *Casa Materna* is leaving behind their children and spouses.

Patient Satisfaction and Repeat Utilization of Casa Materna
There were 5 Patient Satisfaction surveys completed and stored onsite. The responders of the Patient Satisfaction surveys shared comments that the accommodations were well maintained and expressed satisfaction with the *Casa Materna* staff. 35 women returned to the *Casa Materna* for a subsequent pregnancy or OB/GYN consult.

Conclusions:
The *Casa Materna* is providing an important resource as safe shelter, food provision and health care access for pregnant and postpartum women living in remote areas of El Sauce. The program appears to be moderately successful in bringing in women, but it has not reached anywhere near full capacity. There continue to be significant barriers to entering *Casa Materna*, particularly for the women leaving their children, spouses and homes unattended while utilizing the service, and their perception that they live close enough to access the hospital at the time of labor. It will be important to address this obstacle. Health care coverage needs to be expanded to ensure daily health checks for the women. Improved communication between the health posts, hospital and *Casa Materna* will also be crucial in ensuring proper follow-up to meet goals of improved maternal and infant health outcomes. There are valuable opportunities to take advantage of the women's stay to offer them more health education, nutritional enrichment information and workshop skill activities that have not been fully utilized.

Limitations:
Data analysis was limited due to: significant missing data, difficulty deciphering hand-written documentation, discrepancies in the spelling of names and incomplete names without date of birth identifiers to confirm repeat utilizers and re-entry. This investigation is unable to adequately assess outcomes based on not having comparative data to evaluate the difference before and after the *Casa Materna* was established nor an accounting of true total number of pregnancy/births during this time period. *Puesto de Salud* designations and referrals were inferred by listed *comarcas* but it is possible some of these women received prenatal care elsewhere. Some women choose to stay near other relatives or in the urban center of El Sauce during their pregnancy. Nurse interviews were conducted with two representative health posts

to model a relatively high (Sabana Grande) and a relatively low (El Guacucal) referral amount. This does not provide information about the other regional health posts and potentially overlooks additional differences and considerations that could contribute to referral success rates. Time constraints did not permit more extensive data collection and analysis of health outcome measures from *Ficha de Ingreso*, medical chart, hospital and health post documentation.

References:

1. Foundation for Sustainable Development: child and maternal health issues in Nicaragua: http://www.fsdinternational.org/country/nicaragua/healthissues
2. WHO. Maternal mortality in 1990-2013. http://www.who.int/gho/maternal_health/countries/nic.pdf?ua=1
3. The World Bank. Mortality rate, infant (per 1,000 live births). data.worldbank.org/indicator/SP.DYN.IMRT.IN
4. Langman, T. Improving Maternal & Child Health in Nicaragua. Borgen Magazine. 19 July, 2014. http://www.borgenmagazine.com/improving-maternal-child-health-in-nicaragua/
5. Improving Child Health In Nicaragua BASICS III. http://www.basics.org/reports/FinalReport/NicaraguaFinalReport_BASICS.pdf

John Dawson MS2
Katherine Wegman MS1

Preceptors:
Andrew Aligne, MD, MPH
Hoekelman Center Executive Director
Director of Community Health and Advocacy Resident Education
University of Rochester Medical Center

Flavia Nobay, MD
Associate Professor - Department of Emergency Medicine
University of Rochester Medical Center

Andrea Bolnick
Ikhayalami Founder

An analysis and evaluation of fire-related incidents and a solar energy pilot program in Egoli Informal Settlement, Cape Town, South Africa

Background:

Egoli is an informal settlement community located on the outskirts of Cape Town, South Africa. The settlement formed in 1996, in the aftermath of the apartheid era, after black and coloured families evicted from nearby farms began building shack homes on a former soccer field.

Egoli has since grown to its present size of about 2,000 people living in 400 homes. Due to its precarious location on private land, the Egoli community faces the constant threat of eviction. Furthermore, because the community is on private land, it does not currently qualify for the South African government's Free Basic Electricity grant, which provides 50 kWh per household per month to low-income South African families ("Free Basic Electricity"). As a result, the community has no access to electricity and limited access to other municipal services, including waste removal and potable water.

Lacking access to basic electricity is not an issue unique to Egoli. A 2012 General Household Survey found that 11% of South Africans (1.45 million people) did not have access to electricity ("Statistics South Africa"). This number is likely an underestimate given the reality that 1.6 million households - an estimated 6.4 million people - live in informal settlements similar to Egoli.

Those living without basic electricity oftentimes use open flame kerosene stoves for cooking and candles for lighting. This inadvertently leads to a serious risk of fires, which can have devastating consequences for communities, given the tightly packed and extremely flammable building materials typical of informal settlements.

As Davis Projects for Peace Fellows in 2014 we worked with Egoli and Ikhayalami - a non-profit organization dedicated to the implementation of technical solutions for informal settlement upgrading - to implement a solar power project in an effort to address community concerns about shack fires, nighttime safety, and the cost of candles, paraffin, and kerosene. We oversaw the installation of a decentralized solar hub at which Egoli residents can charge portable batteries to power lights and cell phone chargers in their homes. Khaya Power, a South African solar company, developed the solar batteries used in this system.

At the time of installation, Egoli residents choosing to use Khaya Power were required to pay ZAR150 (~$15) – a buy-in cost required to use the batteries and purchase compatible lights and a cell phone charger. Customers then paid ZAR6 ($0.60) each time they charge their battery at the solar hub. When used solely for illuminating homes at night and charging cell phones, the batteries would last up to three days. Income generated from the joining and charging fees is used to pay a salary for the solar hub operator, for repair and maintenance costs of the batteries and solar panels, and for additional solar systems for Egoli and potentially other informal settlements.

Objective:

This study firstly aimed to establish a baseline by which to quantitatively and qualitatively understand the frequency and severity of fire-related incidents in Egoli Informal Settlement. Secondly, this study sought to elucidate the facilitators and barriers to adoption of the novel Khaya Power solar energy system in Egoli. Lastly, this study aimed to evaluate the psychosocial effects of the solar power system on those living in Egoli. Our main objective was to use this information to determine community-wide effects of the technology, as well as elucidate possible correlational relationships demonstrating who is more likely to use solar technology, and for what reasons. This information in turn will be used to inform future work with the Egoli community.

Methods:

Semi-structured door-to-door surveys were used to quantitatively assess the demographic information of Egoli residents, including their candle usage habits and experience with fire-related incidents or injuries in the community. The surveys also sought to assess the financial benefits or risks associated with Khaya Power adoption, and the extent to which the solar technology has reduced fires, burns, and their related stress levels in community members.

Individual ethnographic interviews were used to gain a qualitative understanding of the lived experience of shack fires and fire-related injuries in the Egoli community. Interviews with Khaya Power adopters additionally sought to elucidate the potentially diverse and unanticipated effects of access to solar lighting and cell phone charging. These interviews also sought to determine barriers and facilitators to the adoption of the solar technology.

Results: Surveys

Ikhayalami's December 2014 evaluation of the solar program indicated that 23 households adopted and regularly used the Khaya Power system. All of these homes reported high satisfaction with the Khaya Power battery pack and lights. Adopters reported net financial savings from using Khaya Power and all recommended the system to other community members. The majority of these households (22/23) still used candles to light their homes.

2015 Survey Results

In total, 54 heads of household were surveyed. 95% of those surveyed had witnessed an uncontrolled shack fire in Egoli. 100% of respondents reported using candles in their homes. 70% of respondents also used paraffin or gas lamps or stoves. 11% used electricity, and 6% used Khaya

Power solar lights. 42% of respondents reported experiencing a fire-related incident - defined as a burn or uncontrolled fire - in their homes. The outcomes of these fire-related incidents included destruction of the home (35% of incidents) or property loss or damage to the home (20% of incidents). 69% of those injured by fires in Egoli were individuals under the age of 18. Blistering burns were the most common self-reported injury associated with fire-related incidents. The number of Khaya Power users dropped from 23 to 10 from December 2014 to June 2015. The surveyed Khaya Power users did not report any decrease in fire-related stress or financial savings.

Results: Ethnographic Interviews

The threat of fires and burns was a constant worry of almost every respondent. Beliefs and perceptions on the causes of fires were varied. One of the most common themes was blaming fires on individuals who might knock over candles while under the influence of alcohol or marijuana. When talking about a fire-related death in the community one informant stated, "Because the light, the glass ones (referring to a paraffin lamp), when someone is drunk just knocks it down and there it goes, it goes and starts the fire." Others felt the government was responsible for fires and fire-related incidents in the community because, by not providing the Egoli with free basic electricity, the government was forcing the community to use candles.

For current Khaya Power users, the threat of fire was a key motivator in adopting the system. However, while the system has decreased their candle usage, it has not eliminated it. For example, some informants reported using candles for light when the battery ran out of charge unexpectedly. Typically, the Khaya Power adopters used the lights for 2-5 hours per day. We discovered that most users needed to charge the Khaya Power batteries every day and were paying the solar hub operator on a monthly schedule, contrary to the original pay-as-you-go model. The major issue all Khaya Power users currently have with the program is the limited lifespan of the battery between charges. Despite current challenges, the early adopters and current Khaya Power users believe the system is a good idea and would be adopted more readily in the community if the technical issues are sorted out.

Conclusion:

The Khaya Power system shows great promise in reducing the risk of fires and fire-related incidents in Egoli, though its efficacy is severely limited by ongoing technical issues. We suggest that the relatively slow rate of adoption of the Khaya Power technology is due in large part to the unreliability of the batteries. Similarly, while the Egoli leadership continues to support the Khaya Power program, they believe that the technical issues are the root cause of people opting out of the program. This information was presented to Ikhayalami and Khaya Power in July of 2015. Khaya Power has redesigned the batteries to extend their community lifespan and developed a non-wood-using stove that people can use with the battery system. Their hope is that the stove will address community concerns over open wood fire pit cooking. This intervention could be beneficial to asthmatics as well as the community as a whole by decreasing the chance of uncontrolled fires.

Ikhayalami used this study's results to change monitoring of the Khaya Power program; moving forward, the organization has committed itself to more continuous evaluation of the Khaya Power program through on-site visits and additional training with the solar hub operator.

References:

Drivdal L. Report on flooding in the informal settlement, 'Egoli', in Philippi/Schaapkraal, Cape Town, 2010 and 2011. Available at: http://www.alnap.org/resource/6946
Free Basic Electricity – FAQ's Department of Energy. Available at:
2http://www.energy.gov.za/files/faqs/faqs_freebasic.html

Housing Development Agency. South Africa: Informal settlements Status (2013). Available at: http://www.thehda.co.za/uploads/images/HDA_South_Africa_Report_lr.pdf

Statistics South Africa. General Household Survey 2012. Available at http://www.statssa.gov.za/publications/P0318/P0318August2012.pdf

Wegman, Katherine. "The People on the Floor: Health, Community, and Informality in Egoli Informal Settlement." University of Rochester - Honors Thesis in Anthropology. May 2015.

Gravitz, Zoe, MS2
McCormack, Ellen, MS2
Sandhu, Sandeep, MS2
Sepulveda, Theresa, MS2

Preceptors:
Hanna Mieszczanska, M.D.
Associate Professor
University of Rochester Medical Center
Department of Medicine, Cardiology

C. Luis Vasquez, M.D.
President
Yantaló Perú Foundation

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

Tochukwu C. Ikpeze

Preceptor(s) Name: Raisa Deber, PhD
Title: Accountability in Hospital Care in the US and Canada: Role of Accountability Care Organizations and Other Governing Bodies
Institution: University of Toronto
Department: School of Public Health

Accountability in Hospital Care in the US and Canada: Role of Accountability Care Organizations and Other Governing Bodies

Introduction: Accountability involves the processes and methods by which a body or party justifies and takes responsibility for its actions and activities. In the context of healthcare, it can be defined as the process by which health leaders and organizations pursue the objectives of quality, efficiency, and access to meet the community, commercial, clinical/patient interests and expectations. Hospitals, healthcare organizations, and their respective components are then responsible for measuring and evaluating performance in multiple areas (i.e. quality, access, and efficiency), continually improving performance, and communicating both problems and solutions to accountable bodies (i.e. American Hospital Association, stakeholders, etc.). Failed approaches to accountability evidenced by the substantial rise in healthcare costs have led to the formulation of Accountability Care Organizations (ACOs). These

Objective: The goal of our study was to better understand the role of Affordable Care Organizations in the hospital sector including what approaches are being used for accountability in Ontario and in New York, including who hospitals must be accountable to (e.g., funders, accreditation bodies), for what (e.g., costs, quality, coverage), how (the policy instruments being used, including the measurements), and with what consequences. An emphasis will be placed on the implications for caring for difficult-to-insure patients.

Background: In healthcare, accountability is a valuable tool used to measure and monitor quality performance, access to care, and cost of care. Parameters of interest include accountability for what, to whom, why, and how. Any healthcare systems that utilize accountability are worried about quality, cost, and access. In an effort to reduce costs and improve the quality of patient care in the US, these parameters have been implemented to hold different sectors of healthcare responsible for measures deemed important by accountability bodies. The hospital sector is of particular interest being the last resort for patient care. The differences in healthcare sectors have inevitably led to variability in accountability approaches to better suit each sector. The present, fragmented state of the healthcare delivery system has led to the establishment of Accountability Care Organizations (ACOs). We are focusing on the performance of accountability bodies and what they hope to come across.

Methods: This study involved a systemic and thorough literature review a using a combination of systematic and analytical literature reviews (including of the grey literature)

Results: Increased healthcare costs coupled with low quality of care are a result, both directly and indirectly, of poor accountability approaches. Pilot programs for Accountability Care Organizations have yielded promising results in reducing healthcare-related costs, but the sustenance of those programs remain doubtful. Regarding improvement in quality of care, results are mixed.

Conclusion: The combination of private and public insurers in the US complicates the role of Accountability Care Organizations (ACOs). Prior to the implication of the Affordable Care Act, accountability approaches were unsuccessful in both reducing cost and improving quality of care. Preliminary results show successful savings and cost reductions for ACOs. However, results showing improvement in quality of care are mixed. In comparison to other developed nations, including Canada, the US ranks lower in quality of care provide and healthcare savings.

Latulipe, Ryan
Mark, Tiffany

Preceptors:
David H. Adler, M.D., MPH
University of Rochester
Associate Professor of Emergency Medicine
Associate Professor of Public Health Sciences

Joseph Lanning, Ph.D. Candidate, MA
University of Georgia
Instructor of Anthropology at the University of Rochester

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.

Jennifer Luong
Ben Gertsen

Preceptors:
David H. Adler, M.D., MPH
University of Rochester Associate Professor of Emergency Medicine
Associate Professor of Public Health Sciences

Joseph Lanning, Ph.D. Candidate, MA
University of Georgia Instructor of Anthropology at the University of Rochester

Breast Feeding and Food Insecurity in Rural Malawi

Introduction/ Background:
In conjunction with extreme poverty, Malawi has high rates of infant mortality at 53 deaths per 1,000 live births (compared to 8 deaths per 1,000 live births in the US). Although the under-five mortality rates have decreased in recent years, Malawi's neonatal death toll remains high. Nutritional deficiencies and infectious diseases such as diarrheal diseases and malaria are prominent causes of infant mortality. Breastfeeding has been found to alleviate the risks of these health issues, and both the World Health Organization and the Malawi Ministry of Health recommend exclusive breastfeeding— without introduction of any other types of fluids or foods—for newborns for at least six months. However, while most mothers believe in the health benefits of exclusive breastfeeding, few are able to employ it for six months or more. Factors cited that contribute to early feeding include: the mother's perceived lack of quality breast milk, fear of HIV transmission, and the cultural practice of feeding herbal infusions to the newborns. The average time of exclusive breastfeeding for newborns in rural Malawi is 3.7 months, as drinking water and supplementary foods are introduced before the 6-month period. Early supplementary feeding has been associated with lighter weight and slower growth in newborns, as well as infectious diseases. For example, studies have shown that infants who are not exclusively breastfed have increased risks of death from diarrheal diseases, pneumonia, and parental HIV transmission.

Our study aimed to understand the motivations for early supplementary feeding in a cluster of villages in Ntcheu district, Malawi. We specifically interviewed mother-daughter pairs to better understand the effect of inter-generational dynamics.

Objective:
The purpose of this research project is three-fold:
1) To understand how women engage in the practice of breastfeeding on an individual, familial, and communal level.

2) To identify what factors influence an individual's decision to exclusively breastfeed a child, cease breastfeeding, or supplement breast milk with other foods in the first six months of an infant's life.
3) To determine the alternatives to breastfeeding that women utilize to provide sustenance for their children and at what point these alternative feeding practices are introduced.

Methods:
The research was conducted in a rural community of central Malawi. A 6-page survey was developed to assess women's breastfeeding practices, as well as how these practices are negotiated within the community. Questions were both quantitative (age, number of children, etc.) and qualitative (why they chose to stop breastfeeding, etc.). A series of pilot interviews were conducted to inform any necessary revisions in the survey instrument; results from these interviews were not included for analysis. All interviews were conducted at individuals' homes, and basic demographic data were collected, including gender, age, and number of individuals currently living in the household. De-identified data is being compiled and analyzed with SAS version 9.1. Descriptive statistics will be conducted to draw out emergent themes relating to infant nutrition, cultural norms around motherhood, and breastfeeding practices.

Results:
Final results of the study are pending. Current analysis shows that observed behavioral developments such as sitting up, reaching for and tracking food, as well as crying after feeding are strongly linked to early supplementary feeding. Despite clear guidelines from the local mission hospital for exclusive breastfeeding until 6 months of age, many mothers continue to administer herbal medicines to their children during the first few months of life. Additionally, grandmothers have their own beliefs about early supplementation based on their personal experiences, which can be at odds with the hospital guidelines. Therefore, women are navigating multiple streams of knowledge as they make decisions regarding their breastfeeding practices.

Conclusion:
Early supplementary feeding has contributed significantly to the morbidity and mortality of children in Malawi. Our study approaches this problem from an anthropological perspective to understand the social, cultural, and biological factors involved in decisions to introduce supplementary foods before the WHO-recommended age of 6 months. Understanding the precise reasons for early supplementary feeding such as observed milestones, beliefs about traditional herbal medicines, and intergenerational dynamics will enable local healthcare systems and development organizations to better tailor educational and interventional breastfeeding programs.

References:

1. Doherty, T, et al. "Severe events in the first 6 months of life in a cohort of HIV-unexposed infants from South Africa: effects of low birthweight and breastfeeding status." *Tropical Medicine and International Health.* 19, 10 (2014): 1162-1169.

2. Issaka, A., et al. “Factors Associated with Early Introduction of Formula and/or Solid, Semi-Solid or Soft Foods in Seven Francophone West African Countries.” *Nutrients*. 7 (2015): 948-969.
3. Kafulafula, U, et al. “Exclusive breastfeeding prenatal intentions among HIV-positive mothers in Blantyre, Malawi: a correlation study.” *BMC Pregnancy and Childbirth*. 13, 203 (2013).
4. Kamundoni, PR, et al. “Breastfeeding perceptions in communities in Mangochi district in Malawi.” *Acta Paediatrica*. 99 (2010): 367-372.
5. Kerr, R, et al. ‘‘We Grandmothers Know Plenty’’: Breastfeeding, complementary feeding and the multifaceted role of grandmothers in Malawi.” *Social Science and Medicine*. 66 (2008): 1095-1105.
6. Malawi Statistics. 2003. Retrieved from Unicef: http://www.unicef.org/infobycountry/malawi_2424.html
7. Sellen, D. “Weaning, Complementary Feeding, and Maternal Decision Making in a Rural East African Pastoral Population.” *Journal of Human Lactation*. 17, 3 (2001): 233-244.
8. (2012). “Under five child deaths still high in Malawi.” Retrieved from Nyasa Times Malawi: http://www.nyasatimes.com/2012/10/22/under-five-child-deaths-still-high-in-malawi/
9. Vaahtera, M, et al. “Breastfeeding and complementary feeding practices in rural Malawi.” *Acta Paediatrica*. 90 (2001): 328-332.

Michael Mattiucci, MS2

Preceptor:
Nancy Chin, Ph.D., MPH
Associate Professor
University of Rochester School of Medicine and Dentistry
Department of Public Health Sciences

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 itinerate 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 Ladahki 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; Healis-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/

Lam-Anh (Lamie) Nguyen, MS 2

Preceptors:
Edit Paulik, M.D., Ph.D.
Associate Professor and Director
University of Szeged Faculty of Medicine
Department of Public Health

Andrea Szabo, Ph.D., DrPharm
Assistant Professor
University of Szeged Faculty of Medicine
Department of Public Health

Jennifer Carroll, M.D., M.P.H.
Associate Professor
University of Rochester
Department of Family Medicine
Center for Community Health

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 McLafferty[18] and Kitzinger[19] 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 or 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 publishe 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.

Rachel H Park

Preceptor(s) Name: Dr. Howard Langstein, Dr. Yong Hang Lee
Title: Young Adults' Attitudes and Beliefs Towards Plastic Surgery in South Korea
Institution: University of Rochester School and Medicine and Dentistry
Department

Young Adults' Attitudes and Beliefs Towards Plastic Surgery in South Korea

Introduction: Plastic surgery is a very common and widely popular practice in South Korea. It has become a multi-billion dollar business that not only attracts Koreans, but also foreigners. However, despite its popularity, there is not many studies regarding this phenomenon. This study aims to specifically look at Korean young adults' attitudes and beliefs toward plastic surgery, especially regarding their educational background, gender, and employment. The researchers hypothesize that a significant portion of Korean young adults will have accepting attitudes towards having a cosmetic surgery, especially as a means to increase their chance of employment. We also expect to see both gender-specific and occupation-specific attitudes and beliefs towards such behavior. Lastly, we expect to see one's close family and friends having influence over the decision-making steps in undergoing plastic surgical procedure.

Objective: This study aims to closely look into the Korean young adults' attitudes and beliefs toward plastic surgery, especially regarding their educational background, gender, and employment.

Background: Plastic surgery was first introduced in Korea in the beginning of the 1950s by Western doctors. They performed skin grafts and surgical procedures on facial disfigurations, which many were caused during the Korean War. It was not until 1961, when Dr. Jaeduk Yoo founded the very first plastic surgery department at Yonsei University Severance Hospital, that plastic surgery became an official field of medicine with trained specialists in South Korea.[15] Despite the short history, plastic surgery became incredibly popular and prevalent in this country. In 2013, it was estimated that the cosmetic surgery industry in South Korea is valued at

---

[15] Plasticsurgery.or.kr,. 'History Of Korean Society Of Plastics And Reconstructive Surgeons'. N.p., 2015. Web. 28 Jan. 2015.

about $5 billion USD, with more than 2,000 board-certified surgeons.[16, 17] Although the highest number of procedures take place in the U.S., South Korea shows the highest number of procedures per population, which is 16 procedures in 1000 people.[18] It is very popular among young adults, especially for females - it is estimated that one in five females between the ages of 19 and 49 undergo some sort of cosmetic procedure.[19]

With the rise of "lookism" in the 21st century, plastic surgery has become a very peculiar culture that is planted deeply into the Korean society. One's external appearance is now considered an important factor that contributes to one's interpersonal relationships, achievement, and placement in the society.[20] Such correlation between one's attractiveness and success is not new nor localized to South Korea[21]; however, one's look, or attractiveness, has become increasingly more important in the Korean society over the past few decades. Such phenomenon has led many individuals to receive cosmetic surgical procedures to achieve much desired "beauty," which is believed to be directly linked to popularity and success.

A number of Korean studies and surveys address the influence of the applicants' "looks" during the job interview. The interviewers suggest that one's external appearance is an important factor; often times, they will hire applicants who are more "attractive" over ones with similar or even better qualifications.[8] Since the job market is becoming increasingly more competitive, "external appearance" is even more of an important factor than it ever was. Such favoritism is gender relevant, for women are more often subject to such standard of beauty. A study shows that the three most important factors that an interviewer considers during the interview are: i)general first impression, ii) personality, and iii) external appearance, for males, in the order of significance. However, for females, the order changes to: i) general first impression, ii) external appearance, and iii) personality.[22]

---

[16] Park, Ju-Min. 'Trouble Brewing In South Korea's Plastic Surgery Paradise'. *Reuters* 2014. Web. 28 Jan. 2015.

[17] International Society of Aesthetic Plastic Surgery,. *ISAPS Global Statistics 2013*. 2013. Web. 25 Jan. 2015.

[18] International Society of Aesthetic Plastic Surgeons,. *ISAPS Global Statistics 2010*. 2010. Web. 24 Jan. 2015.

[19] Choe, Sang-Hun. 'In South Korea, Plastic Surgery Comes Out Of The Closet'. *NYTimes* 2011. Web. 24 Jan. 2015.

[20] Kim, Hwa Sook. 'A Study On The Awareness And Interest About Appearance Of Cosmetic Surgery Of Adults'. Master's Degree. SeoKyeong University, 2011. Print.

[21] Hamermesh, Daniel S., and Jeff E. Biddle. *Beauty and the labor market*. No. w4518. National Bureau of Economic Research, 1993.

[22] Kim, Hye Ri. 'Influence Of External Images Of Job Applicants On Interviewers' Judgement'. Master's Degree. Korea International Culture University of Graduate, 2009. Print.

Many employers require their applicants and employees to have "neat, polished external appearance." However, such category poses double standard for male and female. For males, such requirements relate to the overall cleanliness and neat presentation of self. For females, "attractiveness and beauty" is often considered as an unwritten part of the requirement.[23] Such gender disparity should be studied more thoroughly and addressed more clearly, especially when more women are joining the workforce than ever.[24]

This project aims to quantitatively and qualitatively explore the attitudes and beliefs of young adults in South Korea toward plastic surgery. Specifically, this study aims to address the following questions: 1) What is the Korean young adult's attitudes and beliefs towards plastic surgery, especially as a way of increasing the chance of employment? 2) Are there gender-specific attitudes and beliefs toward having plastic surgery procedures to increase the chance of employment? 3) Does one's field of study and anticipated occupational field influence his or her attitude towards plastic surgery? 4) Who influences one's decision in undergoing plastic surgery?

Methods: The study utilized a mixed method, combining a quantitative survey and qualitative in-depth interview. Both the interview and survey participants were recruited from Apgujong BC plastic surgery clinic and through online advertisements. A small booth was set up in the waiting room of ApGuJong BC Plastic Surgery clinic, stationed with the principal investigator, recruitment forms, and a laptop. The visiting patients had a chance to stop by the booth and participate in the study if they were interested. The information letter was made available so the patients can read about the study, participation requirements, and make a voluntary decision.

The survey was generated by REDcap, a secure, web-based application for building and managing online survey and database. The survey had a unique web address, which will allow an easy access by internet connection.

The study was also advertised online. Four biggest online forums for job-searching from <naver.com>, which is one of the biggest search engines in South Korea, was used as online advertisement platforms. Qualifying individuals who were interested contacted the principal investigator via email to schedule an interview. The interviews were carried out on a time and location that the participant and the investigator agreed on. These included coffee shops and private rooms in the clinic. The advertisement had direct link to the online survey, so that qualifying individuals can take it at time and location of their convenience.

All the subjects who participate in the survey will be entered into a raffle to win a gift card (100,000 KRW, about $92 USD) to a restaurant or an equivalent. All subjects who choose to do a personal interview will be given cash (15,000 KRW, about $13.8 USD).

---

[23] Lim, In-Sook. 'Women's Employment And Appearance-Discriminatory Selection'. *Korean Association of Women's Studies* 19.113-144 (2003): n. pag. Print.

[24] Korea National Statistical Office,. *Statistical Data On Female Worker's Number And The Level Of Participation*. 2014. Print.

The data was collected and processed by the REDcap application. The survey was open from June 8th until July 27th, for the total of 7 weeks. The interviewees were recruited on a rolling basis during the same time frame as the survey. The collected survey data was analyzed using the REDcap application and Excel. Graphs and charts were made using Excel.

Results: During this study, online survey of 103 unemployed Korean young adults with college education background was gathered. Among the participants, 27 were male and 76 were females. Qualitative interviews with 19 participants were executed, which included 11 females and 8 males.

Highly educated, unemployed Korean young adults showed positive attitudes towards plastic surgery procedures as means of self-improvement and as tools in enhancing their chances of employment. Such procedures were more common and popular among females who had higher rate of past plastic surgery experiences (22.4%). However, a significant portion of males had past plastic surgery experiences as well (14.8%). Both males and females who has not had any plastic surgery procedures were interested in having them in the future, much more so for the males (39.1%) than females (28.8%). Different types of surgeries were desired by different genders. Nose surgery was the most desirable among the males by the majority, followed by eyes and jaw surgeries. Eye surgeries were overwhelmingly popular among the females, followed by the nose and other minimally invasive procedures for face shapes.

For both genders, the greatest reason for receiving plastic surgery in the past was their personal dissatisfaction with their looks. However, parental influence was just as influential as one's self-dissatisfaction for the females, while it was not one of the main reasons for the males. Hence, self was the most influential figure for male, followed by friends, while parents were the most influential figure followed by self for females. Future employment was not a primary reason. However, they all agreed that their past plastic surgery results would have positive effect on finding a job in the future.

The primary motivation and influential figures differed for the individuals who are planning on getting plastic surgery in the future, compared to the group with past plastic surgery experiences. Although personal dissatisfaction was still the biggest reason for both genders, parental influence and employment became significant factors for the males, while peer pressure became an important factor for the females. Hence, parents became important figures for males and while friends became influential figures for females. This group also anticipated that having plastic surgeries will have positive effect in the employment process. Even though employment is not often the greatest motivation for these individuals, it is considered as one of the many benefits that will come as a result of having more appealing facial features.

The survey participants represented current college students and graduates who studied in various academic fields. Such fields covered the major scholarly disciplines, which are natural and social sciences, as well as humanities. The participants anticipated to find occupations in a variety of job fields, and no significant correlations between one's attitudes towards plastic surgery and anticipated occupational fields was observed. Rather, personal and religious backgrounds seemed to have much stronger influence over one's attitude towards plastic surgery, according to the personal interview cases.

Conclusion: Plastic surgery is a popular and common way of self-improvement and care for both male and female Korean young adults. It is more common among females to have a plastic surgery procedure compared to male, but it is becoming increasingly popular among males as well. Females tend to receive aesthetic surgery in their late teens and early twenties, while men are more likely to get it at older age. Important figures in one's decision to receive plastic surgery procedures were self, parents, and friends. Major reasons for such decision included personal dissatisfaction, parental pressure, peer pressure, and employment. The importance of listed factors showed variation for different gender groups and groups with past surgery experience. Unemployed, young Korean adults expressed that one's looks are an important factor in the employment process, more so for females than males. Such phenomenon can be stemming from a number of reasons that are unique to Korean cultures.

References:

[1] Plasticsurgery.or.kr,. 'History Of Korean Society Of Plastics And Reconstructive Surgeons'. N.p., 2015. Web. 28 Jan. 2015.

[1] Park, Ju-Min. 'Trouble Brewing In South Korea's Plastic Surgery Paradise'. *Reuters* 2014. Web. 28 Jan. 2015.

[1] International Society of Aesthetic Plastic Surgery,. *ISAPS Global Statistics 2013*. 2013. Web. 25 Jan. 2015.

[1] International Society of Aesthetic Plastic Surgeons,. *ISAPS Global Statistics 2010*. 2010. Web. 24 Jan. 2015.

[1] Choe, Sang-Hun. 'In South Korea, Plastic Surgery Comes Out Of The Closet'. *NYTimes* 2011. Web. 24 Jan. 2015.

[1] Kim, Hwa Sook. 'A Study On The Awareness And Interest About Appearance Of Cosmetic Surgery Of Adults'. Master's Degree. SeoKyeong University, 2011. Print.

[1] Hamermesh, Daniel S., and Jeff E. Biddle. *Beauty and the labor market*. No. w4518. National Bureau of Economic Research, 1993.

[1] Kim, Hye Ri. 'Influence Of External Images Of Job Applicants On Interviewers' Judgement'. Master's Degree. Korea International Culture University of Graduate, 2009. Print.

[1] Lim, In-Sook. 'Women's Employment And Appearance-Discriminatory Selection'. *Korean Association of Women's Studies* 19.113-144 (2003): n. pag. Print.

[1] Korea National Statistical Office,. *Statistical Data On Female Worker's Number And The Level Of Participation*. 2014. Print.

Stacy Salerno (1)

Preceptor(s):
Teri Reynolds
Associate Professor of Emergency Medicine and Global Health Sciences
University of California at San Francisco
Lead of Emergency, Trauma and Acute Care Program
World Health Organization

Hendry Sawe
Lecturer and Fogarty Global Health Fellow
Muhimbili University of Health and Allied Sciences
President, Emergency Medicine Association of Tanzania

Juma Mfinanga
Head, Emergency Medicine Department
Muhimbili National Hospital
Secretary General, Emergency Medicine Association of Tanzania

David Adler
Associate Professor of Emergency Medicine and Public Health Sciences
University of Rochester
Department of Emergency Medicine

A Multi-country Assessment of Trauma Documentation, Data Collection Practices, and Facilitators and Barriers to Implementation of the African Federation of Emergency Medicine Trauma Data Project

Introduction: Trauma contributes significantly to the burden of disease and mortality in low and middle-income countries (LMICs). It has been estimated that nearly 2 million deaths, one third of all trauma fatalities, could be prevented in LMICs if case fatality rates among seriously injured persons was reduced to those in high-income countries.[1] Monitoring elements of diagnosis, treatment and outcome has led to significant quality improvement strategies and has become an essential component of developed trauma systems.[2-6] However, the lack of trauma care information systems remains a challenge to trauma system development in LMICs, and limited documentation of the acute disease burden has been identified as a major barrier to global emergency care development.[6-8]

Objective: The African Federation of Emergency Medicine (AFEM) trauma data project was proposed to improve trauma care information systems and systematically collect essential trauma data across multiple countries in Africa. The objective of this study is to identify barriers

and facilitators of current trauma charting practices in developing emergency care systems and to inform the creation of a trauma charting instrument for the AFEM regional trauma data project.

Methods: A cross-sectional qualitative research design with semi-structured interviews was utilized to explore perceptions and practices of trauma charting. Respondents were also asked about their views with respect to a proposed trauma form. 35 interviews were conducted: 10 at Muhimbili National Hospital in Dar es Salaam, Tanzania; 17 at HEAL Africa Hospital in Goma, Democratic Republic of Congo; and 8 at Mulago Hospital in Mulago, Uganda. Respondents included physicians, residents, registrars, nurses, orthopedic officers and one administrator. Interview transcripts were entered into ATLAS.ti qualitative data management and analysis software. Coded emerging themes were integrated into a grounded theoretical framework. Constant comparative methods were used to develop codes, focus interview questions, and make changes to develop the trauma form.

Results: All 35 respondents expressed that it would be helpful to have a specific form for trauma charting. However, 32 out of the 35 respondents reported that they had no current trauma specific charting system at their facility. Respondent themes fell into four major domains (1) trauma form function; (2) trauma form content; (3) useful aspects of the proposed trauma form; (4) difficult aspects of the proposed trauma form.

Conclusion: Majority themes endorsed that a trauma form can serve as a clinical management guide, improve and standardize documentation and data reporting, and increase efficiency. Proposed barriers included time to fill, training and paper use. Utilization of a systematic acute intake trauma charting system can lay the foundation for future outcome data capturing strategies in developing emergency care systems.

References:

1. Mock C, Joshipura M, Arreola-Risa C, Quansah R. An estimate of the number of lives that could be saved through improvements in trauma care globally. World J Surg. 2012 May;36(5):959-63.
2. Hashmi ZG, Haider AH, Zafar SN, Kisat M, Moosa A, Siddiqui F, Pardhan A, Latif A, Zafar H. Hospital-based trauma quality improvement initiatives: first step toward improving trauma outcomes in the developing world. J Trauma Acute Care Surg. 2013 Jul;75(1):60-8; discussion 68.
3. Mock C, Juillard C, Brundage S, Goosen J, Joshipura M. Guidelines for trauma quality improvement programmes. Geneva, World Health Organization, 2009.
4. Moore L, Clark DE. The value of trauma registries. Injury. 2008 Jun;39(6):686-95.
5. Nwomeh BC, Lowell W, Kable R, Haley K, Ameh EA. History and development of trauma registry: lessons from developed to developing countries. World J Emerg Surg. 2006 Oct 31;1:32.
6. O'Reilly GM, Joshipura M, Cameron PA, Gruen R. Trauma registries in developing countries: a review of the published experience. Injury. 2013 Jun;44(6):713-21.
7. Reynolds TA, Bisanzo M, Dworkis D, Hansoti B, Obermeyer Z, Seidenberg P, Hauswald M, Mowafi H. Research priorities for data collection and management within global acute and emergency care systems. Acad Emerg Med. 2013 Dec;20(12):1246-50.

Stacy Salerno (2)

Characteristics of Injured Patients Presenting to an Urban Emergency Department in Dar Es Salaam, Tanzania

Introduction: Trauma contributes significantly to the burden of disease and mortality in low and middle-income countries (LMICs). It has been estimated that nearly 2 million deaths, one third of all trauma fatalities, could be prevented in LMICs if case fatality rates among seriously injured persons was reduced to those in high-income countries.[1] Monitoring elements of diagnosis, treatment and outcome has led to significant quality improvement strategies and has become an essential component of developed trauma systems.[2-6] However, the lack of trauma care information systems remains a challenge to trauma system development in LMICs, and limited documentation of the acute disease burden has been identified as a major barrier to global emergency care development.[6-8]

Objective: The objective of this study is to describe injury epidemiology through the implementation of a standardized trauma data form for patients presenting to Muhimbili National Hospital's Emergency Medicine Department in Dar Es Salaam, the chief academic medical center and largest trauma referral hospital in Tanzania.

Methods: This is a prospective descriptive cross-sectional study of 11,290 injured patients presenting to Muhimbili National Hospital's Emergency Medical Department (MNH EMD) within a two year time period (March 2012 through February 2014). A standardized trauma form was used for both clinical and data collection purposes. Information from the trauma form was entered into an electronic database and analyzed using descriptive statistics on demographic characteristics, mode of arrival to the EMD, mechanism of injury, and place of injury.

Results: Injured patients presenting to MNH EMD are predominately adult males between the ages of 21 and 40. Road traffic incidents, falls, assaults and burns are among the most common mechanisms of injury. Pedestrians are the most frequent victims of road traffic injuries. Of those in vehicles, motorcyclists' injuries are most prevalent. The greatest burden of burn injury is seen in children under the age of 5, and burns most frequently occur in the home.

Conclusion: Implementation of trauma surveillance at MNH EMD has improved knowledge of trauma risk factors and demographics.

References:

1. Mock C, Joshipura M, Arreola-Risa C, Quansah R. An estimate of the number of lives that could be saved through improvements in trauma care globally. World J Surg. 2012 May;36(5):959-63.
2. Hashmi ZG, Haider AH, Zafar SN, Kisat M, Moosa A, Siddiqui F, Pardhan A, Latif A, Zafar H. Hospital-based trauma quality improvement initiatives: first step toward improving trauma outcomes in the developing world. J Trauma Acute Care Surg. 2013 Jul;75(1):60-8; discussion 68.
3. Mock C, Juillard C, Brundage S, Goosen J, Joshipura M. Guidelines for trauma quality improvement programmes. Geneva, World Health Organization, 2009.

4. Moore L, Clark DE. The value of trauma registries. Injury. 2008 Jun;39(6):686-95.
5. Nwomeh BC, Lowell W, Kable R, Haley K, Ameh EA. History and development of trauma registry: lessons from developed to developing countries. World J Emerg Surg. 2006 Oct 31;1:32.
6. O'Reilly GM, Joshipura M, Cameron PA, Gruen R. Trauma registries in developing countries: a review of the published experience. Injury. 2013 Jun;44(6):713-21.
7. Reynolds TA, Bisanzo M, Dworkis D, Hansoti B, Obermeyer Z, Seidenberg P, Hauswald M, Mowafi H. Research priorities for data collection and management within global acute and emergency care systems. Acad Emerg Med. 2013 Dec;20(12):1246-50.

Stacy Salerno (3)

Diagnostic Impact of Emergency Point of Care Ultrasound in Tanzania

Introduction: Access to radiological imaging is limited in Tanzania and other low- and middle-income countries. Point of care ultrasound (PoCUS) is a relatively accurate, efficient, inexpensive, low-maintenance, safe, and portable imaging modality that can be particularly useful in resource-limited settings. There has been a substantial increase in the use of PoCUS in resource-limited settings over the past decade.[1-7] However, there is limited information on the diagnostic impact of PoCUS in such settings.
Objective: The objective of this study is to evaluate the use and diagnostic impact of PoCUS at an urban emergency department in Dar Es Salaam, Tanzania.
Methods: This is a prospective descriptive cross-sectional study of patients receiving PoCUS at Muhimbili National Hospital's Emergency Medical Department (MNH EMD). A convenience sample of PoCUS scan data was collected at MNH EMD over the course of 10 months. Data collection on a standardized form included patient demographics, reported indications for ultrasound, findings, interpretations, and provider reported diagnosis and disposition before and after PoCUS. Descriptive statistics were utilized, including means and standard deviations, medians and interquartile ranges, and counts and percentages, as appropriate. Pearson chi squared tests and p-values were applied to categorical data to evaluate for significant differences.
Results: PoCUS data was collected for 785 patients. The average age of patients receiving PoCUS was 36 years and 55% of patients were male. Top indications for PoCUS included trauma, dyspnea, and abdominal pain. The most frequent PoCUS exams utilized were eFAST, cardiac, and obstetric/gynecologic. Clinicians reported that findings from PoCUS either changed diagnosis or disposition in almost one-third of all cases. Reported change in a patient's diagnosis or disposition increased significantly, from 25-47%, as multiple PoCUS exams types were used.
Conclusion: In resource-limited emergency settings, PoCUS can be utilized for a wide variety of diagnostic indications with significant diagnostic impact.

References:

1. Maru DS-R, Schwarz R, Jason A, Basu S, Sharma A, Moore C. Turning a blind eye: the mobilization of radiology services in resource-poor regions. Glob Health. 2010;6:18.
2. Adler D, Mgalula K, Price D, Taylor O. Introduction of a portable ultrasound unit into the health services of the Lugufu refugee camp, Kigoma District, Tanzania. Int J Emerg Med. 2008 Dec;1(4):261–6.

3. Henwood PC, Beversluis D, Genthon AA, Wilson CN, Norwood B, Silva D, et al. Characterizing the limited use of point-of-care ultrasound in Colombian emergency medicine residencies. Int J Emerg Med. 2014;7(1):7.
4. Groen RS, Leow JJ, Sadasivam V, Kushner AL. Review: indications for ultrasound use in low- and middle-income countries. Trop Med Int Health TM IH. 2011 Dec;16(12):1525–35.
5. Shah SP, Epino H, Bukhman G, Umulisa I, Dushimiyimana JMV, Reichman A, et al. Impact of the introduction of ultrasound services in a limited resource setting: rural Rwanda 2008. BMC Int Health Hum Rights. 2009;9:4.
6. Kotlyar S, Moore CL. Assessing the utility of ultrasound in Liberia. J Emerg Trauma Shock. 2008 Jan;1(1):10–4.
7. Aboud M, Mkony C, Wustner M. Elective Abdominal Ultrasonography by Surgeons at MNH, Dar Es Salaam, Tanzania. East and Central African Journal of Surgery. 2006;11(1):52–6.

Stacy Salerno (4)

Feasibility of Mapping the Distribution of Road Traffic Injuries Presenting to a Trauma Center in Tanzania: A Pilot Study

Introduction: Road traffic injuries (RTIs) are the ninth leading cause of death globally.[1] RTIs constitute a substantial burden for morbidity and mortality in Tanzania and are associated with extensive health care costs.[2-3] Geographic mapping methods can identify areas with high prevalence of injury, guide environmental evaluations, and inform location-specific injury prevention strategies.[4-9] Despite Tanzania's high burden of RTIs, no known GIS studies have been conducted to identify areas of high RTI prevalence.
Objective: This study's objective was to map locations of road traffic events for injured patients presenting at the largest public tertiary care center in Tanzania, Muhimbili National Hospital (MNH) in Dar es Salaam.
Methods: Coordinates were gathered from a convenience sample of trauma patients presenting to MNH during an eight-week pilot study. 89 RTIs were geocoded in ArcGISPro and mapped over a street basemap of Dar Es Salaam. A density analysis was conducted to identify areas of high RTI density.
Results: Most of the RTIs occurred on major roads. Given the data was collected at MNH, most of the injuries mapped occurred near MNH. Within our limited sample, there was an area of relatively high RTI density at the intersection of Morogoro Road and United Nations Road.
Conclusion: GIS can be utilized to indicate areas of high RTI density in Dar Es Salaam, Tanzania. It is feasible to collect geographic information on RTIs at an urban emergency medicine department in Sub-Saharan Africa. With a larger sample size, multi-center sampling, and triangulation of data from other sources (e.g. police or mortuary records), accurate and statistically significant hotspots may be identified for targeted interventions.

References:
1. World Health Organization. Injuries and Violence: The Facts 2014. (2014) Geneva: World Heallth Organization.

2. Chalya PL, Gilyoma JM, Dass RM, Mchembe MD, Matasha M, Mabula JB. (2011). Trauma admissions to the intensive care unit at a reference hospital in Northwestern Tanzania. Scand J Trauma Resusc Emerg Med, 19, 61.
3. Moshiro C, Heuch I, Åstrøm AN, Setel P, Hemed Y, Kvåle G. (2005). Injury morbidity in an urban and a rural area in Tanzania: an epidemiological survey. BMC public health, 5(1), 11.
4. Razzak, J., Khan, U. R., & Jalal, S. (2011). Application of geographical information system (GIS) for mapping road traffic injuries using existing source of data in Karachi, Pakistan--a pilot study. Journal of the Pakistan Medical Association, 61(7), 640.
5. Schuurman, N., Hameed, S. M., Fiedler, R., Bell, N., & Simons, R. K. (2008). The spatial epidemiology of trauma: the potential of geographic information science to organize data and reveal patterns of injury and services. Canadian journal of surgery, 51(5), 389.
6. LaScala, E. A., Gruenewald, P. J., & Johnson, F. W. (2004). An ecological study of the locations of schools and child pedestrian injury collisions. Accident Analysis & Prevention, 36(4), 569-576.
7. Bell, N., & Schuurman, N. (2010). GIS and injury prevention and control: history, challenges, and opportunities. International journal of environmental research and public health, 7(3), 1002-1017.
8. Lord, S. E., Hameed, S. M., Schuurman, N., Bell, N. J., Simons, R. K., & Chir, B. (2010). Vulnerability to pedestrian trauma: Demographic, temporal, societal, geographic, and environmental factors. British Columbia Medical Journal, 52(3), 136-143.
9. Crandall, M., Zarzaur, B., & Tinkoff, G. (2013). American association for the surgery of trauma prevention committee topical overview: national trauma data bank, geographic information systems, and teaching injury prevention. The American Journal of Surgery, 206(5), 709-713.

Stacy Salerno (5)

Characteristics and Management of Burn Patients Presenting to and Urban Emergency Department in Dar Es Salaam, Tanzania

Introduction: Burns contribute substantially to the global burden of injury.[1] An accurate description of burn injury epidemiology can inform more effective prevention and management. However, data on burns is scarce in resourced-limited settings where prevention and management is needed most.[2-3] In particular, there is a disproportionate burden of burn morbidity and mortality in Africa. Burn injuries also account for a substantial proportion of preventable prolonged hospital stays in Africa, where human and material resources for proper burn care are chronically in short supply.[4-5] There is a substantial burden of burn injury in Tanzania.[6-8] A better understanding of the epidemiology, mechanisms, risk factors, and management of burn injuries presenting to Muhimbili National Hospital's Emergency Medicine Department, in Dar Es Salaam, can facilitate effective burn prevention and care interventions in Tanzania.

Objective: This objective of this study is to describe the burden of burn injury presenting to the largest public tertiary care center and emergency department in Tanzania.

Methods: This is a descriptive cross-sectional sub-analysis from a study of all injured patients presenting to Muhimbili National Hospital's Emergency Medical Department (MNH EMD) within a two year time period (March 2012 to March 2014). A standardized trauma form was used for both clinical and data collection purposes. Information from the trauma form was entered into an electronic database and analyzed using descriptive statistics on demographics, burn injury mechanism, place of injury, and clinical management. Stata (v.14) was utilized to generate means and standard deviations, medians and interquartile ranges, counts, percentages and 95% confidence intervals, as appropriate.

Results: Approximately five percent of injuries presenting to MNH EMD are burn injuries. Burn injuries account for over one-third of injuries in children under the age of five. Females presenting to MNH EMD have a higher prevalence of burn injury. Over two-thirds of burn injuries occurred in the home.

Conclusion: Burn injuries disproportionately impact the pediatric population, and more research is needed to improve our understanding of the circumstances predisposing children to high rates of burn injury in the region. Additionally, knowledge of burn management practices at home, during pre-hospital care, and in district and tertiary hospital settings can provide valuable information for future burn care education, training and resource allocation.

References:

1. WHO. The injury chart book: a graphical overview of the global burden of injuries; 2002.
2. Mock C, Peck M, Peden M, Krug E, & World Health Organization (WHO). A WHO plan for burn prevention and care. 2008; Geneva: World Health Organization.
3. Peck M, Pressman MA. The correlation between burn mortality rates from fire and flame and economic status of countries. Burns 2013; 39 (September (6)):1054–9.
4. Mock C, Peck M, Krug E, Haberal M. Confronting the global burden of burns: a WHO plan and a challenge. Burns 2009; 35 (August (5)):615–7.
5. Hyder A, Kashyap K, Fishman S, Wali S. Review of Childhood Burn Injuries in Sub-Saharan Africa: A Forgotten Public Health Challenge. African Safety Promotion 2004; 2: 43-58.
6. Outwater AH, Ismail H, Mgalilwa L, Temu MJ, Mbembati NA. Burns in Tanzania: morbidity and mortality, causes and risk factors: a review. International journal of burns and trauma 2013; 3(1), 18.
7. Chalya PL, Mabula JB, Dass RM, Giiti G, Chandika AB, Kanumba ES, Gilyoma JM. Pattern of childhood burn injuries and their management outcome at Bugando Medical Center in Northwestern Tanzania. BMC Res Notes 2011; 4:485.
8. Roman IM, Lewis ER, Kigwangalla HA, Wilson ML. Child burn injury in Dar es Salaam, Tanzania: Results from a community survey. International journal of injury control and safety promotion 2012;19(2), 135-139.
9. Ringo Y, Chilonga K. "Burns at KCMC: Epidemiology, presentation, management and treatment outcome." Burns 2014; 40: 1024-1029.

Margaret Schoeniger, MS2

Marc Sklar, MD, MPH Clinical Assistant Professor
Albert Einstein College of Medicine Obstetrics & Gynecology and Women's Health
Executive Director of Brick by Brick Uganda

Daniel Murokora, MB, ChB Assistant Professor
Albert Einstein College of Medicine Obstetrics & Gynecology and Women's Health

Elizabeth J. Brown, MD, MPH Assistant Professor
University of Rochester School of Medicine and Dentistry Department of Family Medicine

Needs Assessment to Evaluate Emergency Obstetric and Neonatal Care in Rakai District, Uganda

Background/Introduction:

The Millennium Development Goals (MDG) are eight international development goals established by the United Nations in 2000. As a UN member state, Uganda is committed to achieving these eight goals by the end of 2015. The fourth goal, to reduce child mortality and the fifth goal, to improve maternal health, are of particular interest to Brick by Brick Uganda. While Uganda has made some progress towards attaining MDG 4 and 5, the rate is not adequate to hit the 2015 targets unless the approach to implementation is sharpened and expedited[4]. The 2015 Maternal Mortality Ratio (MMR) target is 130/100,000, yet the 2011 Uganda Demographic and Health Survey (UDHS) reports MMR of 438/100,000 representing only a modest reduction over the past three decades [6,9]. Nonetheless, there has been improvement in skilled birth attendance (SBA) between 2006 and 2011 from 42%-58%, and this needs to be maintained or increased to create further opportunities for reductions in maternal and newborn deaths. Between the years 2000–2010 newborn deaths declined by a mere 2.2% and the neonatal mortality rate remains unacceptably high at 27 deaths per 1,000 live births, calling for further investment in high impact newborn survival interventions [9]. On the whole, causes of maternal and newborn deaths are preventable and associated with one of three delays in seeking or accessing quality care. In spite of the existence of the correct policy, advocacy and improvement in the health facility environment are required to achieve desired results.

In 2011, The Uganda Demographic and Health Survey (UDHS) was completed to obtain current statistical data about Ugandan demographics, including maternal and infant mortality, and information on health care services including antenatal, delivery and postnatal care. Our target district of Rakai is encompassed by the UDHS under the "Central-1" region. According to the 2011 UDHS, the district of Central-1 Uganda is particularly prone to poor Reproductive Maternal Newborn Child Health (RMNCH) indices due to a rapid population growth rate, high Total Fertility Rate (TFR) of 6.9 even when the desired number of children is 4.4 per woman [9].

The 2011 UDHS shows a low birth weight of 11.9%, and a Perinatal Mortality Rate (PMR) of 28/1,000 as well as an Intermittent Presumptive Treatment of Malaria rate (IPT) in antenatal care (ANC) of 12.1%. Although health facility births have increased over the last 2-3 years to 67.1%, the region still suffers a high rate of home births at 32% and i n fact, 8.3% of births are not assisted by anyone, while 9.5% and 11.3% are assisted by traditional birth attendants (TBA) and friends/relatives respectively. Postnatal care is another missed opportunity which if well utilized could help improve maternal and newborn care. For example, 60.2% of postnatal mothers and 88.5% of newborns in the Central Region of Uganda do not receive postnatal care (PNC) [9] .

This study aims to define and direct capacity-building activities which will encompass both training and mentoring for health care staff, as well as initiatives to improve physical infrastructure, medical supplies and equipment. To accomplish this, a needs assessment and baseline survey of knowledge and skills was performed in three Level 4 and twenty-two Level 3 Health Centers in the Rakai District.

Uganda has a tiered structure of public health facilities and operates on a referral basis. Level 1 Health Centers (HC's) are satellite facilities with no definite physical structure where community health workers may operate from. Level 2 HC's are staffed by nurses and serve a community of several thousand for common diseases and ANC. Level 3 HC's serve up to 10,000 people and should have a staff of 18 members led by a senior clinical officer who runs an outpatient clinic and maternity ward. They should also have a functioning laboratory. Level 4 HC's are mini-hospitals serving 20,000 people and should have wards for men, women, and children where patients can be admitted and a senior medical officer, another doctor, and an operating theater. Level 4 facilities are intended to provide blood transfusion services and comprehensive emergency obstetric care. Regional Hospitals (Level 5) have additional specialized services, consultation and research and serve 2 million people [7].

Objective:

The purpose of this phase in the project is to complete and analyze a thorough needs assessment of emergency obstetric and neonatal care in 25 health care facilities in the Rakai District. This is a multi-phased project carried out by the non-profit Brick by Brick Uganda in partnership with the Ugandan Ministry of Health. The data from the needs assessment will be used by this team to direct future programs to improve the identified gaps in care in an effort to decrease maternal and newborn mortality.

The Rakai district is in southwestern Uganda and is bordered by northern Tanzania and Lake Victoria. The population is over 500,000, with 91% of habitants in agrarian villages [2]. This rural region has been identified by the Ugandan Ministry of Health as an area with high maternal and infant mortality rates. The 3 Delays Model developed by McCarthy and Maine at Columbia University provides a framework for analyzing the factors that influence maternal mortality in developing countries [5]. This model presents three different delays in care that cause maternal morality: 1.) A delay in recognizing danger due to unskilled birth attendants, 2.) Delays in reach care due to long distance and a lack of available transportation, and 3.) Delay in receiving care at a Medical facilities due to inadequate staff or supplies[10].

The objective of this research project is to assess the third delay, the quality of medical facilities, medical supplies, and skilled staff in the hospitals in the Rakai District. The team used a Needs Assessment tool adapted from Averting Maternal Death and Disability (AMDD) to survey 25 health care facilities in the district [1]. Based on the trends identified in the Needs Assessment, Brick by Brick Uganda then plans to implement district-wide health system strengthening interventions through an integrated package of quality health initiatives to provide programmatic evidence for impact on maternal and infant health services affecting all three delays.

Methods:

Prior to the start of data collection our Ugandan staff will meet with local Ministry of Health (MoH) officials to ensure full partnership with this project. This included gaining permission to assess all of the aforementioned health care facilities. The MoH also helped provide transportation for our team to reach the extremely rural locations.

Our data collection team consisted of myself, a medical student at URMC, two certified nurse midwives and a Health Information Systems expert. The assessment is a 65 page long document that includes quantitative questions as well as observational and interviewing qualitative data. Photographs of each facility were also taken, particularly of the maternal and antenatal wards, operating theater, and the delivery rooms.

The tool consists of the following sections: Background, Maternity Services, Communication and Transport, Facility Availability, Antenatal Care, Labor and Delivery, Immediate Postpartum Care, Postnatal Clinic, Post Abortion Care, Guidelines and Protocols, Signal Functions, Other Maternal and Newborn health Services, Equipment and Supplies, Operating Theater, Personnel, and Information Systems. The needs assessment was divided amongst the four team members so that each researcher completed the same section of the survey at each facility.

The data was entered in real time into a paper hard copy of the tool at each site. A cross checking mechanism was put in place to ensure completeness. Before leaving the site, each team member would look over another team member's section to certify that each question had an answer or a coded response for "not applicable."

The support staff at the Brick by Brick office in Masaka Town, Uganda were then responsible for entering the data from the hard copy into an excel file. After all of the data from one health facility was entered, another team member would cross-check the excel file to ensure that all of the data had been entered. The data collection team also held a daily de-brief section after returning from the field. During this session, we read through the tool to ensure that all questions were answered properly, and to compile a Narrative Health Facility Summary. This is a qualitative summary of what the team found in each facility.

Results:

Quantitative results are still pending. Preliminary qualitative results compiled from the Narrative Summaries identify several crucial gaps in care:

Background

Many of the facilities are in very remote locations, a long dirt road away from a main thoroughfare, making the facility inaccessible to patients, especially maternity patients.

Maternity Services

Most of the facilities has adequate space to care for their patient load, however, this space was often no adequately organized, cleaned and maintained. The maternity beds need replacement and there is a great need for mosquito nets and privacy curtains for these beds. There is an urgent need for soap and water near the toilets for maternity patients and staff. Several of the level 3 facilities need repair to their rain water harvesting tanks as well as installment of solar lights so that there will be adequate light for the maternity ward at night.

Communication and Transport

Across the board, staff at these facilities have to use their personal cellphones and personal data plans to call for referrals. They are not reimbursed for these calls.
The level 3 health centers to not have a vehicle for patient transport. There are no funds set aside for patient transport or fuel costs. This barrier to referral causes women to go home to deliver (dangerously) instead of reaching a higher level care center that they need.

Facility Availability

The facilities are out of stock of several emergency obstetric medications. The health centers frequently run out of equipment and medication, thus forcing the patient to go to a store to purchase equipment/medication before receiving care.

Antenatal Care

Antenatal care is often delivered in the same area as maternal care, thus, patients do not have adequate privacy. There is need for adequate lighting in the exam rooms. There was a general lack of appropriate patient education posters and EMOC Clinical Guidelines. Across the district, facilities were not routinely screening for syphilis, hemoglobin levels or blood group type due to reagent shortages.Proper documentation of given antenatal care and patient education is not always done, in part because facilities are often out of stock of the proper documents and must resort to using notebooks.

Our team saw evidence of hand washing in only a handful of facilities. Many facilities did not have proper gloves either.

Funding for antenatal community outreach (beyond HIV/AIDS education and testing) was a problem for almost every facility.

Labor and Delivery

Most labor rooms are too small, too cluttered, without adequate light and privacy. We saw many outdated delivery tables.

Delivery equipment and supplies were severely lacking and disorganized. Instruments are not always properly cleaned and decontaminated. Women are often not prepared properly with antiseptic solution prior to delivery.

Midwives do not wear proper protective equipment when conducting deliveries.

Many facilities need new placental pits and incinerators for medical waste.

There was not a single facility that had evidence of routine partograph use by the midwives. There was not a single emergency trolley seen.

Immediate Postpartum Care

Many women want to leave the facility immediately after delivering and do not come back for postnatal care for themselves or their infants. Mothers are not always adequately educated about postpartum danger signs. Midwives are not all aware of the recommendation to bathe newborns 24 hours after birth to decrease incidents of hypothermia. Not all infants receive BCG and Polio vaccines prior to discharge, especially at the smaller facilities.

There is no neonatal intensive care equipment and staff are not trained for any interventions.

Postnatal Clinic

Postnatal patients often return on Immunization Days. They are not given any educational materials. None of the facilities screen for cervical cancer.

The level 3 health centers do not all have 4 or more modern methods of family planning.

Post Abortion Care

Midwives are not trained for Manual Vacuum Aspiration, and level 3 health centers do not have MVA sets. Most patients do not come back for follow up appointments.

Guidelines and Protocols

Antenetal, maternal, newborn care and post abortion protocols were missing in many facilities.

Signal Functions

The majority of the Level 3 health centers do not have $MgSO_4$ in stock, and midwives are not trained to administer this vital medication. Midwives are also not trained on vacuum extraction.

Other Maternal and Newborn Health Services

Midwives need additional training on newborn resuscitation with a bag and mask. Many facilities are missing proper face masks for newborn, especially premature newborns.

Equipment and Supplies

No facility had an infant incubator or warmer. Many facilities lacked mucus extractors and suction aspirators. There is an urgent need at most health centers for new complete delivery sets, MVA sets, resuscitation tables, speculums and blankets for the patients. The level 4 health centers also desperately need more cesarean section kits and proper protective equipment.

Operating Theater

Level 4 and 5 health care facilities do not have adequate equipment and supplies for emergency obstetric and neonatal care. Commonly, facilities did not have enough C-section surgical kits, laparatomy kits, eye-shields, surgical gown, gumboots, and drapes. Infection prevention protocols are not followed. We observed a lack of communication and teamwork between the doctor and the other staff and a lack of knowledge and preparedness for newborn resuscitation post C-section. They need O2 cylinders and proper anesthetic medications, equipment, and staff.

Personnel

All facilities reported less staff members than the MoH recommends for their given health center level. Staff need additional training in emergency obstetric care, newborn care, maternal and perinatal death reporting, and quality improvement. They need emergency response teams. Level 4 and 5 centers need anesthetic technician, anesthetic officers, and pharmacists.

Information Systems

There was an astonishing lack of organized data collection and usage. Many facilities were missing the proper forms and reports. Most facilities did not hold monthly all staff meeting, did not give feedback to staff and did not have data review meetings prior to submitting data to the district headquarters.

Health information assistants and medical records assistants need computer training and data reporting training.

Conclusion:

This study provides insight into many of the challenges health facilities are facing in the Rakai District to provide adequate emergency maternal and newborn health care. The data analysis is not complete but there are general themes that emerge. One such theme is the need for additional staff training. This falls under the third delay that we set out to address and we are currently in the process of planning district wide educational sessions and certifications in partnership with the Ministry of Health. The quantitative data analysis will more specifically guide what changes we can make in the facilities to reduce maternal and newborn mortality rates.

References:

1. Averting Maternal Death and Disability (AMDD). NeedsAssessment: Emergency Obstetrics and Newborn Care. Columbia University. 2015.

2. Estimated Population of Rakai District in 2012. citypopulation.de. Retrieved January 30 2015.

3. Health Sector Strategic and Investment Plan (2010) Ministry of Health, Uganda. www.health.go.ug

4. Hogan MC et al. 2010. Maternal mortality for 181 countries, 1980-2008: A systematic analysis of progress towards Millennium Development Goal 5. *Lancet* (375): 1609–1623.

5. McCarthy, J., Maine, D. "A framework for analyzing the determinants of maternal mortality". Studies in Family Planning 01/1992; 23(1):23-33.

6. Millenium Development Goals Reeport for Uganda, 2013. planipolis.ilep.unesco.org/upload/Uganda

7. Ministry of Health, Government of Uganda. Health Sector Strategic Plan 2000/01- 2004-05. Kampala, Uganda. 2000.)

8. National Development Plan, Uganda, 2010. http://npa.ug/wp-content/themes/npatheme/documents/NDP2.pdf

9. Uganda Demographic and Health Survey (UDHS 2006) Uganda Bureau of Statistics (UBOS) and Macro International Inc, 2007, Claverton, Maryland, USA: UBOS and Macro International Inc.

10. Waiswa P, Kallander K, Peterson S, Tomson G, Pariyo GW. Using the three delays model to understand why newborn babies die in eastern Uganda. Tropical Med Int Health. 2010;15(8): 962–972.

Casey Silver

Preceptors: Sarah Betstadt, Kusum Mathur
Institution: University of Rochester, Seva Mandir

Identification and Referral of Malnourished Children to Treatment: An Evaluation of a Community Health Worker Initiative in Rural Rajasthan

Introduction: Undernutrition is the most important risk factor for illness and death in infants in low-and-middle-income-countries (LMIC) (1). Community Health Workers (CHWs) are a proven intervention used to provide outreach in remote areas burdened with absent, inaccessible, or ineffective healthcare systems (2). Specifically, they often serve as important ties to formal healthcare systems when a child is found to be malnourished (3). This study undertakes implementation research to better understand the capabilities of CHWs and the challenges that beneficiaries face in accessing higher levels of care.

Objective: This study seeks to evaluate the capacity of CHWs to correctly identify and refer malnourished children to an appropriate treatment facility. The two primary aims of this study are 1) to assess the ability of CHWs to correctly identify and refer undernourished children and 2) to verify that patients seek care at the correct referral treatment center.

Background: A CHW program was implemented in 2009 by Seva Mandir, an Indian NGO, to improve practice of newborn care in rural tribal Rajasthan. The CHWs are trained to identify undernourished children and refer them to treatment centers. This is particularly important given that 43% of children in Seva Mandir's working areas are underweight (4).

Methods: Semi-structured interviews were conducted with 10 CHWs who were chosen randomly. They were also tested on their ability to use growth charts. Purposive sampling was then used to identify mothers whose children had been identified as underweight by CHWs in the past 6 months, and 24 of these mothers were interviewed.

Results: 100% of CHWs surveyed were able to demonstrate correct use of growth charts, though 3/10 reported using a method other than weighing to identify malnourished children. 38% of the mothers referred to physicians for malnutrition treatment did not seek care, and the most common reasons cited involved misconceptions about undernutrition.

Conclusion: CHWs are able to accurately use growth charts, though trainings should stress the importance of using these charts as the primary method of identifying malnourished children. In counseling mothers of malnourished children CHWs should emphasize that undernutrition is a medical condition that needs to be treated a physician.

References

1. Muller O, Krawinkel M. Malnutrition and health in developing countries. CMAJ. 2005;173(3):279-86.
2. White et al. Ethiopia Community-Based Nutrition Program Helps Reduce Childhood Malnutrition. Tulane CBN Evaluation Report. 2012.
3. Wollinka O, Keeley E, Burkhalter RB, Bashi. The Hearth Nutrition Model: Applications in Haiti, Vietnam, and Bangladesh. Wheaton, IL, Arlington, VA: World Relief, BASICS; 1997.
4. Banerjee et al. Wealth, Health, and Health Services in Rural Rajasthan. American Economic Review. 2004; 94 (2): 326-330.

Michelle Shankar and Corrie Poelman, MS2

Preceptors:
Dr. Richard Hodes, M.D.
American Jewish Joint Distribution Committee Spine and Heart Program
Addis Ababa, Ethiopia

Dr. Arthur Moss, M.D.
University of Rochester Medical Center
Department of Medicine, Cardiology Heart Research

Dr. David Korones, M.D.
University of Rochester Medical Center
Department of Pediatric Hematology-Oncology

Dr. Addisu Mesfin, M.D.
University of Rochester Medical Center
Department of Orthopaedics

Finger-to-Knee Distance as a Predictor of Lung Function in Pre-operative Spine Patients in Ethiopia

Introduction

Untreated spinal deformities (scoliosis and kyphosis) can result in compression of the thoracic cavity and restrict lung function, damage vital organs, and cause neurological deficits. These are prevalent health concerns in Ethiopia, a country with limited resources to measure, monitor, and intervene.

Dr. Rick Hodes, M.D. is an internist who works with Ethiopian spine patients to provide free surgical intervention with the Foundation of Orthopaedics and Complex Spines (FOCOS) in Ghana and provides care during follow-up. A major challenge of his work is to find low-cost and low-resource ways to predict severity of lung restriction among his spine patients.

Background

Ethiopia is located in the horn of East Africa. With a population of 91 million, it is the third most populous country in Africa. The majority of the population lives in a rural and impoverished setting[1].

Ethiopia ranks third in Africa and eighth among the 22 highest tuberculosis (TB) burdened countries. The TB case detection rate, treatment success rate, and TB cure rate are 74%, 82.5%, and 67%, respectively[2]. Although lungs are the major site of damage caused by TB, the spine and musculoskeletal system can also be affected. TB spinal infection (also known as TB spondylitis or Pott's disease) is more common in Ethiopia compared to worldwide statistics. If left untreated, it can result in severe kyphosis. This deformity may result in compression of the thoracic cavity and restrict lung function, damage to vital organs, and neurological deficits due to compression of neural structures within or adjacent to the spine[3].

In addition to kyphosis secondary to TB infection, congenital scoliosis is prevalent among Ethiopians. It is the most common spinal disorder in children and adolescents[4]. It is caused by failure of formation and/or segmentation of vertebrae during development. It is theorized that vitamin deficiency, particularly Vitamin D, can contribute to the higher rates of spinal deformity in Ethiopia[5].

The primary treatment for scoliosis and kyphosis is surgical intervention. However, current surgical services available in the country do not offer corrective procedures for cases of the most severe spinal deformities[1].

It is evident that scoliosis and kyphosis cause deformity of the thoracic cage, leading to impaired development and compression of lungs as well as limited chest wall movement. Possible consequences of this are restrictive ventilation defect affecting oxygen and carbon dioxide gas exchange[6]. While there is extensive research on the causative effect of spinal deformity on lung function, little has been done to explore the prediction of lung function based on degree of spinal deformity. After performing a PubMed search, we found several studies on prediction of lung function using height and arm span[7,8]. However the results of these studies show that thorax dimensions, arm span, and sitting height were reliable predictors of lung function only in healthy, non-smoking subjects.

Dr. Hodes estimates severity of spinal deformity by estimating the distance from his patients' fingertips to their knees. Patients with a greater degree of curvature have a shorter finger-to-knee distance, sometimes even extending below the knees. These patients display decreased lung function in relation to those with a less severe spinal deformity. He uses this to estimate the relative lung function of his patients. However, the relationship between finger-to-knee distance and lung function has never been tested.

Objective

The goal of this study is to determine if there is a correlation between the finger-to-knee distance and pulmonary function among pre-operative spine patients in Ethiopia. This will help us to determine if such a measure can be used as a proxy for severity of spinal deformity and accurate predictor of lung restriction among spine patients in low resource settings.

Methods

Patients from Dr. Hodes' spine clinic were selected based on the criteria that they were preoperative Ethiopian spine patients who were willing and able to participate in all parts of the study.

Once consented, a tape measure was used to obtain the following measurements at standing posture: standing height, wingspan, left and right distance from acromion to tip of third digit (arm length), left and right distance from floor to anterior superior iliac spine (leg length), and left and right distance from floor to the upper patella and to the tip of the third digit. The distance of floor to upper patella was then subtracted from the measured distance of floor to fingertip to calculate the finger-to-knee distance. An example of this distance is depicted in the image below. (Blue line is floor-to-finger distance, red line is floor to patella distance; the distance between these two is our calculated finger-to-knee measurement of interest.) The subject then performed a pulmonary function test (PFT), with percent-predicted forced vital capacity (%FVC) being our primary outcome of interest.

Figure 1: Measurements Used to Determine Finger-to-Knee Distance

We analyzed our data using Microsoft Excel and PRPP software. The distance between the tip of the third digit and upper patella height during rest posture was calculated in order to determine fingertip-to-knee distance, both right and left, for each patient. In some cases, the fingertip-to-knee distance was different between the right and left, so we used the lowest fingertip-to-knee distance in our calculations.

We then used PRPP software to perform a Pearson two-tailed correlation test to analyze the relationship between average fingertip-to-knee distance and %FVC in each patient.

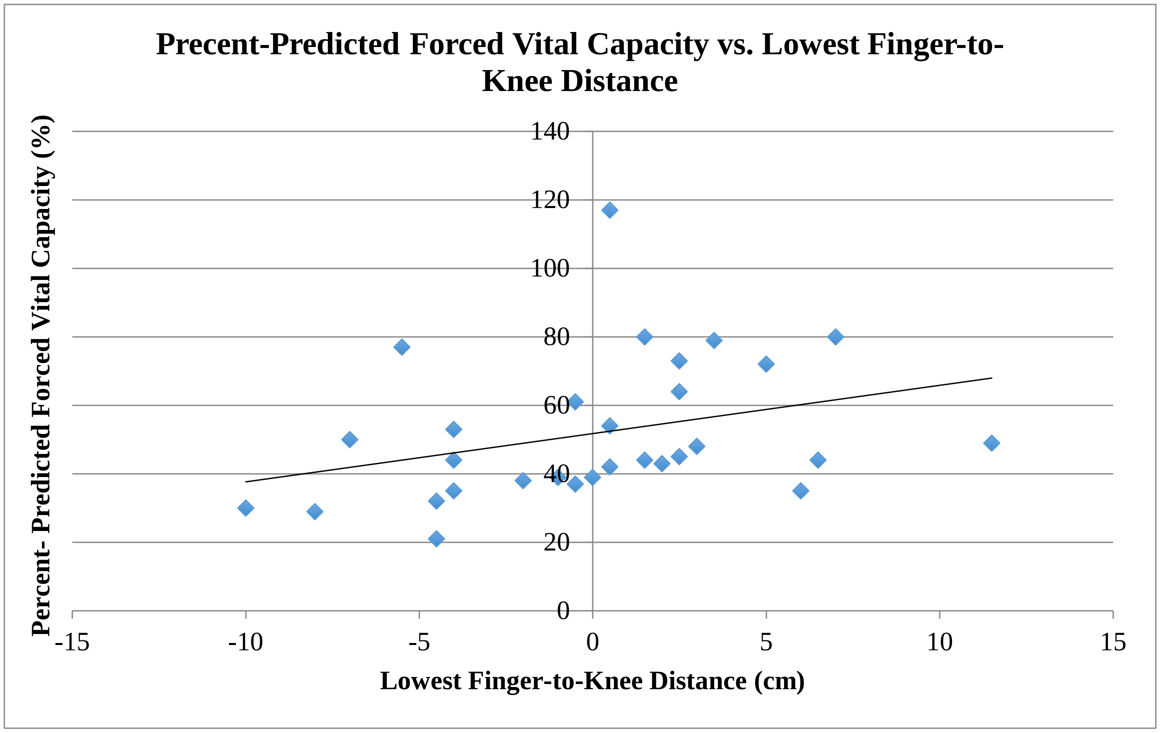
Results

We enrolled 34 pre-operative spine patients at the clinic of Dr. Richard Hodes in Ethiopia. Age range was 8 to 32. Eleven were male, 23 were female. Twelve spines were classified as scoliotic, while seven were classified as kyphotic, and twelve were kyphoscoliotic. At least five subjects reported having had tuberculosis and/or TB treatment.

Of the 34 subjects, 4 were removed because they were unable to perform the PFT, reducing the sample size to n=30. The median finger-to-knee distance was 1.25 cm and 1.75 cm on the patients' right and left sides, respectively. The median %FVC of our population was 44.5 percent-predicted.

We found there to be a Pearson correlation (r value) of 0.33, which indicates a moderate positive relationship between lowest finger-to-knee length and percent FVC. The significance of this correlation (p value) is 0.08, which is not statistically significant. Individual data are shown in the graph below.

Figure 2: Percent-Predicted Forced Vital Capacity vs. Lowest Finger-to-knee Distance



Discussion

Our findings support a moderately positive correlation between finger-to-knee distance and lung function that is not statistically significant.

In considering these results, we reflect on the many challenges of our study. The first challenge was recruiting a large sample size within a short amount of time (6 weeks). With a larger sample size (n >30), we may find results that will allow us to prove or disprove a correlation with greater confidence.

The second challenge was in taking reliable measurements. Finger-to-knee measurements were taken using a measuring tape and using anatomical landmarks based on palpation, which provides room for human error. Though the spirometer used to perform the PFT was functional and accurate, we are wary of the reliability of the readings due to the potential for misinterpretation through a translator that may have affected the outcomes on a case-by-case basis.

It is also worth considering that finger-to-knee distance is variable even in normal populations, and we were presented with the challenge of trying to standardize this measurement. There may be value to comparing our data to the same measurements taken in a healthy population.

Finally, it is likely that lung function is worsened in patients afflicted by kyphosis secondary to tuberculosis, and this should be considered in future studies. The challenge of analyzing this information is that most patients are uncertain about their own personal medical history. In our study population, five patients self-reported having had or been treated for TB, but it is possible that more than this number had been affected.

References:

1. "Ethiopia Scoliosis Profile." Scoliosis Research Society. https://www.srs.org/professionals/global-outreach-program/srs-endorsed-programs/ethiopia-addis-ababa

2. "Comprehensive Analytical Profile: Ethiopia: Tuberculosis" African Health Observatory. World Health Organization. http://www.aho.afro.who.int/profiles_information/index.php/Ethiopia:Tuberculosis

3. Rasouli MR, Mirkoohi M, Vaccaro AR, Yarandi KK, Rahimi-Movaghar V. "Spinal Tuberculosis: diagnosis and management. *Asian Spine J.* 2012;6(4):294-308.

4. Konieczny, M.R. et al. "Epidemiology of adolescent idiopathic scoliosis" *Journal of Child Orthopaedics*. V.7(1); 2013 Feb. NCBI. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3566258/

5. Balaji, V. et al. "Vitamin D Deficiency in Patients with Adolescent Idiopathic Scoliosis (AIS): A Cause for Concern?" *Bone Joint Journal* 2014 v.96-B no. SUPP 6 http://www.bjjprocs.boneandjoint.org.uk/content/96-B/SUPP_6/2.abstract

6. Ran, H. W. Zhi Hong and H. Jiang-Na. "Scoliosis on Pulmonary Function." Rep 1st Ed. Vol 33. N.p.: n.p., 2011. PubMed. Web. 4 Feb 2015. 4.2 (2010):127-36.

7. Golshan, M. RO Crappo, B. Amra, RL Jensen, and R. Golshan. "Arm Span as an Independent Predictor of Pulmonary Function Parameters; Validation and Reference Values." Respirology 12.3 (2007): 361-66. Web.

8. Helms, P., SH Bain, and JO Warner. "Foot and Hand Length for Prediction of Vital Capacity in Scoliotic Children." Spine (Phila Pa 1976) 11.7 (1986): 746-48. Web.

Sujeong Kim, MS2

Dr. Rohit C. Khanna MD, MPH
International Centre for Advancement of Rural Eye Care
LV Prasad Eye Institute, India

Cataract Surgery Visual Outcomes and Associated Risk Factors in Secondary Level Eye Care Centers of LV Prasad Eye Institute, India

Introduction:
Visual impairment affects an estimated 285 million people worldwide, and over 62 million people in India alone. Despite this prevalence of visual disability and the fact that over 80% of visual impairment is treatable, global access to high quality eye care and treatment is far from pervasive. [1]

Globally, cataracts account for 51% of blindness[2] and a loss of over 3.5 million DALYs (disability adjusted life years) each year[3]. Surgery is the only identified treatment for cataracts, and is one of the most common and cost effective surgical procedures preformed worldwide[4]. In India, over the past 25 years, the cataract surgical rate has increased roughly 500%. As the quantity of cataract surgery continues to increase, it is vital to ensure that the quality of care is increasing as well. However, current data is troubling and shows that, particularly in low and middle income countries, up to 20% of patients have 'poor' (visual acuity worse than 6/60 metric) outcomes, with particular inconsistencies between the hospital and community setting.[1]

Studies have shown that monitoring outcomes can effectively improve and ensure quality of cataract surgical outcomes in rural eye care center.[5,6] Evaluation of surgical outcomes is crucial for surgeons, health care management teams, and for public health officials. It encourages eye surgeons to monitor their own results over time, identifies causes of poor outcomes, and enhances the quality of care. It also provides a foundation for further improvements in healthcare delivery.

Study Background:
The LV Prasad Eye Institute (LVPEI) is a not-for-profit, comprehensive eye care network that opened in 1987 in Hyderabad, India and has since expanded to 137 centers across the state of Andhra Pradesh. LVPEI operates on a pyramidal hierarchical network of primary community vision centers, secondary care centers that provide basic surgical services, and tertiary care centers that provide the most comprehensive and advanced eye care. Patients are admitted regardless of their ability to pay for the procedure, and more than 50% of services at LVPEI are provided free of charge. The International Centre for Advancement in Rural Eye Care (ICARE) branch of LVPEI, directed by Dr. Rohit Khanna, specifically aims to make high-quality,

appropriate eye care accessible to previously geographically and economically disadvantaged populations.

Objective:
The purpose of this study was to evaluate cataract surgery visual outcomes and associated risk factors in rural secondary level eye care centers of LV Prasad Eye Institute.

Methods:
The study was retrospective in nature and looked at medical records of patients at secondary care centers. Out of the 11 secondary centers in the LV Prasad Eye Health Pyramid, 3 specific secondary care centers were studied (Nava Bharat Eye Centrein Paloncha, Dr Komma Reddy Raja Ram Mohan Rao Eye Centre in Gudavalli, and Y Mahabaleswarappa Eye Centre in Bellary). All age related cataract surgeries performed in 2014 were included in the initial data collection.

All patients examined at the secondary level eye care centers were given complete ophthalmologic exams prior to surgery (presenting and best corrected visual acuity, intraocular pressure measurement, detail slit lamp examination, and screening for ocular comorbidities). The surgeon determined the surgical method (Extracapsular Cataract Extraction, Small Incision Cataract Surgery, or Phacoemulsification) based on the severity of the cataract, the results of the opthalmic examination, and his particular level of expertise. Surgical procedure details, intra operative and post operative complications, and follow up measures of visual acuity, best corrected visual acuity, and further complications were all recorded in patient medical records. Visual outcomes were assessed at follow-up appointments at intervals of 1 day, 1-3 weeks, andt 4-11 weeks.

Results:
In 2014, a total of 5,580 age-related cataract surgeries were performed across the three secondary centers. Small Incision Cataract Surgery with a Posterior Chamber Intraocular Lens insertion was the most common procedure. Final data analysis is pending, but preliminary data shows that poor visual outcomes are higher in older age groups, in females, those with preoperative comorbidities, those with intraoperative complications, and those undergoing ECCE.

Conclusion:
Preliminary data suggests that post-operative visual acuity will fall within the WHO recommendations of successful cataract surgical outcomes, indicating that quality cataract surgeries can be achieved at rural secondary care centers. Reliable surgical performance in such areas has the potential to provide the reversal of disabling visual impairment to previously unreachable populations.

References:

[1]International Agency for the Prevention of Blindness. State of the world's sight. VISION 2020: The Right to Sight 1999–2010. IAPB, London, 2010.

[2]Pascolini D, Mariotti SPM. Global estimates of visual impairment: 2010. British Journal Opthalmology Online. 2011 December.

[3]Baltussen R, Sylla M, Mariotti S, et. al. Cost-effectiveness analysis of cataract surgery: a global and regional analysis. Bull. World Health Organ. 2004; 82:338-345

[4]Foster A, Gilbert C, Johnson G. Changing patterns in global blindness: 1988-2008. Community Eye Health. 2008;21:37–9.

[5]Gogate P, Vakil V, Khandekar R, Deshpande M, Limburg H (2011) Monitoring and modernization to improve visual outcomes of cataract surgery in a community eyecare center in western India. J Cataract Refract Surg 37: 328-334.

[6]Yorston D, Gichuhi S, Wood M, Foster A. Does prospective monitoring improve cataract surgery outcomes in Africa? Br J Ophthalmol. 2002 May; 86(5):543-7.

Zehui Wang

Preceptor(s) Name: Dr. Shrikant Bharadwaj
Title: Associate Director of Optometry
Institution: LV Prasad Eye Institute
Department: Optometry

Preceptor(s) Name: Dr. Geunyoung Yoon
Title: Associate Professor
Institution: University of Rochester School of Medicine and Dentistry
Department: Ophthalmology

Enhancing the depth of focus of the pseudophakic eye with uncorrected myopic astigmatism

Introduction:
Many cataract surgery patients experience varying degrees of postoperative astigmatism, or blurred vision from irregularities in cornea or lens curvature. Previous studies show that myopic astigmatism can improve near vision acuity at the cost of distance vision acuity, and uncorrected astigmatism has been proposed as an alternative to expensive custom bifocal lenses in developing countries. This project subjectively and objectively evaluates the range of depth of focus (DOF), defined as the range of tolerable blur, in 10 healthy cyclopleged volunteers with different monocular and binocular astigmatism combinations. Our results show that in binocular vision, subjective visual acuity (VA) is determined by the best performing eye. The combination of OS plano and OD 2.5 diopters (D) modeled after Monovision intraocular lens (IOL), which best corrects one eye to distance vision and the other to near vision, yielded the greatest range of DOF as each eye is optimized for near and distance vision.

Objective: This study was designed to evaluate the depth of focus of pseudophakic eyes with uncorrected astigmatism by subjectively and objectively measuring the range of near and intermediate vision.

Background:
In pseudophakic patients with surgically implanted intraocular lenses, the loss of accommodation leads to reliance on multifocal lenses for optimal near and distance vision. Yet beyond near and distance vision, depth of focus (DOF) is another crucial component for visual performance. DOF is defined as the range of image distance that can be tolerated by an optical system with an acceptable reduction in acuity, and its enhancement carries great implications for refractive errors (e.g. astigmatism, myopia and hyperopia) following cataract surgery.

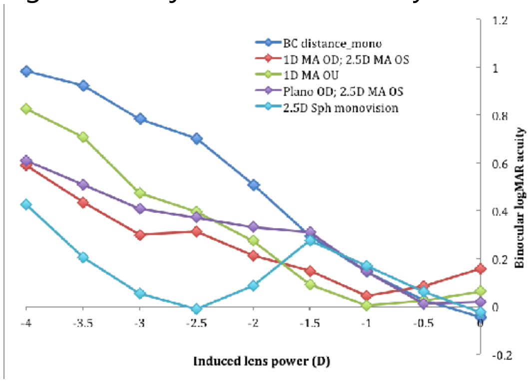
In a previous study, we have shown that the combination of induced astigmatism that leads to the best near vision acuity and stereoacuity is plano/+1.00 DC at 90 degrees axis in the right eye and plano/+2.50 DC at 90 degrees axis in the left eye. Using this combination of induced astigmatism, the current study experimentally determined the DOF of pseudophake patients to better evaluate the range of their best corrected near and intermediate visual acuity. While higher visual acuity has been correlated with lower DOF in previous studies, the optimal combination of visual acuity and DOF for uncorrected astigmatism has not yet been determined. Enhancing the DOF of the astigmatic eye is a research effort to improve quality of life in pseudophake patients.

Methods:
10 cyclopleged healthy volunteers serving as the control group for the pseudophakic patients were evaluated in the laboratory with calibrated examination room for visual acuity measurements using a standard COMPlog thresholding system. Informed consent was obtained from all study participants. Subjective DOF was measured with trial lenses calibrated considering the refractive error status of the subject for distance, desired combination of astigmatism to be induced and the dioptric defocus to be induced. Determined trial lenses were placed in a trial lens frame in front of the eye at vertex distafnce of 12mm. Distance visual acuity measurements were recorded using the thresholding program in COMPlog system at different dioptric defocus levels from -4.0 D to 0 D in intervals of 0.50D, for 4 monocular and 4 binocular astigmatism combinations, totaling 72 combinations tested. Near vision was defined as -4.0 D to -2.0 D, intermediate vision defined as -2.0 D to -0.5 D, and distance vision as -0.5 D to 0 D.

Results:
While the results of the entire study are still pending, subjective visual acuity data from our control group of 10 healthy cyclopleged volunteers have been compiled into defocus curves and DOF ranges below. Figure 1 shows the composite defocus curves from all 10 subjects on a logMAR scale, for which defocus defined as less than 0.3 logMAR units. This value has been used in literature as the cutoff point for tolerable blur. Figure 1 shows the defocus curves for all four binocular combinations, with monocular best-corrected distance vision serving as control and Monovision represented by "2.5 D Spherical" showing best overall visual acuity.

Further experimental data for calculating the range of DOF was first analyzed using the Shapiro-Wilk test which revealed a non-normal distribution, precluding the usage of mean and standard deviation for data analysis. Figure 2 shows the range of DOF for all eight astigmatism with the median, maximum and minimum values, and 25th and 75th percentiles in a box-and-whiskers plot of the obtained subject data.

Figure 1. Subjective Visual Acuity Defocus Curves for Binocular and Monocular Vision



The dark blue line labeled “BC distance_mono” represents monocular plano without astigmatism. The aqua line labeled “2.5D Sph monovision” represents right eye plano and left eye 2.5D Spherical, best corrected for near vision. The red, purple, and green lines represent astigmatism combinations as labeled. Overall, Monovision showed the best performance by remaining below the 0.3 logMAR cutoff point for all defocus levels tested.

Figure 2. Range of Depth of Focus Across Astigmatism Combinations

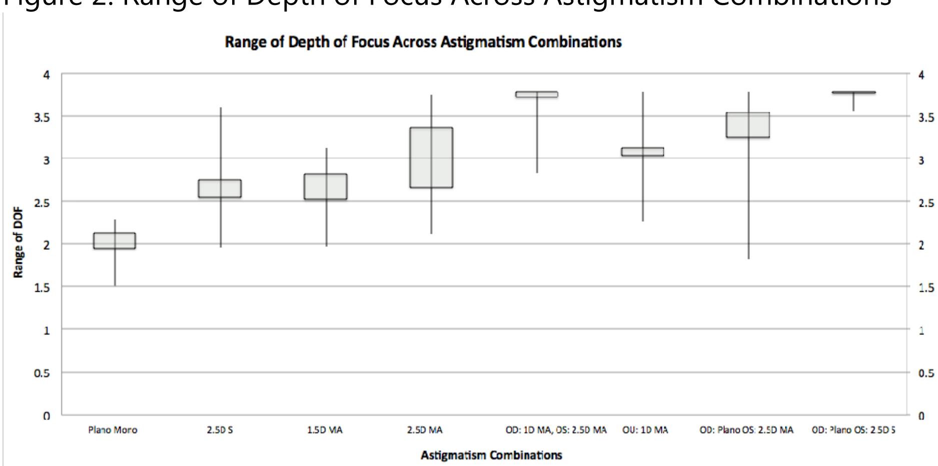


Figure 2 shows the range of DOF with maximum and minimum values, as well as 25th and 75th percentiles. The last combination of Monovision showed the greatest range with the least variation, as the visual acuity data for all defocus levels remained under the cutoff line for tolerable blur.

Conclusion:

The preliminary results from this study support Monovision as the best visual acuity solution for patients who have lost accommodation for near and distance vision. While combinations of uncorrected astigmatism were capable of improving near vision to a certain extent, especially compared to the control of best-corrected distance vision, it did not compare to the binocular performance of Monovision. In relation to previous studies which showed uncorrected myopic astigmatism showing improved stereoacuity over Monovision, this study begs the question of what components are more important in the visual experience. However, we are still awaiting computational data from our control group as well as data from pseudophakic patients, as data collection was not yet complete by the end of my planned research stay. The two pseudophakic patients whose data were collected and analyzed correlated with the trends seen in the control group, albeit with lower visual acuity. This data is not necessarily representative of pseudophakic subjects however and should not be used as a prospective bias for study results.

References:

1. Singh A, Pesala V, Garg P. Relation between uncorrected astigmatism and visual acuity in pseudophakia. Optometry and Vision Science 2013;90:378Y84.
2. Pesala V, Garg P, Bharadwaj R. Binocular vision of bilaterally pseudophakic eyes with induced astigmatism. Optometry and Vision Science 2014;91:1118Y28.
3. Pesala V, Garg P, Bharadwaj R. Image quality analysis of the pseudophakic eyes with uncorrected astigmatism. Optometry and Vision Science 2014;91:444Y51.

Chris Wong

Dr. David Adler

Program Evaluation of LINKS Implementation in Botswana

Task Force for Global Health

Introduction:

Historical Background on NTDs and MDA

Neglected tropical diseases (NTDs) are a collection of 17 diseases that afflict some of the world's poorest populations. Not only are these diseases sources of suffering in and of themselves, but they are also major burdens that propagate a cycle of poverty.

In the last decade there has been a mounting international effort to control NTDs. In 2007, representatives of WHO Member States, United Nations agencies, the World Bank, philanthropic organizations, universities and pharmaceutical companies convened in Geneva, Switzerland to declare the importance of NTDs to the world (WHO, 2007).

This was followed by a WHO report in 2010 discussing progress in the field of NTDs. While this report showed significant gains since 2007, it also revealed significant obstacles. These obstacles were confronted by the Roadmap for Neglected Tropical Diseases published by the WHO in 2011. This document plots a course to accomplish concrete goals by 2020, including regional control of some diseases and global elimination for others (WHO, 2012). Building on this momentum, pharmaceutical companies, donor groups, implementing partners, national NTD programs and supportive partners met in London in January 2012 to establish the London Declaration on Neglected Tropical Diseases in support of the WHO Roadmap (Uniting to Combat NTDs).

Taken as a whole, the international community's recent actions have set the stage for well-funded, large-scale public health interventions capable of distributing the advances of modern medicine to those who have been left behind. It is in this optimistic political landscape that the Task Force for Global Health offers technical assistance to Ministries of Health through their NTD Support Center (NTDSC).

Objective:

Under the supervision of the NTDSC and the Ministry of Health of Botswana, the objective of this study was to (1) identify logistical processes and gaps and (2) determine concrete ways the NTDSC can improve upon these processes.

Background:

Established in 2013, the NTD Support Center (NTDSC) is a part of the Task Force for Global Health focused on researching and assisting interventions to control or eliminate NTDs. Currently, the NTDSC is pushing to finish mapping the prevalence of NTDs during 2015 in order to meet the goals for 2020. To this end, the NTDSC provides Ministries of Health with the equipment and training to utilize the LINKS System, which allows field technicians to directly send results to an online database via smartphone. This system accelerates the workflow from fieldwork to a finished report while minimizing entry errors.

Typically, the NTDSC sends a member of their team to conduct a training session before the field technicians begin the mapping exercise. However, no NTDSC staff has stayed past the training and into the mapping exercise itself. In addition, the NTDSC's involvement with the mapping project is mediated through the WHO, which speaks to the Ministry of Health, which employs a principal investigator who oversees the technicians who benefit from the LINKS system. The number of actors between the NTDSC and the technicians creates an opportunity to find out new information by integrating NTDSC staff for the entire duration of the mapping exercise.

Methods:

As an Intern with the Task Force for Global Health, I provided technical support and general logistical assistance to Botswana's national NTD mapping exercise. I paid special attention to logistical gaps and processes and provided daily updates and weekly reports to staff stationed in Atlanta. Upon returning, I wrote a final report synthesizing my observations and suggestions geared toward improving NTDSC activities.

Results:

Overview of the Mapping Exercise in Botswana

- Surveyors screened school children for STH/SCH and general populations for LF.
- 10 survey teams screened for SCH/STH in all 26 districts and LF in 6 districts.
- For SCH/STH, the workflow for each school consisted of setting up, intaking students, analyzing samples, and entering data with a smart phone.
- For LF, survey teams conducted community based screening with ICT cards.
- Social mobilization primarily consisted of sensitization, consenting, and scheduling. However, social mobilization was the biggest obstacle to the mapping exercise because entire districts were not mobilized.

Lessons Learned and Recommendations

- A team with two phones would be able to assign two people to intake children, halving the required time and allowing the team to move to a second school more quickly. This gives the team greater flexibility when dealing with unforeseen and time-consuming obstacles in the field. It stands to reason that such a team would more consistently complete two schools a day over the course of the exercise. Teams could achieve the same advantages by using multiple paper forms, but this creates extra work and errors when compared with using two phones.
- Timers and results forms provided by the Task Force would be reliably distributed to every lab bench. This is an opportunity to create an environment conducive to SOP adherence. Clocks are not always present in classrooms, so providing a timer guarantees the means to standardize certain steps across teams. The results forms mirror the LINKS forms, and the LINKS forms are only available to the Task Force prior to the phone's arrival. This creates an opportunity to preempt the needs of program managers by distributing USB drives loaded with digital results forms to be printed. While fulfilling this

need, the Task Force can add reminders to the results forms so that every technician reads key parts of the SOP on a very frequent basis.

Conclusion:

The Task Force for Global Health benefits from feedback on their technical support as it pertains to the impact it has on technicians in the field. However, complex organizational structures make such feedback inconsistent and cumbersome. Sending someone to observe the entire mapping exercise provided direct feedback to the NTDSC, elucidating the ways that efforts in the United States translate to an impact on the ground. Continuing to send interns or fellows into the field to observe entire exercises may provide a consistent source of such feedback.

References:

Uniting to Combat NTDs. "Uniting to Combat NTDs & the London Declaration". Retrieved January 12, 2015, from http://unitingtocombatntds.org/uniting-combat-ntds-london-declaration

WHO (2007). *A Report of the Global Partners' Meeting on Neglected Tropical Diseases: A turning point*.

WHO (2012). *Accelerating Work to Overcome the Global Impact of Neglected Tropical Diseases: A roadmap for implementation*.

WHO (2013). Sustaining the drive to overcome the global impact of neglected tropical diseases: Second WHO report on neglected tropical diseases.

Michael Geary

Preceptor
Regis O'Keefe, MD, PhD
Chair, Department of Orthopaedics and Rehabilitation
University of Rochester

"Systemic EP4 Inhibition Increases Adhesion Formation in a Murine Model of Flexor Tendon Repair"

Introduction: Flexor tendons (FT) in the hand run on the palmar side of the digits and transmit the forces that allow for finger flexion. Primary repair of FT injuries in zone II remains a challenging surgical problem with a high rate of post-operative complications [1-4]. Fibrous adhesions between the tendon and surrounding tissue form to some extent in all cases of tendon repair, and up to 30–40% of cases are significant enough to result in loss of digit range of motion (ROM) and impaired hand function [5]. There are more than 30,000 tendon repair procedures a year in the US, with billions in associated healthcare costs [6]. Given this clinical challenge, there is significant interest in optimizing the repair process to improve functional outcomes following FT injury.

Objective: The objective of the present study was to evaluate the effects of systemic EP4 inhibition on adhesion formation and matrix deposition after flexor tendon repair.

Background: Flexor tendon injuries are a common clinical problem, and repairs are frequently complicated by post-operative adhesions forming between the tendon and surrounding soft tissue. Prostaglandin E2 and the EP4 receptor have been implicated in this process following tendon injury [7-8]; thus, we hypothesized that inhibiting EP4 after tendon injury would attenuate adhesion formation.

Methods: A model of flexor tendon laceration and repair was utilized in C57BL/6J female mice to evaluate the effects of EP4 inhibition on adhesion formation and matrix deposition during flexor tendon repair. Systemic EP4 antagonist or vehicle control was given by intraperitoneal injection during the late proliferative phase of healing, and outcomes were analyzed for range of motion, biomechanics, histology, and genetic changes.

Results: Repairs treated with an EP4 antagonist demonstrated significant decreases in range of motion with increased resistance to gliding within the first three weeks after injury, suggesting greater adhesion formation. Histologic analysis of the repair site revealed a more robust granulation zone in the EP4 antagonist treated repairs, with early polarization for type III collagen by picrosirius red staining, findings consistent with functional outcomes. RT-PCR analysis demonstrated accelerated peaks in F4/80 and type III collagen (Col3a1) expression in the antagonist group, along with decreases in type I collagen (Col1a1).Mmp9 expression was significantly increased after discontinuing the antagonist, consistent with its role inmediating adhesion formation. Mmp2, which contributes to repair site remodeling, increases steadily between 10 and 28 days post-repair in the EP4 antagonist group, consistent with the increased matrix and granulation zones requiring remodeling in these repairs.

Conclusion: These findings suggest that systemic EP4 antagonism leads to increased adhesion formation and matrix deposition during flexor tendon healing. Counter to our hypothesis that EP4 antagonism would improve the healing phenotype, these results highlight the complex role of EP4 signaling during tendon repair.

References:

1. Beredjiklian PK. Biologic aspects of flexor tendon laceration and repair. J Bone Joint Surg Am. 2003; 85-A(3):539–50.
2. Lin TW, Cardenas L, Soslowsky LJ. Biomechanics of tendon injury and repair. J Biomech. 2004; 37(6):865–77.
3. Lister G. Pitfalls and complications of flexor tendon surgery. Hand Clin. 1985; 1(1):133–46.
4. Momeni A, Grauel E, Chang J. Complications after flexor tendon injuries. Hand Clin. 2010; 26(2):179–89.
5. Aydin A, Topalan M, Mezdegi A, Sezer I, Ozkan T, Erer M, et al. [Single-stage flexor tendoplasty in the treatment of flexor tendon injuries]. Acta Orthop Traumatol Turc. 2004; 38(1):54–9.
6. Langer R, Vacanti JP. Tissue engineering. Science. 1993; 260(5110):920–6.
7. Wang JH, Li Z, Yang G, Khan M. Repetitively stretched tendon fibroblasts produce inflammatory mediators. Clin Orthop Relat Res. 2004(422):243–50.
8. Khan MH, Li Z, Wang JH. Repeated exposure of tendon to prostaglandin-E2 leads to localized tendon degeneration. Clin J Sport Med. 2005; 15(1):27–33.

Nicholas T. Hogan, CC3

Preceptors:
Casey Romanoski, Ph.D.
Post-Doctoral Fellow
Christopher Glass, M.D./Ph.D.
Professor of Cellular and Molecular Medicine and
Professor of Medicine
Department of Cell and Molecular Medicine
University of California, San Diego School of Medicine.

A Combination of AP-1 and ETS Transcription Factors Co-localize at Human Aortic Endothelial Cell Enhancers Involved in TNFα Signaling

Introduction:

Despite decades of research into the etiology and treatment of atherosclerosis and coronary artery disease (CAD), these diseases remain leading causes of morbidity and mortality. While these conditions can display a complex pattern of heritability, the predisposing genetic sequence variants have remained largely unknown[1]. The advent of affordable high throughput genomic sequencing technology has allowed for the study of disease-associated genetic variants in large genome-wide association studies (GWAS) of patients and control subjects[2,3,4]. The results of these studies have revealed that the vast majority of loci correlated with CAD, and other prevalent diseases, are located in intronic or intergenic regions of the human genome rather than within the exome[5]. How sequence variation in these non-coding regions exerts an effect on susceptibility to atherosclerosis has yet to be fully understood. One possible explanation for the observed association between non-coding sequence variations and atherosclerosis is that these variations alter the activity of regulatory elements such as enhancers, thus changing levels of transcription for their associated target genes.

Objective:

We aimed to study how combinations of transcription factors interact with enhancers and regulate transcription in human aortic endothelial cells (HAEC). One of our primary goals was to define key lineage determining and signal dependent transcription factors (LDTF, SDTF) that are particularly influential in HAEC. We hypothesize that a set of AP-1 and ETS transcription factors collaborate to establish key endothelial cell enhancers.

Background:

Simple combinations of lineage-determining transcription factors (LDTF) have been shown to prime cell-specific enhancers that establish cellular identity. By generating open regions of chromatin, these factors also facilitate binding of signal-dependent transcription factors (SDTF) including the NFκB subunit p65. Here we present evidence that, in human aortic endothelial cells

(HAEC), members of the AP-1, and ETS transcription factor families prime enhancers that establish endothelial cell identity and enable endothelial cell-specific responses to the pro-inflammatory cytokine TNFα.

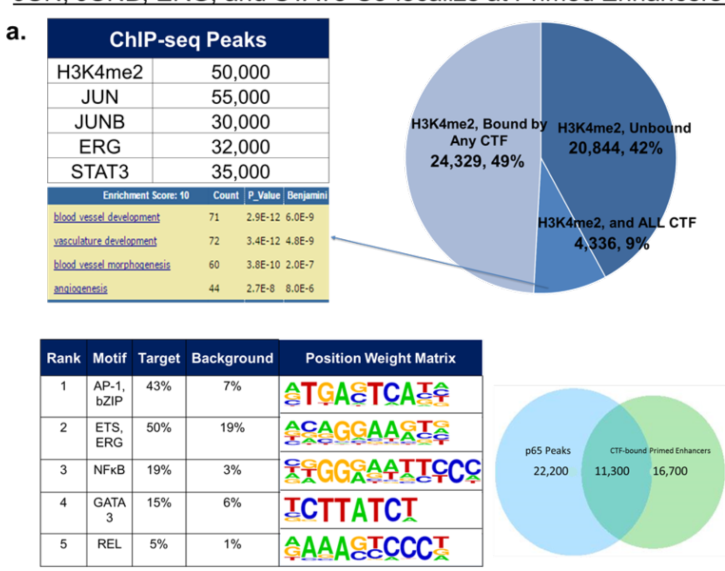
Methods:

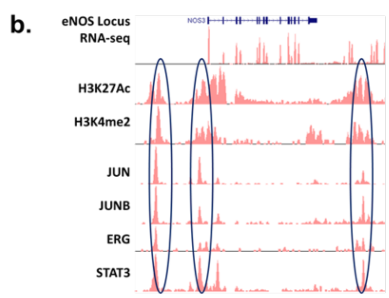
Working in HAEC treated with and without 2 ng/mL TNFα, we measured primed and active enhancers using ChIP-seq for the epigenetic histone modifications H3K4me2 and H3K27Ac, respectively. We employed de novo motif analysis to infer combinations of transcription factors required for enhancer priming and activation and performed ChIP-seq for these candidates. Knockdowns of JUN, ERG, and STAT3 followed by RNA-seq were used to evaluate altered enhancer function and corresponding gene targets.

Results:

De novo motif analysis revealed that motifs for ETS and AP-1 transcription factors are highly enriched at HAEC enhancers, basally and after TNFα treatment. ChIP-seq for JUN, JUNB, ERG, and STAT3 identified 25,000-55,000 intergenic peaks associated with each transcription factor. These peaks bind 50% of poised enhancers, with a subset co-localizing at these sites. Gene ontology analysis showed that gene targets of these enhancers are involved in endothelial-specific functions. Additionally, over 11,000 TNFα-induced p65 binding sites occur at these enhancers. These findings are summarized in the following figure. Further, knockdown of JUN, ERG, and STAT3 resulted in a twofold or greater change in expression of hundreds of HAEC transcripts.

<u>JUN, JUNB, ERG, and STAT3 Co-localize at Primed Enhancers and Enhancers Targets of NFκB Subunit p65</u>





<u>JUN, JUNB, ERG, and STAT3 Co-localize at Primed Enhancers and Enhancers Targets of NFκB Subunit p65.</u> **a**. Candidate CTF bind the majority of primed HAEC enhancers. Gene ontology analysis shows genes near sites of co-localization are enriched for endothelial-specific functions. **b.** Candidate CTF co-localize at the eNOS locus. Loci exhibiting similar patterns include vWF, PECAM-1, and VE-Cadherin. **c.** *De novo* motif analysis showing enrichment for AP-1 and ETS motifs at TNFα-induced p65 binding sites. CTF-bound primed enhancers account for many p65 binding sites.

Conclusion:

The genome-wide pattern of JUN, JUNB, ERG, and STAT3 co-localization at poised enhancers and at enhancer targets of TNFα-induced p65 suggests that these factors collaboratively modulate endothelial-specific gene expression and prime inflammatory transcriptional programs in HAEC.

These transcription factors and the regulatory loci they bind may prove important targets for further study of vascular biology, and diseases such as atherosclerosis.

References:

1. The Wellcome Trust Case Control Consortium. Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls. *Nature* 447, 661-678 (2007).
2. Erdmann, J. *et al.* Genome-wide association study identifies a new locus for coronary artery disease on chromosome 10p11.23. *European heart journal* **32**, 158-168, doi:10.1093/eurheartj/ehq405 (2011).
3. Reilly, M. P. *et al.* Identification of ADAMTS7 as a novel locus for coronary atherosclerosis and association of ABO with myocardial infarction in the presence of coronary atherosclerosis: two genome-wide association studies. *Lancet* **377**, 383-392, doi:10.1016/S0140-6736(10)61996-4 (2011).
4. Schunkert, H. *et al.* Large-scale association analysis identifies 13 new susceptibility loci for coronary artery disease. *Nat Genet* **43**, 333-338, doi:10.1038/ng.784 (2011).
5. Hindorff, L. A. *et al.* Potential etiologic and functional implications of genome-wide association loci for human diseases and traits. *Proc Natl Acad Sci U S A* 106, 9362-9367, doi:10.1073/pnas.0903103106 (2009).
6. Shlyueva, D. et al. Transcriptional enhancers: from properties to genome-wide predictions. *Nature Rev Genet* **15,** 272-284 (2014).
7. Heinz, S. et al. Simple Combinations of Lineage-Determining Transcription Factors Prime cis-Regulatory Elements Required for Macrophage and B Cell Identities. Mol Cell **4,** 576-589 (2010).
8. Heinz, S. *et al.* Effect of natural genetic variation on enhancer selection and function. *Nature*, doi:10.1038/nature12615 (2013).
9. Glass, C. K. & Witztum, J. L. Atherosclerosis. the road ahead. *Cell* **104**, 503-516 (2001).
10. Lusis, A. J. Atherosclerosis. *Nature* **407**, 233-241 (2000).

Victor Kucherov

Preceptor:
Guan Wu, M.D., Ph.D.
Institution: URMC
Department of Urology

Characterization of kidney cancer exosomes

Introduction: Renal cell carcinoma (RCC) is the most lethal genitourinary cancer and the sixth most common cause of cancer-related death in the United States. Investigation into RCC biomarkers has the potential to reveal important prognostic indicators that may inform therapeutic options and be used to monitor disease course. Exosomes, which are 50 – 200 nm particles produced by cells and released into the extracellular space, are a potential source of such biomarkers and have been studied for their role in cancer biology, particularly in promoting tumor invasion and metastasis. Exosomes carry information specific for their host cells and are readily found in blood and urine.

Objective: To develop a cell-line model for RCC that could be used to study RCC exosomes. Exosomes would be collected from this cell-line model and characterized by their morphology and protein content. Any proteins that might serve as potential RCC biomarkers would be identified for further study.

Background: In multiple cancer types exosomes have been demonstrated to promote tumor invasion and metastasis resulting in more aggressive cancer phenotype. Additionally, exosomes contain protein elements potentially unique to their cells of origin making them suitable targets for biomarker research.

Methods: Four RCC cell lines (786-O, ACHN, A498, and A704) were cultured and exosomes were harvested from each cell culture supernatant. Exosomes for each line were isolated and concentrated through serial ultracentrifugation and density sorting by ultracentrifugation over discontinuous sucrose gradient. Density fractions from the sucrose gradient were analyzed by western blotting to identify the presence of exosome-associated protein markers (e.g. ALIX, CD63). Exosome-marker enriched fractions were further analyzed by transmission electron micrography (TEM) to characterize exosome morphology and by nanoparticle tracking analysis to characterize exosome size. Exosomal protein discovery was undertaken through tandem mass tag mass spectrometry (TMT-MS).

Results: Three of the four RCC cell lines (7860-O, ACHN, and A498) produced exosomes in sufficient quantity to analyze. Western blotting for typical exosome-associated protein markers revealed enrichment of Alix, CD63, syntenin-1, and CD9. These markers were enriched in the density range 1.08 – 1.12 g/cm^3, consistent with the density of exosomes reported in the literature. Analysis with TEM revealed particle morphology consistent with exosomes. Nanoparticle tracking analysis identified average particle sizes between 65 – 93 nm in diameter. TMT-MS of exosomal protein derived from ACHN and A498 cells revealed several proteins enriched in exosome fractions compared to non-exosome fractions and each respective cell lysate. These proteins include galectin-3 binding protein (GAL3BP), alpha-2 macroglobulin (A2M), and ferritin light chain (FTL),

Conclusion: Particles consistent with the morphology, density, and protein markers of exosomes were isolated from the cell culture supernatant of three RCC cell lines (786-O, ACHN, and A498). Protein analysis by TMT-MS found several proteins in ACHN and A498 exosomes that warrant further study including GAL3BP, A2M, and FLT. Further work includes confirming these proteins via western blot. The next step of the project would be to repeat these experiments with fresh cell cultures to confirm the results.

References:

1. Théry C, Amigorena S, Raposo G, et al. Isolation and characterization of exosomes from cell culture supernatants and biological fluids. Curr Protoc Cell Biol. 2006 Apr;Chapter 3:Unit 3.22.
2. Chen CY, Hogan MC, Ward CJ. Purification of exosome-like vesicles from urine. Methods Enzymol. 2013;524:225-41.
3. Vlassov AV, Magdaleno S, Setterquist R, et al. Exosomes: current knowledge of their composition, biological functions, and diagnostic and therapeutic potentials. Biochim Biophys Acta. 2012 Jul;1820(7):940-8.
4. Yang C, Robbins PD. The roles of tumor-derived exosomes in cancer pathogenesis. Clin Dev Immunol. 2011;2011:842849.
5. Wang D, Sun W. Urinary extracellular microvesicles: isolation methods and prospects for urinary proteome. Proteomics. 2014 Aug;14(16):1922-32.
6. Lötvall J, Hill AF, Hochberg F, et al. Minimal experimental requirements for definition of extracellular vesicles and their functions: a position statement from the International Society for Extracellular Vesicles. J Extracell Vesicles. 2014 Dec 22;3:26913.
7. Baietti MF, Zhang Z, Mortier E, et al. Syndecan-syntenin-ALIX regulates the biogenesis of exosomes. Nat Cell Biol. 2012 Jun 3;14(7):677-85.
8. Raimondo F, Morosi L, Corbetta S, et al. Differential protein profiling of renal cell carcinoma urinary exosomes. Mol Biosyst. 2013 Jun;9(6):1220-33.
9. Cvjetkovic A, Lötvall J, Lässer C. The influence of rotor type and centrifugation time on the yield and purity of extracellular vesicles. J Extracell Vesicles. 2014 Mar 25;3.
10. Beckham CJ, Olsen J, Yin PN, et al. Bladder cancer exosomes contain EDIL-3/Del1 and facilitate cancer progression. J Urol. 2014 Aug;192(2):583-92.

Nancy T-M Kung

Preceptor:
Dr. Babak S. Jahromi
URMC
Department of Neurosurgery

Cerebrovascular hemodynamics measured using near-infrared spectroscopy during carotid endarterectomy: A prospective study

Introduction: Near-Infrared Spectroscopy (NIRS) is a non-invasive optical technique for monitoring cerebral blood flow (CBF). While NIRS has been used extensively in functional studies in the pediatric population, it has rarely been used to monitor CBF during neurovascular procedures.

Objective: To prospectively investigate cerebral hemodynamics using NIRS in patients undergoing carotid endarterectomy (CEA).

Background: The carotid endarterectomy (CEA) was chosen as an ideal procedure to study cerebral hemodynamics as it involves temporary clamping of the internal carotid artery (ICA) and thus its blood supply to the ipsilateral hemisphere during the procedure. Adequate perfusion to the operative hemisphere is then achieved from flow across the Circle of Willis, or augmented with shunts used selectively (using neuromonitoring criteria) or routinely.

Methods: Cerebral hemodynamics was measured using NIRS in 45 patients. Patients were separated into three cohorts depending on shunt use: not shunted, selectively shunted (by neuromonitoring criteria), and routinely shunted. Data were analyzed using custom MatLab algorithms.

Results: ICA occlusion resulted in a transient drop in oxygenated hemoglobin and a concomitant rise in deoxygenated hemoglobin in the operative hemisphere in non-shunted patients. Oxygenated hemoglobin levels recovered in the minutes following ICA occlusion, while the increase in deoxygenated hemoglobin levels persisted for the duration of occlusion. These changes were reversed following flow restoration. Routine shunt placement during ICA occlusion did little to rescue oxygenated hemoglobin levels in the operative hemisphere and did not reduce deoxygenated hemoglobin levels. In one patient, who required selective shunting, a more pronounced deviation in oxygenated and deoxygenated hemoglobin concentrations was observed 8 minutes after ICA occlusion - shunt placement in this patient gradually reversed neuromonitoring changes but NIRS showed only partial restoration of CBF. No adverse events were noted due to use of NIRS during the study period.

Conclusion: Use of NIRS during CEA is safe and feasible, with preliminary data suggesting early detection of physiologically relevant changes in cerebral blood flow during ICA occlusion. Further studies and correlation with operative events and clinical outcomes are warranted.

References:

1. Villringer, Arno, et al. "Near infrared spectroscopy (NIRS): a new tool to study hemodynamic changes during activation of brain function in human adults." *Neuroscience letters* 154.1 (1993): 101-104.
2. Cope, M., and David T. Delpy. "System for long-term measurement of cerebral blood and tissue oxygenation on newborn infants by near infra-red transillumination." *Medical and Biological Engineering and Computing* 26.3 (1988): 289-294.
3. Kim, Meeri N., et al. "Noninvasive measurement of cerebral blood flow and blood oxygenation using near-infrared and diffuse correlation spectroscopies in critically braininjured adults." *Neurocritical care* 12.2 (2010): 173-180.
4. Chongruksut W, Vaniyapong T, Rerkasem K. **"**Routine or selective carotid artery shunting for carotid endarterectomy (and different methods of monitoring in selective shunting)." Cochrane Database Syst Rev. 2014;6:CD000190. PubMed PMID: 24956204.
5. Radak D, Sotirovic V, Obradovic M, Isenovic ER. **"**Practical use of near-infrared spectroscopy in carotid surgery." Angiology. 2014 Oct;65(9):769-72. PubMed PMID: 24176911.

Year-Out Research

Caitlin Orner

Preceptors:
Regis O'Keefe M.D., Ph.D.
Alayna Loiselle, Ph.D.
University of Rochester
Center for Musculoskeletal Research

Low-dose and short-duration Matrix Metalloproteinase 9 inhibition does not affect adhesion formation during murine flexor tendon healing

Introduction: After flexor tendon injury and repair, adhesion formation is a substantial concern as it can result in loss of motion and functional disability. There is a need for pharmacological interventions to reduce scar formation during flexor tendon healing.[1, 2]

Objective: The purpose of this study was to investigate whether systemic administration of Ro 32-3555, an Mmp9 inhibitor, can improve murine flexor tendon healing by limiting adhesion formation or enhancing remodeling of scar tissue following tendon injury and repair

Background: Mmp9 is a gelatinase that contributes to degradation of extracellular matrix and is expressed during flexor tendon healing.[3, 4] Our lab has previously shown that *Mmp9*$^{-/-}$ (genetic knockout) mice have accelerated remodeling of adhesions during flexor tendon healing, relative to wild type mice.[5] Therefore, modulation of Mmp-9 activity is a potential therapeutic target. Ro 32-3555 is a competitive gelatinase inhibitor that binds to Mmp9 in place of the substrate, collagen. It has been used in animal studies as a potential treatment for osteoarthritis, rheumatoid arthritis, and meningitis.[6-8] This study was designed to investigate whether pharmacological inhibition of Mmp9 with Ro 32-3555 during healing improves tendon gliding, reduces adhesion formation, or enhances scar tissue remodeling. The effect on tendon biomechanical properties was also evaluated, since repair strength should ideally not be compromised in a healing tendon.

Methods: Flexor digitorum longus laceration and repair was performed in female C57BL/6J mice. Mice were treated with vehicle or the Mmp9 inhibitor Ro 32-3555 for 8 days via intraperitoneal injection. Analysis was performed for digit range of motion and gliding function, biomechanics including stiffness and maximum load at failure, gene expression, and Mmp9 activity.

Results: An Mmp9 activity assay as well as zymography confirmed suppression of Mmp9 activity in mice treated with Ro 32-3555. There was no significant difference in tendon gliding or range of motion between vehicle and Ro 32-3555 treated mice. There was also no difference in tendon biomechanical properties (stiffness and maximum load at failure) between the two groups

Conclusion: Local inhibition of Mmp9 gelatinolytic activity at the flexor tendon repair site is insufficient to alter adhesion formation, remodeling of adhesions, and mechanical properties of healing murine flexor tendons.

References:

1. James, R., et al., *Tendon: biology, biomechanics, repair, growth factors, and evolving treatment options.* J Hand Surg Am, 2008. **33**(1): p. 102-12.
2. Beredjiklian, P.K., *Biologic aspects of flexor tendon laceration and repair.* J Bone Joint Surg Am, 2003. **85-a**(3): p. 539-50.
3. Visse, R. and H. Nagase, *Matrix metalloproteinases and tissue inhibitors of metalloproteinases: structure, function, and biochemistry.* Circ Res, 2003. **92**(8): p. 82739.
4. Loiselle, A.E., et al., *Remodeling of murine intrasynovial tendon adhesions following injury: MMP and neotendon gene expression.* J Orthop Res, 2009. **27**(6): p. 833-40.
5. Loiselle, A.E., et al., *Bone marrow-derived matrix metalloproteinase-9 is associated with fibrous adhesion formation after murine flexor tendon injury.* PLoS One, 2012. **7**(7): p. e40602.
6. Lewis, E.J., et al., *Ro 32-3555, an orally active collagenase inhibitor, prevents cartilage breakdown in vitro and in vivo.* Br J Pharmacol, 1997. **121**(3): p. 540-6.
7. Brewster, M., et al., *Ro 32-3555, an orally active collagenase selective inhibitor, prevents structural damage in the STR/ORT mouse model of osteoarthritis.* Arthritis Rheum, 1998. **41**(9): p. 1639-44.
8. Liechti, F.D., et al., *Matrix metalloproteinase inhibition lowers mortality and brain injury in experimental pneumococcal meningitis.* Infect Immun, 2014. **82**(4): p. 1710-8.

Year-Out Research

Student Name: Kyle E. Rodenbach

Preceptor:
George J. Schwartz, MD
Renal Reserve: Development of a Kidney Stress Test
University of Rochester Medical Center
Department of Pediatrics

Renal Reserve: Development of a Kidney Stress Test

Introduction: Protein loading is an effective, non-invasive method for assessing renal reserve (RR, difference between stimulated and baseline glomerular filtration rate) and is conceptually similar to other stress testing modalities including cardiac stress testing and glucose tolerance testing. Lack of RR in the setting of a normal GFR suggests glomerular hyper-filtration exists at baseline. Normal values for creatinine and BUN are maintained by hyper-filtration despite the loss of functional renal mass in this pre-clinical state [1]. Over time, hyper-filtration likely causes progressive decline in renal function, as in diabetic nephropathy [2].

Objective: The purpose of this study was to compare a meat versus liquid protein load in a cystatin-C-based (Cys-C) RR test using cimetidine-inhibited creatinine clearance (Cr Cl) and iohexol infusion clearance (Io Cl) for validation.

Background: Cystatin C-estimated RR was previously developed in a population of healthy, young adults [3]. Individuals consumed a beef burger containing 60 grams of protein following a baseline blood draw for serum Cystatin C (Cys-C). A second Cys-C sample was obtained 125141 minutes after the protein load. Subjects showed a mean increase in Cys-C estimated GFR (eGFR) of 12.0 +/- 5.2 (P=0.0003) following the protein load, which represented 12.2% of the mean baseline eGFR (98.1 +/- 9.1 mL/min/1.73m2).

Methods: Participants (N=18) were screened for health status, blood pressure, and proteinuria. They followed a low protein diet and took cimetidine (20 mg/kg) for two days prior to the study. Water loading was used to maintain urine flow, and two hours were allotted for iohexol steady state equilibration. Participants 1-10 received a hamburger (1 g/kg protein); 11-15 received a ProCel® shake (1 g/kg protein); and 16-18 received a high dose ProCel® shake (1.5 g/kg protein). Data were analyzed for significance of RR. Cystatin-C estimated GFR (Cys-C eGFR) was calculated using the CKD-EPI Cys-C formula following IFCC calibration using ERMDA471/IFCC.

Results: Participants (N=18) had a mean (SD) age of 22 (2) years and were 39% male and 72% white. Baseline GFR (SD) in mL/min/1.73m^2 averaged 103.4 (14.7) for Cr Cl; 108.9 (9.0) for Io Cl (N=8); and 117.4 (6.1) for Cys-C eGFR. For the hamburger group (N=10), mean RR (SD) in mL/min/1.73m^2 was 17.1 (11.6) for Cr Cl (P=0.001); 8.4 (4.3) for Io Cl (P<0.001); and 4.7 (2.4) for

Cys-C eGFR (P<0.001). For 1.0-1.5 g/kg shakes (N=8), mean RR (SD) in mL/min/1.73m^2 was 15.8 (5.8) for Cr Cl (P<0.001), 11.7 (9.0) for Io Cl (P=0.008), and 2.4 (2.9) for Cys-C eGFR (P=0.05). The hamburger and shake groups did not differ significantly in RR determined by Cr Cl, Io Cl, or Cys-C but Cys-C-based RR was significantly less than Io-based RR for both groups. There were no differences in post-load versus pre-load Cr/Io clearance ratios.

Conclusion: Cys-C-based RR following a hamburger provides a simple stress test of kidney function which was validated by classical renal clearances and can be applied to those who recover from acute kidney injury. Why Cys-C-based RR was smaller than Io RR, the reference standard, is a topic for future investigation. This might be due, in part, to the dilutional effect of water loading on biomarker estimates of GFR.

References:

1. Thomas DM, Coles GA, Williams JD. What does the renal reserve mean? Kidney Int. 1994;45:411-16.
2. Ruggenenti P, Porrini EL, Gaspari F, et al. Glomerular hyperfiltration and renal disease progression in type 2 diabetes. Diabetes Care. 2012 Oct;35(10):2061-8.
3. Fuhrman DY, Maier PS, Schwartz GJ. Rapid assessment of renal reserve in young adults by cystatin C. Scandinavian journal of clinical and laboratory investigation. 2013:10.3109/00365513.2013.765964. doi:10.3109/00365513.2013.765964

Rachel Rodenbach

Preceptor:
Ronald Epstein MD
Center for Communication and Disparities Research, University of Rochester
School of Medicine and Dentistry
Department of Family Medicine

Relationships Between Oncology Clinicians' Personal Attitudes About Death and Communication with Terminally Ill Patients

Introduction/Background: There are many barriers to delivering clear communication at the end of life, which leads to missed opportunities for patients to prepare for death, make informed decisions, and avoid aggressive medical care near death. Despite suggestions that clinicians' attitudes about death affect the care they provide to dying patients, this phenomenon has not been well studied.

Objective: To explore oncology clinicians' attitudes and emotions surrounding their own death and how these attitudes both affect and are affected by their care of dying patients and their communication with them.

Methods: Semi-structured personal interviews were conducted with physicians (n=25), nurse practitioners (n=7), and physician assistants (n=1) in medical or hematologic oncology clinical practices in the Rochester, New York, area. Audio-recordings were transcribed and qualitatively analyzed to examine clinicians' communication styles, attitudes toward their own mortality, and reflections on how caring for dying patients affects their personal perspective about death and vice versa.

Results: Clinicians described three communication styles with patients about death and dying: direct, indirect, or selectively direct. Most expressed a conditional acceptance of their mortality, realizing that they could not fully know how they would respond if actually terminally ill. For many, caring for dying patients affected their outlook on life and death, and their own perspectives on life and death affected their approach to caring for dying patients. No general pattern was observed between clinicians' self-reported communication styles and acceptance of their own death.

Conclusion: An awareness of personal mortality may help clinicians to discuss death more openly with patients. Efforts to promote both self-awareness and communication training are key to facilitating clear communication with and compassionate care of terminally ill patients.

References:

1. Wenrich MD, Curtis JR, Shannon SE, Carline JD, Ambrozy DM, Ramsey PG. Communicating with dying patients within the spectrum of medical care from terminal diagnosis to death. *Arch Intern Med*. 2001;161(6):868-874.

2. Fallowfield LJ, Jenkins VA, Beveridge HA. Truth may hurt but deceit hurts more: Communication in palliative care. *Palliat Med*. 2002;16(4):297-303.
3. 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(14):1665-1673.
4. Quill TE. Initiating end-of-life discussions with seriously ill patients: Addressing the elephant in the room. *JAMA*. 2000;284(19):2502-2507.
5. Baile WF, Lenzi R, Parker PA, Buckman R, Cohen L. Oncologists' attitudes toward and practices in giving bad news: An exploratory study. *J Clin Oncol*. 2002;20(8):2189-2196.
6. Rodriguez KL, Gambino FJ, Butow P, Hagerty R, Arnold RM. Pushing up daisies: Implicit and explicit language in oncologist–patient communication about death. *Supportive care in cancer*. 2007;15(2):153-161.
7. The AM, Hak T, Koeter G, van Der Wal G. Collusion in doctor-patient communication about imminent death: An ethnographic study. *BMJ*. 2000;321(7273):1376-1381.
8. Mack JW, Cronin A, Taback N, et al. End-of-life care discussions among patients with advanced CancerA cohort study. *Ann Intern Med*. 2012;156(3):204-210.
9. Granek L, Krzyzanowska MK, Tozer R, Mazzotta P. Oncologists' strategies and barriers to effective communication about the end of life. *J Oncol Pract*. 2013;9(4):e129-35.
10. Russell BJ, Ward AM. Deciding what information is necessary: Do patients with advanced cancer want to know all the details? *Cancer Manag Res*. 2011;3:191-199.
11. Friedrichsen M, Milberg A. Concerns about losing control when breaking bad news to terminally ill patients with cancer: Physicians' perspective. *J Palliat Med*. 2006;9(3):673-682. 12. Broom A, Kirby E, Good P, Wootton J, Adams J. The troubles of telling: Managing communication about the end of life. *Qual Health Res*. 2014;24(2):151-162.
13. Clayton JM, Butow PN, Arnold RM, Tattersall MH. Fostering coping and nurturing hope when discussing the future with terminally ill cancer patients and their caregivers. *Cancer*. 2005;103(9):1965-1975.
14. Elit L, Charles C, Gafni A, Ranford J, Gold ST, Gold I. Walking a tightrope: Oncologists' perspective on providing information to women with recurrent ovarian cancer (ROC) during the medical encounter. *Supportive Care in Cancer*. 2012;20(10):2327-2333.
15. Christakis NA, Lamont EB. Extent and determinants of error in doctors' prognoses in terminally ill patients: Prospective cohort study. *BMJ*. 2000;320(7233):469-472.
16. Mackillop WJ, Stewart WE, Ginsburg AD, Stewart SS. Cancer patients' perceptions of their disease and its treatment. *Br J Cancer*. 1988;58(3):355-358.
17. Quirt C, Mackillop W, Ginsburg A, et al. Do doctors know when their patients don't?: A survey of doctor–patient communication in lung cancer. *Lung Cancer*. 1997;18(1):1-20.
18. Butow PN, Kazemi JN, Beeney LJ, Griffin A, Dunn SM, Tattersall MH. When the diagnosis is cancer: Patient communication experiences and preferences. *Cancer*. 1996;77(12):2630-2637.
19. Jenkins V, Solis-Trapala I, Langridge C, Catt S, Talbot DC, Fallowfield LJ. What oncologists believe they said and what patients believe they heard: An analysis of phase I trial discussions. *J Clin Oncol*. 2011;29(1):61-68.
20. McCue JD. The naturalness of dying. *JAMA*. 1995;273(13):1039-1043.
21. Baider L, Wein S. Reality and fugues in physicians facing death: Confrontation, coping, and adaptation at the bedside. *Crit Rev Oncol*. 2001;40(2):97-103.
22. Miller WL, Crabtree BF. The dance of interpretation, in: Crabree BF, Miller WL, (Eds.), Doing qualitative research, second ed., Sage Publications, Thousand Oaks, 1999, pps. 127-143 23. Ernest Becker. The Denial of Death, The Free Press, New York, 1973.

Serena Shung, CC4

Preceptors:
Douglas L. Stockman, M.D
Clinical Associate Professor, Department of Family Medicine
University of Rochester

Jennifer K. Carroll, M.D., M.P.H
Network Director
American Academy of Family Physicians

Elvin D. Suero Jorge, M.D.
Medico Nutricional
Hospital Municipal de Altamira

Intervention on diet and physical activity: An effort to prevent and control noncommunicable diseases in rural Dominican Republic

Introduction: Non-communicable diseases (NCDs), including cardiovascular diseases, cancers, chronic respiratory diseases and diabetes, are the leading cause of mortality worldwide.[1,2] NCDs disproportionately affect the poor, and 80% of deaths attributable to NCDs occur in low-and middle-income countries (LMICs).[1,2] The Dominican Republic (DR), for example, is a middle-income country in which NCDs are the number one cause of mortality and account for 68% of all deaths,[3] and in which the poorest quintile of the population have the worst access to healthcare,[4] an integral part of NCD management. Los Claveles and La Jagua are two poor rural communities in the DR where high rates of NCDs have been both self-reported and observed.[5]

Tobacco use, unhealthy diets, physical inactivity and harmful alcohol use are four modifiable risk factors for NCDs.[1] The World Health Organization (WHO) estimates that elimination of these risk factors would prevent 80% of deaths due to cardiovascular disease, stroke and diabetes.[2] A community education intervention called *Pasos Adelante* addresses these risk factors and was able to significantly reduce unhealthy dietary habits and physical inactivity in several low-literacy Spanish-speaking communities in the US[6,7] and in Mexico,[8] with evidence for long-term sustainability in behavior change.[8,9]

Objective: To adapt, implement and evaluate the *Pasos Adelante* intervention in the Dominican communities of Los Claveles and La Jagua, in an effort to decrease risk factors for NCDs.

Methods: Program implementation: The Pasos Adelante intervention is a 12-week educational course delivered by health promoters to their own communities, paired with a weekly walking club. The co-principle investigator worked closely with community leaders to adapt the intervention to the local context, and to identify and train three health promoters in Los Claveles and La Jagua. Participants were recruited door-to-door in Los Claveles, and during social gatherings in La Jagua. The *Pasos Adelante* program was implemented once in each community.

<u>Program Evaluation</u>: Outcome measures included knowledge, dietary habits, and physical activity assessed via health questionnaires, and physiological data. All measures were assessed pre- and post- intervention. Qualitative interviews were also conducted post-intervention. Due to the small number of intervention completers, analyses include simple comparison of paired pre- and post-intervention values, and examination of qualitative data.

Results: A total of 40 participants were recruited, and 7 participants completed the program. All 7 completers were from La Jagua. The intervention was terminated in Los Claveles due to lack of interest and local support.

<u>Demographics</u>: The average age of participants recruited was 56.4 years old, and the majority were married (67.4%), unemployed (70.2%), and had not graduated from high school (81.0%). More than half of participants recruited reported being diagnosed with hypertension (53.1%), almost half with hyperlipidemia (48%), and one fifth with diabetes (20.0%). Compared with non-completers, completers from the Jagua community were older (mean age 64.7), significantly more likely to be single (57.1%) and insured (100%), and had higher rates of diagnosed hypertension (71.4%), hyperlipidemia (71.4) and diabetes (42.9%).

<u>Outcomes</u>: *Knowledge*: The 7 completers scored an average of 68.4% higher in every knowledge category of the questionnaire and stated 15.7% fewer misconceptions. *Dietary habits*: Completers reported a significant increase in weekly intake of fruits and vegetables by 56.7% and 115.6% respectively, and a significant reduction of intake of sugary beverages by 51.2%. *Physical activity*: On average completers report 51 minutes more of walking per week, but a reduction of 990 minutes less participation per week in other forms of moderate level physical activity, most notably in farming. *Physiological measures*: Outcomes were unchanged except a mean drop of 14.9% in LDL levels and reduction of 17.3% in triglyceride levels. *Qualitative interviews*: 5 out of 6 completers reported changes in eating habits and 6 out of 6 completers reported a significant increase in participation in physical activities. Many spontaneously described that their bodies felt healthier and "more able" after making these changes.

Conclusion: The most glaring observation from this study is the low completion rate by participants (17.5% of participants recruited). This can mostly be accounted for by the 0% completion rate in Los Claveles, one of the poorest communities in the area and one that lacked central leadership, did not actively pursue community improvement, and from which most individuals were not held accountable to participate in any type of scheduled event. Although La Jagua program completers had comparable unemployment rates and low education levels, they belonged to a community that had an active leadership that frequently held meetings and scheduled community improvement projects. They also lived in closer proximity to the local hospital and were significantly more likely to be insured and connected to primary care providers. This probably led to better health awareness and explains the higher rates of diagnoses related to NCDs, which may have been a major source of motivation for health improvement. Notably, program implementation was limited by having only one research personnel and limited funding, which affected access to transportation, quality of project resources used, and reliability of laboratory testing. These factors probably also contributed to the high drop-out rate.

There was an evident increase in knowledge regarding NCDs (mean increase of 68.4% correct responses per knowledge category). The dramatic self-reported improvement in dietary habits may be more a reflection of the increase in knowledge and awareness rather than an accurate assessment of behavior change. During the questionnaires, it was observed that the idea of calculating number of servings consumed per week per food type was a very foreign and difficult concept for the participants.

The program completers reported a small increase of 51 minutes of walking per week, and were observed to be walking more often. They also reported an average of 990 minutes reduction of other moderate physical activity. This probably demonstrates the seasonal halt in farming activities during the time post-intervention data was taken.

Physiological measures were likely inaccurate. The partner hospital that provided laboratory equipment for these measures had unreliable availability and equipment failures. Transportation to this facility was unpredictable and led to poor testing compliance. Participants may or may not have truly fasted. There is a question of whether certain participants' cholesterol results were mixed with those of other patients of the hospital.

Overall this project increased local knowledge about NCDs, and may or may not have achieved its goals to improve health behaviors related to NCD prevention. However, it noticeably increased health awareness in both Los Claveles and La Jagua. Qualitative interviews reveal behavior changes in cooking methods, food choices, and increased voluntary physical activity. Participants from both sites report feeling healthier after making these changes. Anecdotally, the exposure to the hospital led many previously non-insured participants to pursue health insurance and access professional healthcare more regularly. This increased health awareness, although not the primary objective of this project, may have been a necessary first step to health improvement. Future implementation of this intervention would benefit from having a larger team of research personnel with better quality project resources and on-site laboratory testing.

References:

1. Alwan A et al. Global status report on noncommunicable diseases 2010. World Health Organization 2011. www.who.int/publications/ncd_report2010/en
2. 2008-1013 action plan for the global strategy for the prevention and control of noncommunicable diseases: prevent and control cardiovascular diseases, cancers, chronic respiratory diseases and diabetes. World Health Organization 2008. http://whqlibdoc.who.int/publications/2009/9789241597418_eng.pdf

3. Noncommunicable diseases country profiles 2011: Dominican Republic. Noncommunicable Diseases and Mental Health, World Health Organization 2010. http://www.who.int/nmh/countries/dom_en.pdf
4. Report of Dominican Republic. World Health Surveys, World Health Organization. 2003. http://www.who.int/healthinfo/survey/whsdom-dominicanrepublic.pdf
5. Shung SY. Perceptions of a Healthcare Facility and Barriers-to-Care in Rural Dominican Republic. 2012 Abstract Journal: International Medicine research.
6. Staten LK, Scheu LL, Bronson D et al. Pasos Adelante: the effectiveness of a community-based chronic disease prevention program. Prev Chronic Dis 2005; 2(1):A18.
7. Staten LK, Cutshaw CA, Davidson C et al. Effectiveness of the Pasos Adelante chronic disease prevention and control program in a US-Mexico border community, 2005-2008. Prev Chronic Dis 2012;9:E08.
8. Denman CA, Rosales C, Cornejo E et al. Evaluation of the community-based chronic disease prevention program Meta Salud in Northern Mexico, 2011-2012. Prev Chronic Dis 2014; 11:140218.
9. Carvajal SC, Miesfeld N, Chang J et al. Evidence for long-term impact of Pasos Adelante: using a community-wide survey to evaluate chronic disease risk modification in prior program participants. Int J Environ Res Public Health 2013; 10(10):4701-17.