PATIENT-CENTERED CARE: STUDENT PERSPECTIVES ON THE BENEFITS AND CHALLENGES

Victoria L. Boggiano, Yufan Wu, and Erika Schillinger, MD. Stanford Family Medicine Group

In light of the increasing emphasis on incorporation of patient-centered care techniques into health care services, we sought to explore the greatest impediments to and benefits from student engagement in patient-centered care. A secondary aim of this research was to explore possible improvements in the way patient-centered care is taught to medical students. Third-year medical students on family medicine rotations at Stanford School of Medicine were provided the following open-ended prompt: *"Describe a patient-centered care challenge or surprise in the family medicine core clerkship."* 326 free responses were collected. Transcripts were inductively coded by a primary researcher and reviewed by two secondary researchers. Coding discrepancies were resolved through a multi-step adjudication and consensus process. The primary researcher reviewed coded transcripts to identify preliminary themes. The entire research team worked collaboratively to iteratively refine representative themes until consensus was achieved.

Four primary aspects of patient-centered care were mentioned by medical students. First, several students discussed the meaning of patient-centered care and its impact on patient health and adherence. One student, for example, wrote that "letting patients take control and guide their own action plans gets them motivated and excited in a way that having a physician tell them exactly what to do doesn't have that effect." Second, students frequently discussed the relationship between doctor and patient in the patient-centered care model. Third, students discussed communication issues that impact patient-centered care, such as language or cultural barriers that impact engagement with patients. Finally, students discussed how the patient's psychosocial context affects patient-centered care.

Our study suggests that students find the patient-centered care model for healthcare delivery to be challenging but worthwhile. Our results demonstrate a need for improved medical education about patient-centered care that will better enable students to implement the model in a variety of psychosocial and medical contexts.

AN ASSESSMENT OF ESSENTIAL CLINICAL KNOWLEDGE AND PROCEDURAL SKILLS OF PRACTICING INDIAN EMTS

Chattopadhyay, A., Coggins, N., Strehlow, R., Mantha, A., Youngblood, P., Pirrotta, E. Strehlow, M.C., Mahadevan, S.V. , Stanford University

To our knowledge, prior studies have not assessed the capacity of practicing EMTs in resource-poor countries to retain critical, life-saving knowledge and skills from their inaugural prehospital care training programs.

We assessed practicing EMTs' retention of essential clinical knowledge and vital procedural skills in three Indian states during Jul-Aug, 2013.

All study participants were practicing EMTs who had previously completed an adapted six-week EMT-basic training course. Each EMT was assigned a unique ID and completed a demographics survey. Theoretical knowledge was assessed through a 60-question multiple-choice exam testing fifteen essential subjects; the exam was validated prior to the study with US EMTs and Indian EMT instructors. Clinical acumen was assessed through an OSCE of nineteen vital skills. Five examiners observed the participants performing each OSCE skill and determined whether they passed/failed by utilizing a predetermined checklist.

255 practicing EMTs were assessed in Karnataka (n=87), Tamil Nadu (n=102), and Gujarat (n=65). Eighty-one percent were male, mean age was 26 years, and mean length of experience was 39 months (range 3-63). For the knowledge assessment, the mean written test score was 47.2% (range 28-70%). Participants were less knowledgeable about chest pain (27.2% correct) and delivery (30.6%) and more knowledgeable about abdominal/pelvic injury (77.9%). Of the fifteen clinical skills assessed, participants performed poorly on neurovascular assessment before/after splinting (pass rate 2.8%), log-rolling (5.2%), pelvic binding (6.7%), and bag-mask ventilation (6.7%), and performed better on suctioning (62.1%) and oxygen administration (79.4%).

This novel assessment of practicing Indian EMTs has identified critical gaps in their knowledge and skill retention, highlighting the need for a highly focused educational intervention.

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TARGETING KIT IN COLON CANCER

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Colon cancer is a leading cause of cancer deaths, and treatments for advanced disease are generally ineffective. Our lab has shown that human colon cancer is driven by self-renewing cancer stem cells (CSCs) that are marked by the surface protein CD44; thus, targeting these cells may be an alternative treatment strategy. To characterize the tumorigenic $CD44^+$ colon cancer cells, we found that Kit (CD117), a receptor tyrosine kinase (RTK) that promotes cellular proliferation, is expressed in a subset of $CD44^+$ cells. We hypothesize that Kit signaling promotes growth in colon cancer.

In immunohistochemical stains of 334 primary human colon tumors and xenografts, we report that 49.7% of the tumors stained positively for Kit. Notably, Kit is expressed in the $CD44^+$ CSC compartment, and in limiting dilution assays, we found that $CD44^+Kit^+$ cells were more tumorigenic than $CD44^+Kit^-$ cells. To investigate whether Kit signaling promotes proliferation in colon cancer cells, we knocked down Kit with lentivirus-mediated shRNA in several cell lines and xenografts. Kit knockdown cells exhibited decreased growth in vitro and formed smaller xenografts in vivo. Staining for markers of proliferation was decreased, while expression of pro-apoptotic proteins increased. As predicted, Kit^+ cells were inhibited in vitro by the small molecule Kit inhibitor ISCK03, and this inhibition was lost with Kit knockdown. Interestingly, we did not find oncogenic mutations in Kit in the Kit^+ tumors that we studied, but these tumors did express Kit ligand (Kitlg), suggesting that tumorigenic Kit^+ colon cells may receive Kit signaling in an autocrine manner. To test this, we generated Kitlg knockdowns and saw decreased proliferation in vitro with in vivo results pending.

Our work on elucidating the role of Kit in colon cancer may enable the use of presently available RTK-inhibitors, such as imatinib, in the treatment of these cancers.

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INTRA-ARTERIAL DELIVERY OF NEURAL PROGENITOR CELLS AT 3 DAYS AFTER STROKE RESULTS IN OPTIMAL ENGRAFTMENT

Raymond Choi, Josh Chua, Nancy Wang, Raphael Guzman

Intravascular transplantation of neural progenitor cells (NPCs) represents a minimally invasive therapeutic approach for the treatment of central nervous system (CNS) diseases. The timing of intravascular injection and its effect on cellular recruitment after stroke needs to be analyzed to ensure that the maximal number of cells reach the brain. Here we evaluated the absolute number of cell transmigration and the relative percentage of cells that remained in the brain at various time points.

$5x10^5$ NPCs labeled with a trifusion reporter gene were injected into the intracarotid artery at 6 hours, 24 hours, 3 days, 7 days and 14 days after inducing hypoxia ischemia in mice. *In vivo* BLI was used to non-
invasively assess NPC recruitment into the ischemic brain following intra-arterial delivery.

As early as 6 hours, BLI revealed that there was luciferase activity intracranially when animals were imaged immediately after injection. However this activity was low, and luciferase activity did not peak until NPCs were delivered 3 days after stroke. Luciferase activity with NPCs transplanted 7 days after stroke persisted at levels close to day 3. However, this effect dropped significantly when NPCs were transplanted 14 days after stroke.

These results demonstrate that 3 days may be the optimum time for NPC adherence along the vasculature in the ischemic brain following intra-arterial transplantation.

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TUMOR VACCINATION FOR FOLLICULAR LYMPHOMA

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The Levy group focuses on using the body's immune system to fight lymphoma. One method is to stimulate the immune system using a "tumor vaccine," in which a compound injected into the patient activates the patient's immune cells to attack the cancer. One tumor vaccine uses CpG, an oligonucleotide that activates Toll-like receptor 9 (TLR9) on immune cells. It has been previously shown in a phase I/II study that in situ vaccination with CpG results in systemic antilymphoma clinical responses (Brody et al, 2010). A current phase II clinical trial is investigating the use of higher dose CpG vaccination in follicular lymphoma patients. The purpose of this Med Scholars project was to measure patient outcomes via radiographic response and time to progression and next treatment, and to investigate whether patients had a higher incidence of subsequent autoimmune disease compared to other patients with follicular lymphoma.

(1) Radiographic response: Patients underwent a baseline full body CT scan before initiation of therapy, then had repeat scans every 3 months thereafter until disease progression was noted. Six index lesions per patient were followed and the Cheson criteria were used to evaluate radiographic response. Time to progression and next treatment were measured and compared between previously untreated and previously treated arms of the trial. The previously untreated arm was also compared to previously untreated patients subsequently treated with rituximab. Kaplan-Meier curves were generated and data compared using log-rank tests. Preliminary data suggest that a majority of patients have either regression of their tumor burden or maintenance of stable disease with CpG vaccination; however, most patients eventually progress. (2) Autoimmunity: The STRIDE database was used to collect records from CpG patients. These records were queried for autoimmune diagnoses and ICD-9 codes. True positives were defined as new autoimmune disease diagnosed after 1st CpG vaccination. The records of a matched cohort of follicular lymphoma patients not treated with any CpG vaccination was similarly queried; true positives were defined as new autoimmune disease diagnosed after diagnosis of follicular lymphoma. Fisher's exact test was used to determine significance. Preliminary data suggest no difference in development of autoimmune disease between patients treated or untreated with CpG vaccination.

Preliminary findings suggest that CpG vaccination appears to either induce tumor burden regression or maintain stable disease in a majority of patients; however, most patients go on to progress in their disease following several months. Interestingly, most of these patients have not yet gone on to require further treatment, suggesting that these progressions are the result of aggressive monitoring rather than significant clinical progression. We are continuing to track the patients who have not yet progressed. Regarding autoimmunity, CpG vaccinated patients do not appear at increased risk for autoimmunity. However, larger sample sizes and more detailed follow up are required for a definitive conclusion.

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DOES URINARY BPA CHANGE AFTER BARIATRIC SURGERY?

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One of the world's highest volume chemicals is bisphenol A (BPA), an organic compound with high solubility in fat. BPA levels have been correlated with generalized obesity, abdominal obesity, and insulin resistance in middle aged and elderly adults. No studies have yet examined whether a change in weight results in a change in BPA levels. This study aims to determine if BPA levels influence weight loss after bariatric surgery. Demographic, preoperative, and 3- and 6-month postoperative urine and laboratory data were prospectively collected on 22 bariatric surgeries. Laboratory values included hemoglobin A1C, fasting insulin (FI), and fasting glucose. Urinary BPA analysis was completed by NMS labs.

At the time of data analysis, all 22 patients were at or beyond the 6-month postoperative time point with a 3 and/or 6-month urine sample. Preoperative patient demographics included an average BMI of 45.2 kg/m^2, age 47, 63.6% white, 86.4% with private insurance, and 4 total preoperative comorbidities. While there was no difference between preoperative and 3-month postoperative urinary BPA excretion ($p= 0.71$), at 6-month we saw a trend toward significantly increased urinary BPA levels ($p= 0.12$). Heavier patients had lower excretion of BPA preoperatively (1.51 vs. 2.46, $p= 0.05$) but by 6-months postoperative, no difference was seen between the two groups ($p= 0.87$). Higher urinary excretion of BPA preoperatively correlated with lower 6-month patient weight ($r= -0.557$, $p= 0.025$). Patients with preoperative fasting insulin >25 were more likely to have decreased BPA excretion at 6 months. Higher preoperative fasting insulin correlated significantly with reduced BPA excretion at 6-months postoperative ($r= -0.5366$, $p= 0.032$).

As patients lose weight, BPA excretion increases in the bariatric patient population. Given the correlation between insulin and BPA levels, patients with worse diabetes, or higher insulin levels may store BPA longer in their adipose tissue. Higher urinary BPA preoperatively predicts more postoperative weight loss indicating an environmental predictor for weight loss.

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PARALLEL RAREBITS: A NOVEL, LARGE-SCALE VISUAL FIELD SCREENING METHODOLOGY

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Studies in both the developed and the developing regions of the world have concluded that there is a need for a simple, cost-effective visual field screening tool for the early detection of ophthalmic disease. Humphrey 24-2 fast test (H24-2) and Frequency Doubling Perimetry (FDT) are popular glaucoma screening techniques, but are generally too costly and too time consuming to employ in large-scale screenings. As a result, there has been great interest in lowcost, high sensitivity techniques to screen large groups Rarebit Perimetry (RBP) is a computer-based perimetric testing program with sensitivity and specificity for detection of visual field defects comparable to traditional automated perimetry. In order to make large-scale screening more efficient, we developed a parallel RBP method to screen groups of subjects simultaneously. We then used this method to report the mean hit rate (MHR) among subjects aged 13-19.

RBP was installed on computers in an existing school computer laboratory. All subjects provided medical/demographic information, and underwent a basic visual exam. Testing instructions were provided to groups of up to 35 subjects, and the RBP test was subsequently administered. 2-3 test supervisors answered questions and ensured that subjects were well aligned with their test screens. MHR, reaction times, error rates and testing time were calculated, and time estimates for Rarebit, FDT and Humphrey were compared.

A total of 364 RBP tests were conducted on 182 subjects. 154 of these subjects met our inclusion criteria for the reference range (3 testing errors or less and visual acuity 6/9 or better). The average MHR was 94.3 ± 4.63%. Screening of 500 subjects using this parallel RBP method would require approximately 9 hours - far less than an estimated 77 hours required for FDT C-20 screening tests or an estimated 127 hours required for Humphrey 24-2 SITA fast tests.

Using our methodology, RBP can be administered in parallel to groups of subjects. The MHR was found to be comparable to that reported in previously published studies. This parallel technique may improve the efficiency of large-scale visual field screenings and offer a cost-effective opportunity for screening populations in underserved areas for visual field defects. More studies reporting sensitivities in various age groups and in different screening situations are needed to better understand the utility of Rarebit perimetry.

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DRUG REPORPOSING IN DERMATOLOGY: PURCUTANEOUS MTOR INHIBITOR THERAPY FOR DIFFICULT-TO-TREAT SKIN DISEASES.

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Significant developments in the use of *mammalian target of rapamycin (mTOR)* inhibitors as immunosuppressant and anti-proliferative agents have been made in recent years. MTOR inhibitors, such as sirolimus, everolimus and temsirolimus have shown promise in many areas of difficult-to-treat dermatological disease, including cutaneous malignancy, autoimmune diseases, genodermatoses, keratinopathies, vascular anomalies and inflammatory disorders. However, systemic mTOR inhibitor therapy is associated with significant side effects, and often demands drug holidays. Percutaneous delivery of mTOR inhibitors may allow effective long-term therapy while avoiding systemic toxicities.

Topical mTOR inhibitor formulations are typically made from sirolimus, the oldest and most widely used mTOR inhibitor, and consist of crushed tablets compounded with petrolatum or other bases to form ointments or creams. Topical mTOR inhibitor therapy has been attempted off-label in case reports and clinical trials for facial angiofibromas in tuberous sclerosis complex, chronic erosive oral lichen planus, port-wine stain, and familial multiple discoid fibromas. For most of these diseases, current treatment options are suboptimal, resulting in undue morbidity, treatment failures, and disease recurrence. This is particularly problematic, as most of the disease burden is present in children, a vulnerable population. All reports available on treatment of these diseases with topical mTOR inhibitors observed clinical improvement after treatment, and the only adverse event experienced was local skin irritation. When applied to small body surfaces, such as the face, no reports have found detectible blood drug levels.

MTOR inhibitor therapy has shown increasing promise in the field of dermatology, and percutaneous drug delivery may allow for effective long-term therapies with minimal adverse events and avoidance of systemic toxicities. Given the increasing importance of cost minimization in medical science, this development represents a potential breakthrough. Large placebo-controlled, double-blinded, randomized studies are needed to assess the efficacy, safety, duration and tolerability of treatment.

MORTALITY AMONG FORMER JUVENILE OFFENDERS IN CALIFORNIA

Greg Gaskin, Paul Wise, and Arash Anoshiravani, Stanford University Department of Pediatrics

A combination of age, developmental stage, risky health-related behaviors, and poor healthcare access contribute to the increased morbidity experienced by adolescents involved with the juvenile justice system, especially with respect to mental health, substance abuse, and reproductive health**.** Previous studies in adult inmate populations have demonstrated significantly increased rates of mortality following release into the community as compared to matched controls. However, to date, no work has been done to examine the mortality rates, causes or time-courses of mortality among released adolescents. Such insights could then help guide systemic strategies and quality improvement efforts directed at enhancing the quality of diagnosis, in-detention therapy, and coherent follow-up planning.

We have conducted a retrospective cohort study examining all deceased individuals released from DJJ facilities between 1980 and 2010. This data provides information for approximately 20,000 individuals who have transited through the juvenile justice system in California. With this data, we have calculated mortality rates among released youths and described the time-course and chronology of risk upon re-entry into the community.
Our results thus far indicate that youths experience a spike in risk in the first 2 weeks after leaving detention. As expected in this population, the leading cause of mortality is overwhelmingly homicide-related, followed by motor vehicle accidents. Next steps for this project are to compare the mortality rates among released juvenile offenders with those of an age, gender and race-matched control population.

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UNIQUE STROMAL DERIVED FACTOR-1 (SDF-1) INFUSED HYDROGEL CARRIERS FOR HEALING OF VOLUMETRIC BONE DEFECTS

Benson M. George, Robert Carrera, Chris Crowe, Hung Pham, James Chang, and Alesha B. Castillo. Stanford University Department of Plastic and Reconstructive Surgery

Victims of blast and crush injuries generally present with complex bone defects that can eventually require amputation. Typical limitations to proper bone healing are inadequate vascularization and suboptimal cellular recruitment. To address these issues we hope to create a unique hydrogel, which will serve as the scaffold for recruiting factors. Hydrogels are an interesting therapeutic vehicle because they can undergo biodegradation, minimize inflammatory responses, and provide a rich environment for cellular seeding due to their collagen structure. Additionally, hydrogels are injectable, allowing for easy, localized administration to injury sites.

In this study, we explored SDF-1 as a potential recruiting factor in hydrogels. SDF-1 has been strongly implicated with increased angiogenesis, cellular recruitment, cellular proliferation, and osteogenesis; these features make SDF-1 an attractive candidate for bone regeneration therapies. Additionally, our preliminary research indicated that blocking SDF-1 signaling by knocking out its receptor, CXCR4, attenuates load-induced bone healing. To assess SDF-1's chemoattractant potential, we used a migration assay and saw that increasing concentrations of SDF-1 embedded in hydrogels enhanced recruitment of preosteoblast progrenitor cells. With a concentration of 10,000ng/mL of recombinant SDF-1, we witnessed a three-fold increase in recruitment.

In the future, we hope to perform more *in vitro* migration assays using varying concentrations of SDF-1 and gel to find the optimal environment for cellular recruitment. We will then use the hydrogel carrier *in vivo* to assess the ability of SDF-1 to enhance healing of a large cortical bone defect in rat models.

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DYNAMIC LOADING ASSESSMENT IN ELITE ATHLETES USING A WIRELESS PRESSURE INSOLE SYSTEM

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Foot and ankle injuries are common in the athletic population, particularly in athletes participating in field and court sports. Fractures of the proximal metaphysis of the fifth metatarsal (i.e., Jones fractures) generally require surgical fixation and missed time from sports participation to optimize healing rates and return to sport. Subtle hindfoot varus alignment, which likely results in greater forces at the fifth metatarsal, has been associated with increased risk of Jones fractures. Corrective Orthotic devices are often used during rehabilitation for these injuries. A better understanding of dynamic loading at the base of the fifth metatarsal may allow identification of athletes at risk for this injury before it occurs, and aid in the development of appropriate preventive devices and exercises. We hypothesize that athletes who have suffered Jones fractures will apply significantly higher loads at the fifth metatarsal base during sporting activities compared to matched uninjured athletes.

Athletes with a history of Jones fracture showed a significantly increased peak pressure, mean pressure, and maximum force at the 5^{th} metatarsal base during walking and running compared to uninjured matched controls (all $P<0.05$). A 30% increase in force-time integral (impulse) at the 5^{th} metatarsal was observed in Jones fracture athletes during running, but did not reach statistical significance ($P=0.07$). There was a significant increase in maximum force and force time integral in Jones fracture athletes during cutting ($p<0.05$). The 41% increase in peak pressure and 52% increase in mean pressure at the 5^{th} metatarsal base in Jones fracture athletes during cutting did not reach statistical significance with available data ($p=.078$). Use of corrective orthotic device did not significantly reduce peak or mean pressure, maximum force, or impulse at the 5^{th} metatarsal base during running or cutting.

These results indicate that athletes with a history of Jones fracture exert significantly increased peak and mean forces at the base of the fifth metatarsal during common athletic activities. Standard orthoses do not appear to offload this region in all cases. These increased loads may contribute to the development of stress injury to the fifth metatarsal during repetitive loading, and ultimately fracture of the bone. Identifying patients at risk for these injuries may facilitate an injury prevention program. Further study of orthotic devices, shoe wear, and materials designed to offload the fifth metatarsal is necessary.

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THE IMPACT OF MATERNAL AGE AT MARRIAGE ON MALNUTRITION OF HOSPITALIZED CHILDREN IN DHAKA, BANGLADESH

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Childhood malnutrition is a worldwide health problem that continues to cause numerous deaths in children under five years of age without any significant improvement for last several decades especially in south-east Asia. This cross sectional study study focuses on understanding more about the maternal and childhood characteristics associated with malnutrition of children under five (1-59 months) at the Dhaka Hospital of the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) in Dhaka, Bangladesh. Specifically, in this study we asked if younger maternal age at marriage, younger current age of the mother, and lower birth order relates to more severe malnutrition in hospitalized children admitted to the short stay unit, long stay unit, malnutrition ward, and intensive care unit (ICU) of the hospital between July 8-August 6, 2013.

A total of135 subjects were enrolled according to eligibility criteria. Data analysis shows no statistically significant relationship between maternal age at marriage of the mother or current age of the mother and the child's malnutrition level. However, this study supports other findings in which decreased educational years and decreased BMI of the mother relates to more severe childhood malnutrition.

Due to small sample size, low power of the analysis, and other limitations, we cannot draw conclusions on the relationship between maternal age at marriage and childhood malnutrition, but we do see that, even with this underestimated number, 62.96% of the mothers married under the age of 18 (the legal marrying age for Bangladeshi females). The child, mother, and household characteristics we studied allow us to have a holistic perspective on the social situations of hospitalized children at icddr,b. Future study with large sample and adequate power may help in further understanding the health of the mother in obtaining gravidity and parity and the child through collecting health outcomes of the hospitalized children.

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OPTOGENETIC TECHNIQUES TO DEMONSTRATE NEURON ACTIVITY-DEPENDENT PROLIFERATION OF PEDIATRIC GLIOMA CELLS *IN VIVO*

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Pediatric high-grade gliomas (pHGG) are devastating primary brain tumors carrying a uniformly grim prognosis, representing the leading cause of mortality from childhood tumors of the CNS overall. They arise in neuron-rich areas, and tumor cells are known to characteristically surround neurons. However, the role of neurons and neuronal activity in the tumorigenic microenvironment is not well understood. Our research group has recently demonstrated a mitogenic effect of neuronal activity on normal oligodendrocyte progenitor cells *in vivo*, as well as a neuronal activity-dependent mitogenic effect on ppHGG cells *in vitro*. Using optogenetic techniques, we have developed a system to probe the possible mitogenic effect of neuronal activity on HGG cells *in vivo* in a murine model.

Human pediatric cortical glioblastoma cells were xenografted in area M2 (premotor cortex) in juvenile immunocompromised NSG-Thy1:ChR2 mice, which express a light-sensitive excitatory opsin (channelrhodopsin, or ChR2) under control of a neuron-specific promoter (Thy1). After 8-10 weeks, an optical-neural interface was placed at M2 and optogenetic stimulation (blue light of 470 nm wavelength at frequency 20Hz) was applied. A robust and consistent motor response was elicited, confirming effective, behaviorally-relevant neuronal activation. Following stimulation, the thymidine analog EdU (5-ethynyl-2'-deoxyuridine) was administered to label dividing cells, and the animal was sacrificed after 24 hours. Using confocal microscopy, we plan to quantify activity-dependent proliferation of engrafted tumor cells in optogenetically stimulated mice compared with identically-mainpulated wildtype littermates that do not respond to light stimulation; findings are forthcoming.

We thus present a novel system to demonstrate the role of neurons and neuronal activity within the intact tumor microenvironment of a living mouse. Further studies should probe the viability of this system in modeling neuron-glioma interactions in the pons and thalamus, and should investigate the possible regional specificity or glioma subtype specificity of this effect. Efforts to identify the activity-dependent mitogenic factor and its mechanism, which would represent a novel therapeutic target for pHGG, are ongoing.

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FIGHTING FOOD INSECURITY DURING THE SUMMER: EVALUATION OF A PUBLIC-PRIVATE PARTNERSHIP MODEL

Steve Ko, Jenna Nolan, Janine Bruce, Jennifer Puthoff, Megan Haughey, Delayzio Amerson, Lisa Chamberlain. The Pediatric Advocacy Program.

Child hunger rates increase during the summer when children no longer receive reduced-price school meals. Summer hunger is increasingly prevalent in low-income communities. To address this growing need, the *Summer Feeding Program* was developed out of a public-private partnership between the Ravenswood City School District, YMCA and Stanford pediatric residency program. Parents of children enrolled in a summer school were surveyed (N=141) to identify barriers to participation in the program, and validated USDA measures were used to assess family levels of food insecurity. Qualitative interviews were conducted among participating families (N=29) to gauge program satisfaction.

The *Summer Feeding Program* served 4,043 meals to 120 families (238 children, 119 adults) over 23 days by a team of YMCA staff (N=6), school district staff (N=3), and pediatric residency staff (N=5). Survey results revealed that 29.2% of district families were “food insecure” over the past year, more than twice the 2012 U.S. national average. 10.2% of families experienced “very low food security” (vs. 5.7% nationally) and reported multiple indications of disrupted eating patterns and reduced food intake. One parent commented, “This was a very good program. Sometimes, families just don’t have enough money for food.” Despite the overall success, 36% of district families identified barriers to attending the program, such as waiting in long lines.

This inter-disciplinary partnership demonstrated feasibility of uniting public, non-profit, and private partners to address food insecurity. More rigorous evaluation should be conducted to assess the sustainability and scalability of the program.

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CHARACTERIZATION OF NSP1 AND PKR-MEDIATED EFFECTS ON ROTAVIRUS REPLICATION

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Infection with rotavirus (RV) destroys enterocytes, leading to severe diarrhea. Interactions between RV and host innate immune components regulate virulence and host range restriction (HRR). While HRRs were recently harnessed to generate effective vaccines, mechanisms mediating HRRs remain incompletely characterized, hindering understanding of RV pathogenesis.

The host IFN response restricts RV replication. RV encodes NSP1, a sequence-variable protein that antagonizes the innate immune response by targeting IRFs or β-TrCP to the proteasome, suppressing induction of type I IFN; or by inhibiting STAT1 activation, blocking IFN response amplification. The domains responsible for these interactions remain poorly characterized, as do interactions with other innate immune factors. To define these domains and other NSP1-interacting factors, plasmids encoding NSP1s from virulent and attenuated strains, truncated NSP1s, and NSP1s comprised of recombined domains were generated. These constructs are currently undergoing interactome analysis. Future experiments employing IRF and β-TrCP degradation assays will characterize domains responsible for NSP1- and IFN-dependent RV replication restriction.

Other innate immune factors limit RV replication. PKR senses cytosolic RV dsRNA, inactivating eIF2α and inhibiting viral and host protein translation. Using PKR-KO mice, our lab uncovered a novel requirement for PKR in promoting IFN-β secretion during infection; the mechanisms of modulating IFN secretion are uncharacterized. While PKR-KO mice lack detectable PKR protein, they express shorter in-frame PKR transcripts lacking exons 2-3. To better characterize PKR's role during RV infection, we used a small molecule inhibitor of PKR kinase activity in fibroblasts. While our results confirmed that kinase activity is necessary for IFN-β secretion during infection, specific inhibition of kinase activity modestly decreased IFN-β transcript levels *in vitro*. This suppression was polyadenylation-independent. Further experiments to examine kinase domain substrates during infection, and effects on IRF3 and NF-kB activity, will reveal the role and mechanism of PKR in modulating the IFN response to rotavirus infection.

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CREATING A PILOT TRANSITION-TO-INTERNSHIP CURRICULUM FOR GRADUATING STANFORD MEDICAL STUDENTS

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The transition from medical student to intern is inherently stressful. New residents are faced with critical patient care responsibilities and challenges, as well as the professional obligations of entering the workforce – many for the first time. The potential for negative consequences to patients and their providers is real, including an increase in medical errors and low clinician confidence at the beginning of residency. There has been a recent trend in undergraduate medical education to introduce integrative courses and "capstones" into the fourth year of medical school, but no explicit learning objectives exist on an institutional or national level. The purpose of this project was to create a pilot curriculum for graduating Stanford medical students to facilitate the challenges of transitioning to internship.

A needs-assessment of Stanford medical students graduating in 2013 was performed which identified specific areas of concern to transitioning students. With support from clinician educators in several different departments at Stanford, a 3-day curriculum was developed which included small group sessions, immersive simulations, procedural skills training, and case-based lectures. This pilot curriculum was offered to 12 graduating students in May 2013. Pre- and post-course assessments showed significantly increased confidence in 28 of 34 key learning objectives. The course was also evaluated highly with overwhelmingly positive feedback.

Based on the success of the pilot course, there are multiple opportunities to expand and integrate transitional curricula into the fourth year of medical school. Such a course should foster key competencies for graduating medical students that prepare them for the smooth transition from medical school to internship, increase problem solving skills and ability to apply knowledge to common patient care scenarios, and provide a meaningful conclusion to medical school. Future work has already begun in implementing a 1-week "capstone clerkship" for graduating students in 2014.

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LONG-TERM OUTCOMES OF RECTOSIGMOID NEOCOLPORRAPHY IN MALE-TO-FEMALE GENDER REASSIGNMENT SURGERY

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Our group has previously reported favorable outcomes of rectosigmoid neocolporraphy. Unfortunately, rectosigmoid transfers are still perceived negatively, usually relegated to secondary vaginoplasties. Our group aims to go beyond these misconceptions to provide an objective investigation into the safety and efficacy of rectosigmoid neocolporraphy for primary vaginoplasty in the male-to-female (MTF) patient.

A retrospective review was performed on MTF patients who had undergone primary rectosigmoid neocolporraphy with the senior author, Dr. Laub. Patient data including demographics, medical history, complications, and the need for revisional surgery were obtained. Direct inquiries were conducted to determine patients' level of satisfaction with appearance, sexual function, and ease of post-operative recovery.

Eighty-three patients were included over the course of 22 years with an average clinical follow-up of 2.2 years (85 patients) and phone interview follow-up of 23 years (21 patients). Overall, the patients were healthy with minimal comorbidities. Forty-eight patients (58%) had complications, but the majority were minor and consisted mainly of stricture or excessive protrusion of the corpus spongiosum. Smoking was associated with higher complication rates, especially stricture formation. Excessive muccorrhea occurred in 28.6% of our cohort. Overall patient satisfaction with appearance and sexual function (among those who were sexually active) was high.

Our study is one of the largest and longest reported series of rectosigmoid transfers for primary vaginoplasty. Advantages include long vault length, self-lubrication, a natural appearance, sensibility, and lack of malodor. Disadvantages include strictures or leaks of the intestinal anastomosis, and the need to enter the abdomen, which adds a layer of complexity to the procedure. Rectosigmoid neocolporraphies have many times been recommended for secondary or revisional surgery when other techniques, such as penile inversion, have failed. However, we believe the rectosigmoid transfer is safe and efficacious, and it should be offered to MTF patients for primary vaginoplasty.

LOW-DOSE INTRAVENOUS PAMIDRONATE IN CHILDHOOD OSTEOPOROSIS

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Bisphosphonate administration for more than five years has been associated with an increased risk of atypical femur fractures and osteonecrosis of the jaw in adults. A drug holiday has been recommended for this reason. In children with osteoporosis, bisphosphonate therapy has been recommended until final height is reached. The balance of risks to benefit for prolonged therapy with bisphosphonates has not been established in pediatric patients. We performed a retrospective, observational, open-label study of 32 children with osteoporosis treated with low dose intravenous pamidronate for up to 8 years. The aims of the study were to review changes in bone mineral density and fracture rates during therapy and to document adverse events with throughout therapy up to 8 years.

Pamidronate was administered in a dose of 4 mg/kg/year for 36 months (treatment phase) followed by a reduced maintenance dose of 2 mg/kg/year until the condition resolved or epiphyses closed. Bone mineral density or lateral spine x rays were performed at baseline, six, 12, 24 and 36 months. Complete blood counts and serum chemistries were monitored with each infusion.

Gains in bone mineral density in response to therapy varied considerably by disorder but all patients experienced a reduction in fractures relative to pretreatment. Mild adverse effects including fatigue, myalgia, bone pain, fever, and nausea occurred in 30 % after the first pamidronate infusion. Symptoms resolved within 3 –5 days and recurred in only 7% patients after one or more subsequent infusions. There were no episodes of clinically significant hypocalcemia, atypical femur fractures, osteopetrosis or avascular necrosis of the jaw.

Low-dose pamidronate appears to be effective in reducing in children with osteoporosis and is well tolerated during long term use.

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PREDICTING SURVIVAL OF CARDIOPULMONARY ARRESTS AT THE PALO ALTO VETERANS AFFAIRS CARE SYSTEM

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In-hospital cardiac arrests events occur 350,000-750,000 annually in the United States with a small percent surviving cardiopulmonary resuscitation (CPR). There is currently no widely accepted quality metric that allows hospitals to determine if patients that arrests should have survived. Without quality metrics there is no means of measuring code blue response teams' training. The Palo Alto Veteran Affairs (VA) Hospital is a tertiary care center with 325 beds, 15 ICU beds, 15 intermediate ICU beds, and an emergency department. During the arrest the code blue team that responds generates a hand-written code blue sheet that documents specific characteristics about the patient and the arrest. The document is provided to the Cardiopulmonary Resuscitation (CPR) Committee for record keeping.

Records of all the hand-written code blue sheets from 2005 to 2013 were obtained from the CPR Committee and coded. Additional medical history and pertinent information leading to the cardiopulmonary event were obtained from the patients' medical records that are stored in Veterans Health Information Systems and Technology Architecture (VistA). We expect to create an analytic layer to be able to assess the validity of the Cardiac Arrest Survival Post-Resuscitation In-Hospital (CASPRI) score card for our VA patient cohort. In addition we will use STATA to perform a multivariate logistic regression analysis on other predictor variables of survivability that are not used in the CASPRI score card to improve predictability.
The Palo Alto Veteran Affairs Hospital is a tertiary care center with 325 beds, 15 ICU beds, 15 intermediate ICU beds, and an emergency department. From October 2005 to September 30, 2011, 606 files exists for which a "code blue" was called. The data set of actual cardiopulomary arrest events is closer to 215. Preliminary results show that 85% of the events are witnessed, 80% are due to pulseless electrical activity, 47% have return of spontaneous circulation, and 31% survive 24 hours after an event.

Understanding predictors of surviving a cardiopulmonary arrest can lead to better outcomes and policy changes in preventing an event in the first place. By having a scoring system will help the VA hospital and other hospitals understand how their code blue response teams are performing. If the VA's code blue team training is improving the number of patients surviving an arrest event then their training could be adopted by other hospitals and improve the outcomes of all patients across the nation that experience a cardiopulmonary arrest.

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EXPLORING THE HEALTH AND SOCIAL NEEDS OF AT-RISK TRANSITION AGE YOUTH IN SAN JOSE, CALIFORNIA

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In a given year, it is estimated that there are 1 to 1.6 million homeless youth in the United States. Transition age youth (TAY), aged 16 to 24, are a unique sub-population of homeless youth that are particularly at risk of suffering from the effects of being disconnected, homeless, and underemployed as they negotiate the difficult transition into adulthood. While there is an abundance of literature focusing on homeless youth in general, less is known about the specific challenges faced by homeless TAY. Using a community-based participatory research model, we collaborated with a local community organization to assess the health and social needs of at-risk TAY in San Jose, California.

Interviews were conducted at a local center that provides services to TAY. All interviews were audio recorded, transcribed, and a thematic analysis was performed. A total of thirteen 25-minute interviews with male (n=7) and female (n=6) TAY were completed and included in the final analysis. The following major themes emerged:

- Lack of stable support during their childhood fosters a strong sense of independence and self-sufficiency among TAY.
- Unemployment and lack of housing are the primary concerns of TAY and are major sources of stress.
- TAY's self-reliant nature and history of negative health provider experiences result in many being averse to seeking help for their health concerns.
- TAY find themselves in an important transition in their lives and struggle to find ways to define their adulthood and accept increased responsibilities.
- Successful programs and services employ trusted case managers and health providers that respect TAY's autonomy and understand their daily challenges.

TAY highly value independence and self-reliance, which plays a significant role in their attitudes about seeking out both health and social services. Programming and outreach targeting TAY must be designed with this in mind to best serve the needs of this uniquely vulnerable population.

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A USABLE AND COMPREHENSIVE TOOL TO ESTIMATE CUMULATIVE LIFETIME UV EXPOSURE

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Accurate assessment of cumulative lifetime ultraviolet (UV) exposure is critical for clinical and research purposes, as UV exposure is the leading risk factor for many cutaneous cancers, and results in photo-damage and premature skin aging. To date, instruments for assessing cumulative lifetime UV exposure (CLUE) have relied on time-consuming surveys. Additionally, these instruments do not account for the geographic location of exposure, a highly relevant factor due to increasing geographic mobility among patients.

Our objective was to develop an easy-to-use, comprehensive measure of CLUE that integrates both duration and geographic location of ambient UV exposure. After a review of the literature on validated instruments for cumulative UV exposure, we modified these instruments into an 18-item survey to capture individual outdoor exposures. Historical UV index data from the National Oceanic and Atmospheric Administration (NOAA) and the National Weather Service (NWS) was used to calculate the average annual UV indices for 58 anchor cities in the United States. This tool was tested on 400 volunteers aged 18-93 years who had lived in various locales throughout their lifetimes. The CLUE was obtained by multiplying the duration of exposures by the average annual UV index for the closest anchor city, and then summing over all reported exposures.

The generated CLUE is useful for statistical adjustment and for identifying individuals with high lifetime UV exposures. Incorporation of the UV index into the calculation for CLUE can improve accuracy and validity compared to current methods. The NWS-calculated UV index is pre-adjusted for both environmental factors (such as cloud cover and elevation) as well as for the wavelength dependence of actinic skin damage. Thus, our measure is both physiologically relevant and representative of real-world conditions. This new measure CLUE will allow for more precise assessments of patients' sun exposures for clinical care and research purposes.

INTEGRATIVE MEDICINE & THE UNDERSERVED: WHAT ARE THE BARRIERS?

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Integrative Medicine (IM), is a board certified medical specialty that combines conventional medicine with Complementary and Alternative Medicine (CAM), encompassing a wide range of practices, including: acupuncture, naturopathy, chiropractic care, ayurveda, meditation, and nutrition. While integrative medicine is widely popular and is gaining an increased presence in the medical community, very little research has been done specifically evaluating the intersection of integrative medicine and the underserved. The goal of this project is to first assess what models of integrative medicine delivery have been implemented, and the ways in which, if any, they have ensured that services are accessible to lower income populations and/or ethnic, racial, and linguistic minorities.

This study will assess barriers to IM delivery among underserved populations in the Bay Area through two avenues: 1) by conducting a web search of IM practices in the area and documenting mention of sliding-scale fees, acceptance of public insurance, and availability of interpreter services; and 2) by interviewing IM providers to determine current practices to mitigate barriers, or perceived barriers to ensuring equal access to care.

Data was analyzed via an open, inductive coding method. Findings suggest that majority of IM providers are eager to provide services to underserved populations, however those in a private practice setting do not know what modes are available to do so. Practices that are held at a Federally Qualified Health Center (FQHC) have demonstrated the greatest facility in implementing IM into their clinics. Language access remains an issue outside of FQHC settings, and often providers are not cognizant of language as a potential barrier to services. With greater collaboration and sharing of ideas in the field of IM, there are numerous ways in which accessibility could be increased.

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HIGH-THROUGHPUT MOLECULAR PROFILING OF EGFR GENE AMPLIFICATION ACROSS DISTINCT BRAIN REGIONS OF TUMOR FORMATION IN HUMAN GLIOBOASTOMA USING FLUORESCENCE IN SITU HYBRIDIZATION ON TISSUE MICROARRAYS (TMA-FISH)

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It remains unclear whether different brain regions give rise to brain tumors that differ in underlying pathogenesis and molecular characteristics. Epidermal growth factor receptor (EGFR) gene amplification has been reported in association with recurrence and treatment resistance across a number of cancers, including brain tumors. This study evaluates the utility of high-throughput molecular analysis using fluorescence in situ hybridization (FISH) on glioblastoma tissue microarray (TMA) to study the relationship between distinct brain regions of tumor formation and the presence of EGFR gene amplification.

72 males and 51 females (ratio 1.4:1) with a mean age of 61.6 ± 13.6 years with newly diagnosed WHO grade IV glioblastoma were included in a single microarray paraffin block. Distinct brain regions of tumor formation included 29 (23.6%) tumors arising from the anterofrontal subventricular zone (SVZ), 62 (50.4%) arising from the posterolateral SVZ, and 32 (26.0%) from the temporal horn SVZ. A total of 53 (43.1%) tumors were FISH positive for EGFR gene amplification. EGFR gene amplification was associated with the posterolateral SVZ region of tumor formation (OR: 2.3, 95% CI: 1.1-4.8, *P*=0.02). EGFR status was not associated with any other clinical variable, including age, gender, and overall survival. The posterolateral SVZ region of tumor formation was also associated with dense macrophage infiltrates (OR: 3.1, CI: 1.5-6.3, *P*=0.002).

EGFR status varies across distinct brain regions of tumor formation in human glioblastoma. EGFR gene amplification is associated with a posterolateral SVZ cluster of glioblastoma formation characterized by dense macrophage infiltrates. These findings carry important implications regarding which patients might benefit from enrollment in clinical trials involving drugs targeting EGFR kinase activity and/or anti-EGFR immunotherapy. Furthermore, these data serve to highlight TMA-FISH as an efficient and scalable new method for large-scale tumor molecular profiling.

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DOES A DIETITIAN IMPROVE BARIATRIC SURGERY OUTCOMES?

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Bariatric surgery is the only effective and enduring treatment for morbid obesity. Postoperative care is an important mediator of surgical effectiveness and patient safety. It is recommended that postoperative care be managed by both the surgeon and a registered dietitian (RD). However, few studies have validated these guidelines with clinical evidence. In this natural experiment, we aim to determine if an RD improves bariatric outcomes. Patients undergoing bariatric surgery were seen postoperatively by their surgeon at 2- and 6-weeks, followed by 3-, 6-, and 12-months. A new policy required either the two or six-week follow-up appointment to include both a surgeon and a dietitian. We performed a retrospective analysis of patients who underwent surgery during equivalent timeframes before and after adoption of the new policy. Pre- and postoperative data collected included patients' demographic, anthropometric, and biochemical laboratory information. Any incidence of complications and readmissions were also recorded.

302 patients followed-up by a surgeon alone, and 268 followed-up by both a surgeon and dietitian were included in this study. Preoperative demographic and anthropometric features were similar in both groups. Using a multivariate logistic regression model controlling for race, age greater than 50, private insurance, BMI greater than 50, and male sex, we found that having a combined follow-up predicted 3-month decrease in total cholesterol (OR=1.60, p=0.03) and triglycerides (OR=1.57, p=0.03), as well as increase in HDL cholesterol (OR=1.76, p=0.008) and thiamine (OR=2.46, p<0.001). Patients with combined follow-up had a significantly lower incidence of readmissions due to dietary-related problems (0 vs. 3.03%, p=0.004).

In this study, we demonstrate the significant value of a combined surgeon-RD postoperative visit. Adding a dedicated RD post-operative visit significantly decreased readmissions and cardiac risk factors, and improved micronutrient levels. Future studies should explore how a dietician can improve weight loss maintenance long-term in bariatric surgery patients.

DO SALIVARY CORTISOL LEVELS CHANGE AFTER BARIATRIC SURGERY?

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Obesity is a complex disease associated with many different physical illnesses and psychological stresses. Cortisol has a broad physiological impact on the body and has been shown to have wide variability due to physical and mental stresses. Among its many effects on the body, cortisol plays a role in insulin resistance and sodium retention, two disorders that are comorbid with obesity. This study aims to improve our understanding of the relationship between cortisol and weight-loss after bariatric surgery. Demographic, preoperative, and 1-day, 3- and 6-month postoperative salivary cortisol and laboratory data were prospectively collected on 25 bariatric patients. Laboratory values included hemoglobin A1C, fasting insulin, and fasting glucose. Salivary cortisol analysis was performed using a highly sensitive enzyme immunoassay.

All 25 patients were at or beyond the 12-month postoperative time point. Preoperatively, patient's had an average BMI of 45.0 kg/m^2, age 48.5, 60.0% white, and 80% with private insurance. Absolute salivary cortisol levels preoperatively were 0.287, 0.672 at 1-day postoperative, 0.252 at 3-months postoperative, 0.367 at 6-months postoperative, and 0.386 at 12-months postoperative. No significant difference in cortisol levels was found between time points with the exception of preoperative versus 1-day postoperative cortisol levels. Patients with higher than average cortisol levels at post-op day 1 have greater 3-month percent excess weight loss (PEWL) (40.1% vs. 48.8%, p=0.073). A pairwise correlation showed that PEWL at 3-months is significantly correlated to1-day post-op cortisol levels (p= .024, R = 0.51). Additionally, there is a significant correlation between preoperative cortisol and CRP (R= 0.59, p= 0.006)

The immediate postoperative period is a well-known period of increased stress, and our results support this understanding as well as a positive correlation between cortisol and CRP. Interestingly, our results also suggest that although cortisol levels remain relatively stable over time, patients with greater than average cortisol levels at 1-day postoperative may have increased success with weight loss indicating a possible metabolic receptivity to weight loss via inflammation.

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OPTOGENETIC STIMULATION OF THE CEREBELLAR DENTATE NUCLEUS AS A NOVEL THERAPEUTIC TECHNIQUE TO PROMOTE NEURONAL ACTIVITY, PLASTICIY, AND FUNCTIONAL RECOVERY AFTER STROKE

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Stroke is a leading cause of disability in the United States. To date, there are no therapeutic agents to aid in recovery. Studies have demonstrated that brain remodeling due to increased activity in the perilesional areas holds promise as a method of treatment. Previously, our lab demonstrated that optogenetic neuronal stimulation of the ipsilesional primary motor cortex (iM1) promotes functional recovery. To determine an optimal brain stimulation target, we test whether optogenetic neuronal stimulation of the contralesional cerebellar dentate nucleus (cLCN) can promote recovery. Stimulation of cLCN may be more effective, as it sends excitatory outputs to multiple motor and premotor areas. We hypothesize that stimulation of cLCN after stroke will cause widespread perilesional activation, leading to enhanced neuronal activity, plasticity, and functional recovery.

Stroke mice were stimulated from day 5-14 post-stroke and a sensory-motor behavior test was used to evaluate recovery. The rotating beam test demonstrated that stimulated mice recovered quickly, with statistically significant improvement in distance traveled as early as day 7, and faster speed at day 10 post-stroke. To evaluate whether the effect of stimulation was persistent, we tested the effects of short stimulation (day 5-14) and long stimulation (day 5-28) on recovery. Our data showed that the effect of cLCN stimulation is persistent, as the short stim group continued to recover after day 14 without further stimulations and had a comparable recovery outcome to the long stimulation group. This indicates that prolonged stimulation may not be necessary to achieve persistent recovery. Analysis of pCREB activation demonstrates that cLCN stimulation activates premotor and motor areas, as well as thalamic regions.

Ongoing studies examine the underlying mechanisms of cLCN-induced recovery, including synaptic and plasticity markers. Our study demonstrates that cLCN is a promising target for promoting recovery after stroke.

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UTILIZATION OF THE AMERICAN PSYCHIATRIC LEXICON: OUTCOMES OF EVOLUTION AND DIASPORA

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The contemporary medical lexicon has been plagued by a history of inconsistencies, misinterpretations, and digressions. These include any or multiple elements of 1.) morphological, 2.) interdisciplinary or cross-cultural, 3.) linguistic, 4.) colloquial developmental progressions. This is especially evident in psychiatric circles, a multidisciplinary specialty where pathological delineations are often equivocal. Particular diagnostic terms from this arena have intercalated into the casual public discourse, perhaps to a greater extent than diction deriving from other subspecialties.
The objectives of this project are to 1.) research and describe the evolution, dispersal, and semantic employment of certain psychiatric words and syntax , and 2.) synthesize the opinions of physicians within the mental health field (supplemented by medical humanists and writers) regarding implications of the adoption of their specialized discourse into colloquial and vernacular usage.

Utilize the historical resources present in academic libraries, ie archived historical (dating to medieval times, if necessary) documents and the medical literature (most of which is available electronically). This will include Latin, Greek, and German psychiatric lexicons, as well as the preliminary editions of the Diagnostic and Statistical Manual of Mental Disorders (DSM). Compare semantics of definitions with lay glossaries. Also, conduct interviews with members of the psychiatry and linguistics departments at academic and community institutions.

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OUT-OF-POCKET COST BURDEN IN PEDIATRIC INFLAMMATORY BOWEL DISEASE

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Pediatric inflammatory bowel disease (IBD)— consisting of Crohn's disease and ulcerative colitis varieties— is a chronic condition with peak incidence in adolescent and young adult years that can result in significant morbidity. While it is known that the overall financial impact of pediatric IBD is significant, the direct impact on pediatric patients and their families has not been adequately explored. Traditional studies have largely relied on claims, medical records, and other large data sets. Furthermore, family and patient-specific attributes that might correlate with increased pediatric IBD cost burden have never been determined from the direct perspective of patients and families themselves. We hypothesized that children with moderate-to-severe pediatric IBD, and those in families of lower socioeconomic strata, disparately absorb substantial financial stress. To test that hypothesis, we are completing a cross-sectional, survey-based study that encompasses the development of an online Qualtrics survey, collection of results from pediatric IBD patients and their families, and analysis of results using multivariate conditional logistical regressions.

Initial descriptive results demonstrate that for pediatric IBD patients across a spectrum of ages, the financial impact of IBD is variable. While 67.5% of families had annual out-of-pocket (OOP) costs <$1,000, 32.5% had expenses that were greater, including a few families who spent on more than $5,000 annually on IBD-associated expenses. 35% of patients required ED visits over the past year, which resulted in nearly 30% of families spending more than $1,000 on ED copays. OOP costs for procedures and tests was bimodal: 32.5% of families spent <$100, while 27.50% spent >$2,000. Moreover, 30% of families had to travel more than 60 miles for clinic visits, 80% missed work, and 35% subsequently experienced lost wages. The results of this study have the potential to influence the health policies around the financing and medical care of pediatric IBD.

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SUSTAINED HIGHER INFLUENZA VACCINATION RATES IN PREGNANT WOMEN FOLLOWING H1N1 PANDEMIC: ASSESSMENT OF FOUR CONSECUTIVE SEASONS 2008-2012

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Pregnant women are at increased risk for severe complications and mortality as a result of influenza infection when compared to the general population. However, vaccine uptake during pregnancy has historically been low amongst pregnant women. Although studies reported that influenza vaccination rates among pregnant women increased during the 2009-10 H1N1 pandemic season, data is limited regarding subsequent years. Our goal was to assess vaccination rates in pregnant women preceding, during, and following the H1N1 pandemic influenza season. We conducted a retrospective study at a university medical center obstetrics outpatient clinic, in which we assessed vaccination rates for four consecutive influenza seasons: season prior to the H1N1 pandemic (2008-09), the H1N1 pandemic season, (2009-10) and two seasons following the H1N1 pandemic (2010-11, 2011-12). We compared demographic and medical characteristics for patients who were eligible for vaccination during these respective seasons to assess for any differences between cohorts. Descriptive statistics and logistic regression were used for statistical analysis.

Influenza vaccination rates for pregnant women were 33.8% in 2008-09 season, 70.6% in 2009-10 (H1N1 pandemic) season, 58.8% in 2010-11 season, and 63.4% in 2011-12 season. For the H1N1 pandemic season, 98 (14.9%) women received the H1N1 vaccine only, 78 (11.8%) received seasonal 2009-2010 vaccine only, and 289 (43.9%) women received both H1N1 and seasonal 2009-2010 vaccines. Multivariate logistic regression analyses demonstrated that pregnant women were most likely to receive influenza vaccination during the H1N1 pandemic (aOR3.0, 2.4-3.5), but there was a significant sustained increase in vaccination rates from the baseline year in the 2010-11 (aOR 2.0, 1.7-2.5) and 2011-12 seasons (aOR 2.1, 1.7-2.4).

Our findings demonstrate that increased public awareness, stronger physician recommendation, and our obstetrics clinic's systems improvements for vaccination during the H1N1 pandemic influenza season were important potential factors influencing successful vaccination not only during the 2009-10 pandemic but also in subsequent years. While respect for patient autonomy and decision-making is always essential, this study reinforces the critical role of public health awareness and the unique opportunity obstetric physicians have to improve understanding of vaccination and improve women's health during pregnancy -- a crucial period of health care provision.

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PREDICTORS OF APPENDICITIS ON COMPUTED TOMOGRAPHY AMONG CASES WITH BORDERLINE APPENDIX SIZE

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Borderline appendix size complicates the diagnosis of appendicitis. We identified 56 consecutive patients with 6-7 mm appendix on contrast-enhanced CT prior to appendectomy over a 10-year period at Stanford Hospital in order to determine which imaging features are reliably detected and accurate in diagnosing appendicitis when the appendix is borderline in size. Two independent blinded readers noted the presence of intraluminal (air, appendicolith), wall (hyperemia, focal mucosal enhancing defect, thickening), periappendiceal (fat stranding, fluid, phlegmon, abscess, lymphadenopathy), and extraluminal (appendicolith, air) features. Interrater reliability of each feature was calculated with Kappa (K). Receiver Operating Characteristic following logistic regression was used to compare the accuracy of features in predicting pathology-proven appendicitis to the institution's historic sensitivity (sens) and specificity (spec) of CT radiology reports.

The absence of intraluminal air was noted with substantial reliability (K=0.79, p<0.001), and was strongly predictive of appendicitis on both reads (OR=5.45, p=0.005); it was 68.6% sensitive and 71.4% specific for appendicitis. In a comparison of ROC Area Under the Curve, absence of intraluminal air and historic CT reports had comparable accuracy in predicting appendicitis (0.70 vs. 0.68, P>0.05). Despite similar overall prevalence on paired reads (34/56=60.7%; 38/56=67.9%), wall hyperemia was detected with fairly low reliability (K=0.23, p=0.04) and was sensitive and significantly associated with appendicitis for only one reader (sens 80%, spec 52.4%, OR 4.4, p=0.015; sens 65.7%, spec 47.6%, OR 1.74, p=0.33). Wall thickening (K=0.63, p<0.001) and periappendiceal fat stranding (K=0.63, p<0.001) were more sensitive than specific for appendicitis, while intraluminal appendicolith and periappendiceal fluid optimized specificity over sensitivity (K=0.77, p<0.001; K=62.2, p=0.001). The remaining features were not prevalent (<20%) on CT.

The absence of intraluminal air was both reliably detected and relatively accurate in predicting appendicitis. We continue to add tiebreaker reads for features, and will incorporate reads for CT scans of nonsurgical patients.

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Study data were identified through the STRIDE Cohort Discovery Tool and STRIDE Patient Cohort Data Review Tool, and were managed using REDcap electronic data capture tools hosted at Stanford University with support from the Stanford Center for Clinical Informatics grant support (Stanford CTSA award number UL1 RR025744 from NIH/NCRR).

STRUCTURAL AND ARCHITECTURAL REGENERATION OF THE NEONATAL MOUSE LIVER

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The capacity of the mammalian liver to undergo compensatory growth after physical injury is well understood. Liver mass is precisely regulated in proportion to total body mass; mature hepatocytes first re-enter the cell cycle and are induced to proliferate after partial hepatectomy. Though the final mass of the regenerated liver remains consistent, the lobular architecture is lost following resection, implying that the adult liver does not undergo regeneration following acute injury. Chronic injury models do not ablate pre-existing hepatic architecture and therefore fail to address the questions of pattern formation and architectural regeneration of the damaged liver.

Here we show that 0.5 day old mice are able to regenerate lobular architecture following a partial lobular hepatectomy. Multi-color fluorescent based lineage tracing and clonal analysis demonstrate increased proliferation at the resected lobe and full regeneration 56 days after surgery. Regenerated livers were often indistinguishable from age-matched controls seen through the reconstitution of all lineages, with no functional differences observed. Lineage restriction of proliferating clones suggests that lobular regeneration is a result of the expansion of unipotent progenitors. 14 day old mice receiving similar lobular amputations were unable to achieve the full scale of regeneration as their newborn counterparts and instead other lobes underwent compensatory growth. Our results demonstrate that the mammalian liver has the capacity for structural and architectural regeneration for a brief time window before transitioning to a hypertrophic mode of compensatory growth. These results may serve as a starting point for further studies in mammalian liver and tissue regeneration.

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IMMUNE PATHWAYS IN LARGE VESSEL VASCULITIS

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Giant Cell Arteritis (GCA) is a form of vasculitis that affects the aorta and its extracranial branches. In GCA, dendritic cells in the blood vessel walls secrete cytokines that promote the differentiation of CD4 T cells into Th1 and Th17 cells. Th1 and Th17 cells secrete IFN-γ and IL-17A, respectively, which facilitate the formation of lesions that damage the structure of blood vessels. Glucocorticoids, the standard treatment for GCA, selectively suppress Th17 cells but leave Th1 cell responses unaffected.

We hypothesized that novel immunosuppressive therapies for GCA can be developed by interfering with CD4 T cell differentiation. Specifically, we reasoned that the regulation of target gene transcription through the removal of H3K27 trimethylation by Jumonji C domain containing protein 3 (JMJD3) demethylase plays a significant role in supplying vasculogenic Th1 and Th17 cells in GCA. Accordingly, we investigated the immunosuppressive effects of GSK-J4, a small molecule inhibitor of JMJD3, *in vivo* in a humanized mouse model of medium and large vessel vasculitis and *in vitro* on CD4 T cells from a patient with GCA and an age-matched control.

The *in vivo* studies in the mouse model showed that the mRNA expression levels of IFN-γ, a cytokine that is secreted at high levels by Th1 cells, and T-bet (TBX21), a master transcription factor indispensable for Th1-cell differentiation, were lower in the human artery tissue grafts, blood cells, and spleen cells of mice treated with GSK-J4 than in mice treated with a vehicle control. Similarly, the *in vitro* cell culture studies of isolated human CD4 T cells from a patient with GCA showed that the concentration of IFN-γ was lower in the supernatant of cells exposed to 10 μM GSK-J4 than in the samples exposed to 1 μM GSK-J4 and 4% DMSO after 24 and 48 hours. These findings suggest that the GSK-J4 inhibitor may be able to prevent Th1 cell differentiation and, thereby, potentially impede a Th1-mediated inflammatory response.

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IDENTIFICATION AND TARGETED INHIBITION OF A FIBROBLAST LINEAGE RESPONSIBLE FOR SCARRING AND CANCER STROMA

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Fibrosis represents the underlying pathology for a spectrum of clinical entities, including hypertrophic scarring following burns, loss of cardiac function following ischemia, and the development of cancer stroma. Fibroblasts, a heterogeneous population of stromal cells, are central to the fibrotic response. However, few fibroblast lineages have been identified and fibroblast heterogeneity remains poorly understood. Using a new murine model, we reveal the presence of multiple lineages of dermal fibroblasts within the dorsal back of mice. We traced *En1*-derived fibroblasts into the dorsal dermis by crossing $En1^{Cre}$ transgenic mice with $ROSA26^{mTmG}$ mice, which harbor a double-fluorescent reporter that replaces the expression of membrane-bound tomato red with membrane-bound green fluorescent protein following *Cre*-mediated recombination. *In silico* approaches and flow cytometry allowed for the isolation of *En1*-derived fibroblasts from wild type mice on the basis of highly expressed surface molecules. Transplantation methodologies and small molecule-based inhibition functionally corroborated these surface markers in the context of both wounding healing and cancer stroma formation. Lineage-specific cell ablation using transgenic-mediated expression of the simian diphtheria toxin receptor in conjunction with localized administration of diphtheria toxin confirmed the fibrogenic role of *En1*-derived fibroblasts during wound healing and cancer stroma formation.

The lineage of fibroblasts defined by embryonic expression of *Engrailed-1* were found to be responsible for the majority of connective tissue deposition during cutaneous development, wound healing, radiation-induced fibrosis, and cancer stroma formation. Lineage-specific cell ablation using transgenic-mediated expression of the simian diphtheria toxin receptor in conjunction with localized administration of diphtheria toxin led to markedly diminished scar formation following cutaneous dorsal wounding and significantly reduced melanoma growth ($*p<0.05$) in the dorsal skin of mice. Using flow cytometry and *in silico* approaches, we identified CD26/DPP4 as a surface marker that allows for the isolation of this fibrogenic, scar-forming lineage and demonstrated that small molecule-based inhibition of CD26/DPP4 led to significantly reduced scar formation ($*p<0.001$) in a humanized mouse model of wound healing.

We have identified a distinct tissue-resident fibroblast lineage responsible for the majority of connective tissue deposition during wound healing, radiation-induced fibrosis, and cancer stroma formation in the dorsal skin of mice. Targeting this lineage holds promise for the development of therapeutic approaches to fibrotic disease, wound healing, and cancer progression.

STATIN USE IS ASSOCIATED WITH INCREASED RISK OF NON-MELANOMA SKIN CANCER: PROSPECTIVE RESULTS FROM THE WOMEN'S HEALTH INITIATIVE

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The relationship between statin use and non-melanoma skin cancer (NMSC) is unclear with few prospective studies. Laboratory research has suggested both protective and detrimental effects of statin use on NMSC risk, and statins carry a photosensitivity warning. We investigated this relationship among post-menopausal non-Hispanic white (NHW) women in the large prospective Women's Health Initiative (WHI) cohort. The WHI study (Observational Study and Clinical Trial arms) enrolled women aged 50-79 years from 1993-1998 at 40 U.S. clinical centers. Among 161,808 participants, 120,292 NHW women with no cancer history at baseline (excluding skin cancer) and complete medication/covariate data comprised the analytic cohort. The association of NMSC incidence and statin use (baseline, duration, type, potency, lipophilicity) was determined using logistic regression models.

Over 10.5 mean follow-up years, 12,156 NMSC cases were identified. Compared to women with no statin use, use of any statin at baseline was associated with significantly increased NMSC incidence (ORadj 1.18, 95% CI 1.05-1.33). In particular, lovastatin (OR 1.58, 1.11-2.24), simvastatin (OR 1.41, 1.15-1.73), and lipophilic statins (OR 1.32, 1.12-1.56) were all associated with increased NMSC risk. Low and high, but not medium, potency statins were associated with higher NMSC incidence. Longer statin use duration was not associated with increased NMSC risk. No significant effect modification of the statin-NMSC relationship was found for age, BMI, smoking, solar irradiation (Langleys), Vitamin D use, and skin cancer history.

In conclusion, our preliminary results suggest that statin use, particularly lipophilic statins, may increase NMSC risk. Future studies should examine this relationship in the context of randomized controlled trials. As new cholesterol guidelines may broaden statin use, understanding of its effect on NMSC risk will help inform prevention and treatment approaches.

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PATTERNS IN PSORIASIS GENE EXPRESSION

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Psoriasis is a common chronic inflammatory skin disease involving abnormal keratinocyte proliferation and differentiation.. Psoriasis manifests as scaly, itching erythematous epidermal plaques and is in severe cases associated with arthritis and an increased risk of cardiovascular disease. We have through transgenic overexpression of an epidermal-specific (under a K14 promoter) constitutively active mutant of a small GTPase Rac1, discovered and established a model closely mimicking human psoriasis. In this study, we have set out to compare the early transcriptional events initiating the disease progression in our model, and its significance to human disease.

Microarray analysis was performed on early lesional Rac1 mouse (day 7) skin using Illumina MEEBO mouse arrays, and the expressional profiles of human lesional psoriasis skin derived from 4 publicly available datasets found on the NCBI Gene Expression Omnibus (www.ncbi.nlm.nih.gov/geo): GSE13355, GSE14905, GSE30999, and GSE41664. In total 209 non-lesional psoriasis skin samples, 214 lesional psoriasis skin samples and 85 non-psoriasis skin samples were analyzed. Differentially expressed genes were identified using $p \leq .005$.

Through this approach, we have identified an array of transcripts deregulated in both murine Rac1 and human psoriastic skin. We have through bioinformatic analysis (Partek G.S, IPA, DAVID, transfac) overlaid these expressional profiles and identified overlapping canonical pathways, biological functions and predicted upstream regulators (through motif enrichment) involving pathways such as STAT and NFKB signaling. By identifying key pathways and nodes involved in the initiating events driving the aberrant signaling loop between the epidermis and the immune system, we can now test the potential for molecules targeting these pathways in our model.

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PRACTICE-BASED CHALLENGES AND IMPROVEMENT OPPORTUNITIES: CLERKSHIP STUDENTS' PERSPECTIVES

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Medical students are immersed in complex healthcare settings but receive limited standard education in evaluating, analyzing, or improving these environments. There is a current need for undergraduate medical education to integrate "practice-based learning and improvement (PBLI)", which is the ability to engage in life-long learning, identify strengths, deficiencies, and limits to one's own knowledge, and partake in quality improvement (QI) of a practice. To date, there are limited reports regarding students' PBLI in clinics, their challenges and insights, and how to implement this material into curricula. Our study aims to identify the PBLI challenges faced by students on an outpatient clinical rotation. Second, we will examine students' perceived PBLI challenges during clerkships, so that methods of teaching ways to tackle these challenges or alleviating them can be developed.

Data was collected from medical student logs during their required family medicine core clerkship at Stanford University School of Medicine. One of the log questions required students to: "please log a patient encounter in which you experienced a practice-based challenge or improvement opportunity, and how you addressed the challenge or what unfolded." 206 qualitative responses collected, and inductively coded by the study authors. A team-based approach was used to identify representative themes. The themes were revised and condensed through an iterative process until study authors reached consensus. Four general clusters of themes emerged: (1) students were moderately proficient in skills required for PBLI, (2) students commonly faced a set of personal challenges (e.g., limited time during patient encounters, difference in patient's and provider's perspective of care), (3) students commonly recognized a set of system challenges (e.g., lack of patient continuity, limited medical resources & staff), and (4) students' proposed insightful ideas for QI, whether personal or systems-based.

This report reveals students' practice-based challenges and their perspectives regarding QI opportunities. The data on students' proficiency of their PBLI skillset, their perspective of challenges faced, and their proposed QI methods reveal potential gaps in PBLI education that may inform curricular changes both at the pre-clerkship and clerkship levels.

THE COST-EFFECTIVENESS OF ENDOSCOPIC DIAGNOSIS OF COLORECTAL POLYPS

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More than 90% of polyps found at colonoscopy are small; further, half of these polyps are hyperplastic and lack malignant potential. Currently, the standard of care for these polyps is universal resection and pathologic evaluation. Advances in endoscopic imaging, however, have allowed for improved endoscopic distinction between hyperplastic and adenomatous polyps with malignant potential. Leaving benign polyps in the colon while resecting and discarding endoscopically-identified tubular adenomas could potentially reduce pathology and accessory costs while improving patient outcomes by reducing unnecessary polypectomies. This study examines the cost-effectiveness of such a “resect and discard” strategy in relation to the current standard of practice.

We developed Monte Carlo models to compare the lifetime clinical and economic consequences of the two strategies. The base-case is a 50-year-old American undergoing first screening colonoscopy with Markov states reflecting the natural history of polyp development and cancer. Initial distributions of polyps, transition and complication probabilities and cancer survival data were derived from the literature. The feasibility, sensitivity and specificity for endoscopic diagnosis of small and diminutive polyps were derived from the Veterans Affairs Lesion Interpretation and Diagnosis (VALID) study. TreeAge Pro 2011 software was used to conduct simulations with 100,000 patients with a lifetime horizon. Outcomes measured were costs, quality-adjusted life years (QALYs) and incremental cost–effectiveness ratios (ICER). Parameters were tested with probabilistic sensitivity analysis.

The initial single-polyp model indicated that endoscopic diagnosis of small colorectal polyps with a “resect and discard” strategy reduces the cost of colorectal cancer screening, but is less cost-effective than traditional colonoscopy. Further development of the model to allow for multiple polyps has also found that neither strategy dominates.

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