A student-led research publication of the George Washington University School of Medicine and Health Sciences | Spring 2022, Volume XV

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### WILLIAM H. BEAUMONT RESEARCH PRIZE WINNERS

The William Beaumont Research Awards are given to three students for outstanding research accomplishments from work submitted for publication in Fusion, the student-run research magazine at GW School of Medicine and Health Sciences.

The recipients of the 2022 William Beaumont Research Awards are:

- Alisa Malyavko, Mentor, Tushar Patel, Washington Orthopedics and Sports Medicine, "Decreased 5-Year Anterior and Posterior Revisions Following Single-Level Cervical Disc Replacement When Compared to Single-Level Anterior Cervical Discectomy and Fusion in Patients with Cervical Radiculopathy"......p. 78

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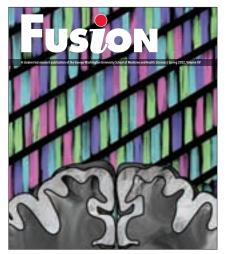
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Thomas Kohout

### Fusion

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This research journal is published by students in collaboration with the Office of the Dean and the Office of Communications



**ON THE COVER:** Illustration by Valory Vailoces, MD Program Class of 2025

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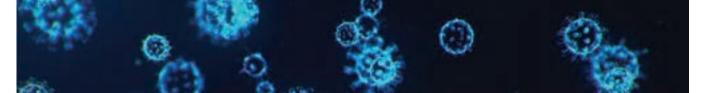
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### Evidence-Based Medicine Through Biomedical Research



Jake Adelman, MSI



Mary Pasquale, MSI

As members of the Fusion Editorial Board, we have the privilege of sharing our colleagues' research accomplishments with the GW community. The COVID-19 pandemic has highlighted the need for timely and effective communication of biomedical research to inform the practice of evidence-based medicine. Most of this effort has been underscored by the surgance of preprint services and larger journals, increasing the volume of knowledge such that researchers can help bring the pandemic to an end.

Despite students working through COVID-19-related challenges, Fusion is proud to share the largest edition to date, with over 70 abstracts from students across all MD classes and across several disciplines. As highlighted by our cover, this year we noticed a trend in pieces about neurology, psychology, and that several students took advantage of molecular biology techniques to further characterize disease pathologies.

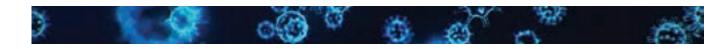
Fusion is a student-run publication that aims to showcase the research achievements of medical students at GW SMHS. The 2022 edition of Fusion includes abstracts from the basic sciences, clinical and translational research, public health, and medical education. The top abstracts from Fusion were awarded the William Beaumont Research Award and their authors will deliver oral presentations at Medical Student Research Day on April 28, 2022.

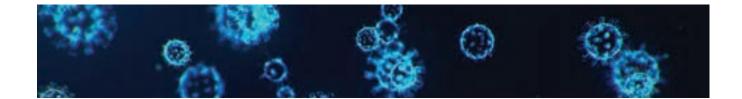
We gratefully acknowledge the following individuals without whom this edition of Fusion would not be possible: David Leitenberg, MD, PhD, associate professor of microbiology, immunology, and tropical medicine at the GW SMHS; medical director of flow cytometry and immunology at Children's National Hospital; and director of medical student research at GW SMHS and Thom Kohout, director of publications at GW SMHS. We would also like to extend appreciation for last year's Fusion editors and current Beaumont Medical Research Honor Society Co-Presidents Alice Chen, MSII and Isabel Park, MSII.

We are very proud of all of our submissions this year and hope that you enjoy this year's edition of Fusion.

Fusion Co-Directors Jake Adelman Mary Pasquale

Fusion Editors Anthara Gnanakumar Esin Namoglu Leyn Shakhtour





### Performance Despite the Pandemic

In reflecting on the past year, I think it's fair to say that it has been another year dominated by the COVID pandemic. But I am optimistic that there is an end in sight. The huge increases in cases related to the Omicron variant is clearly subsiding, and we are all adjusting to a new normal where COVID will become another endemic disease, and less of a public health emergency. There is a lot to be proud of, in terms of how the medical community has responded to the COVID pandemic. The rapid development of effective vaccines as well as new anti-viral therapeutics has been remarkable. Also, critical has been the role of physician scientists in communicating to the public about the importance of vaccines and other public health measures in limiting the spread of infections. At the same time, the COVID pandemic has also revealed unexpected challenges in the way that medical information is provided and evaluated by a significant proportion of the population. The widespread availability of unreliable and/or distorted medical guidance has made it more clear than ever that training medical students to evaluate evidence and become effective communicators is a critical skill. Encouraging and fostering student participation in research activities is an important mechanism to provide these skills.

As seen in this issue of Fusion, medical student research at the George Washington University is thriving. Despite the challenges and restrictions to on-site access due to the COVID pandemic, medical students submitted a record number of abstracts for publication in Fusion. The studies contained in this issue demonstrate significant breadth of research interest spanning basic science research, clinical studies in a wide variety of disciplines, as well as public health and medical education research.

Student participation in extracurricular research activity is also shown by the record number of students joining scholarly concentrations. 95% of the class of 2025 joined a scholarly concentration which provides support and structure to student research participation. These efforts are clearly productive, not only as shown by abstracts in Fusion, but by record participation in Medical Student Research Day (165 abstracts presented in 2021), as well as scholarly output defined by presentations at national meetings and publications in peer-reviewed journals. In the most recent graduation questionnaire that standardizes responses of students to other medical schools nationally, 74% of our students report authorship on a manuscript compared to 61% nationally.



David Leitenberg MD, PhD, associate professor of microbiology, immunology, and tropical medicine at SMHS, and medical director of flow cytometry and immunology at Children's National Hospital

These accomplishments would not be possible without the active engagement of faculty mentors. The significant effort of faculty in mentoring and training our students cannot be overstated. On behalf of our students, I thank you for your efforts!

#### David Leitenberg MD, PhD

associate professor of microbiology, immunology, and tropical medicine at SMHS, and medical director of flow cytometry and immunology at Children's National Hospital



# GW MEDICAL STUDENT RESEARCH



Alex Dobek (left) and Sarthak Shah (right) are members of the student-organized Orthopedic Summer Medical Student Fellowship program that supports students interested in Orthopedic Surgery. Several members of this group were accepted to present their research at the American Academy of Orthopedic Surgery 2022 Annual Conference in Chicago.

### NEIL ALMEIDA RECEIVES 2021 SPECK AWARD

Neil Almeida, MD '21, was selected as the 2021 recipient of the annual Doris DeFord Speck, BA '41, and George Speck, MD '41,



Neil Almeida, MSIV

Endowed Prize for outstanding accomplishments in medical student research.

Almeida, who is continuing his medical education as a neurosurgical resident at the University of Buffalo School of Medicine, is also a Class of 2021 Alpha Omega Alpha (AOA) honor society inductee, a former William H. Beaumont Research Award winner, and the recipient of a competitive fellowship from the American Brain Tumor Association and the AOA Carolyn Kuckein student fellowship.

His record of research accomplishment throughout his years at medical school includes 14 peer-reviewed manuscripts predominantly related to neurosurgery and neuro-oncology while in medical school, with five first-author submissions.

Significantly, Almeida also has played an important leadership role in medical student research organizations at GW by serving as co-president of the Beaumont student research organization and was co-founder and president of the GW student chapter of the American Association of Neurological Surgeons.

### RESEARCH FELLOWSHIP OPPORTUNITIES



A number of competitive scholarship programs are available to assist in funding exceptional projects in health care and medicine, including diversity targeted fellowships, including the Jean L. Fourcroy, MD, Research Award; Health Services Scholarships; the Lazarus Family Scholarship Program; and the WT Gill Fellowship, among others.

In 2021, 22 students were awarded a Gill Summer Research Fellowship and 54 students were earned Health Services Scholarships, both of which are internally funded programs providing stipend support for medical student summer research.

For a list of SMHS student research funding opportunities, timelines, and application tips visit the website *smhs.gwu.edu/research/ research-workforce/medical-studentresearch/medical-student-fundingopportunities.* 

### METEOR PROGRAM

The Mentored Experience to Expand Opportunities in Research (METEOR) program is a competitive fellowship for underrepresented-inmedicine students. For more information, visit the website smhs.gwu.edu/academics/ md-program/admissions/ METEOR.

### INNAUGURAL AKMAN INNOVATION AWARD

Wyn Dobbs, a rising fourth-year medical student at the George Washington University (GW) School of Medicine and Health Sciences (SMHS), was selected as the inaugural undergraduate recipient of the Akman Innovation Fund – created in honor of Jeffrey S. Akman, MD '81, RESD '85, former GW SMHS dean, and designed to foster ideas, support mentorship, and promote clinical innovation, Through his award, Dobbs will delve into the exploration, understanding, and treatment of COVID-19.

His interest in COVID-19 began as a contact tracer for the Mississippi Department of Health before shifting to more clinical work at GW SMHS. He served as a research assistant on the Moderna COVID-19 vaccine trial at GW and as senior research assistant and project manager of the GW Medical Faculty Associates (MFA) COVID-19 Recovery Clinic and Biorepository.

While researchers are still untangling the effects of post-acute sequelae of COVID-19 (PASC), or Long COVID, Dobbs, thanks to his time at the clinic, has identified a potential relationship between the disease and pre-existing asthma. As part of the mentorship component of the fund, Dobbs will work with Adrienne Poon, MD, MPH, assistant professor of medicine at GW SMHS. With the Akman Innovation Fund, he's planning to use the clinic's unique data to pinpoint patients with asthma and varying levels of COVID severity to "observe any differences in pulmonary symptoms.

# SMHS STUDENTS WIN NIH MEDICAL RESEARCH SCHOLARS FELLOWSHIPS

The National Institutes of Health (NIH) awarded fellowships to Allison Distler, MD '21, and Mario Pita, MSII, as part of the Medical Research Scholars Program.

Just 50 students representing 35 U.S.-accredited universities were selected for the

robust, mentored training fellowship. The yearlong research immersion program fosters career development for students interested in

Allison Distler, MD '21

becoming physician scientists.

Distler's project was in the National Cancer Institute's Lymphoid Malignancies Branch, working with Mark Roschewski, MD, senior clinician and clinical cirector of the NCI's Lymphoid Malignancies Branch of the Center for Cancer Research. Disltler focused on the use of a next generation sequencing assay to detect tumor clonotypes in the plasma of follicular lymphoma (FL) patients at diagnosis and with serial monitoring for detection of minimal

### WALTER FREEMAN RESEARCH WINNER

The Freeman Award is given to the graduating senior who submits the best scientific paper based on original research. For 2021, this award was split and given to two equally deserving students: Aslam Akhtar for his manuscript titled "Inducible Expression of GDNF in Transplanted iPSC-Derived Neural Progenitor Cells" published in Stem Cell Reports; and Kendrah Osei for the manuscript; "Abbreviated Breast MRI for Screening High-Risk Women: Comparison with the Full Clinical Protocol", published in the Journal of Breast Imaging.

residual disease.

Pita worked in the Social Determinants of Obesity and Cardiovascular Risk Laboratory within the National Heart, Lung, and Blood Institute (NHLBI). Under the mentorship of Tiffany Powell-Wiley, MD, MPH, Stadtman Tenure-Track Investigator with the NHLBI, Pita's project focused on the effects of neighborhood deprivation and catecholamines on the migration

of inflammatory monocytes towards arterial plaques.

"The future of medicine hinges upon developing clinician-scientists who will make

Mario Pita, MSII

and translate discoveries at the bench, achieve success against rare and refractory diseases, and address disparities in health and medicine," said Thomas R. Burklow, M.D., director of the MRSP. "[The program] offers a transformational training experience that will promote students to become leaders in American medicine."

# Effect of Mesenchymal Stromal Cell Delivery Through Cardiopulmonary Bypass in a Piglet Model

#### Alice Chen, MSII

ADVISORS:

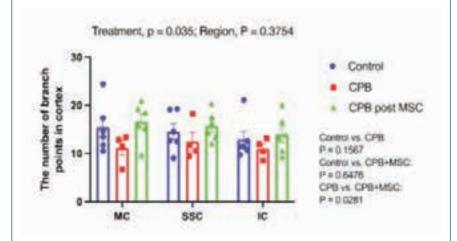
Kei Kobayashi, MD<sup>1,2,</sup> Nobuyuki Ishibashi, MD<sup>1,2,3</sup>



Department of Cardiac Surgery
 Center for Neuroscience Research,
 Children's National Hospital
 George Washington University
 School of Medicine and Health Sciences

Congenital heart disease (CHD), a structural abnormality of the heart or great vessels at birth, affects approximately 1% of live births worldwide each year. Research shows that increased severity of CHD is associated with increased frequency of neurological deficits, suggesting a direct correlation between the functioning of the heart and brain, resulting in an increased incidence of structural abnormalities of the brain in children with structural cardiac abnormalities. Young children with more complex CHDs who require cardiac surgery, including cardiopulmonary bypass (CPB), have a significantly higher incidence of developmental abnormalities and neurological deficits, including academic difficulties, behavioral abnormalities, motor delays, etc.1

Microglia, the resident immune cells in the central nervous system, play a key role in neural immune function. In a previous study, CPB and circulatory arrest increased microglia number three days after surgery. Microglia expansion was prolonged for up to four weeks.<sup>2</sup> Mesenchymal stromal cells (MSCs) are multipotent, non-hematopoietic cells that possess



**FIGURE 1:** The number of branch points in microglia in three regions of the cortex. Data values are expressed as mean  $\pm$  SEM. P-values were evaluated by two-way ANOVA with Tukey comparison (n=6, 4, 4,).

immunomodulatory and regenerative properties and regulate microglia activation. It is hypothesized that intraarterial MSC delivery through CPB in a survival porcine model is neuroprotective by modulating systemic and brainspecific inflammatory responses.<sup>3</sup>

To mimic the effects in young CHD patients, two-week old female piglets were randomly assigned to one of three treatment groups: control, CPB, and CPB+MSC. The CPB+MSC group consisted of a CPB surgery, followed by administration of MSC before weaning. Microglia undergo morphological changes from a naïve, ramified shape to an amoeboid shape under activated condition. To analyze the effects of MSCs on microglia activation, changes in the length of microglial processes and number of branch points from the nuclei were assessed.

Four weeks post-surgery, analysis using Imaris software showed that CPB reduced both the length of processes and number of branch points compared to control in three different cortex regions. CPB+MSC revealed significantly longer processes (p=0.0281) and more branch points (p=0.0232) than CPB alone, indicating that morphological changes in microglia were normalized after MSC delivery.

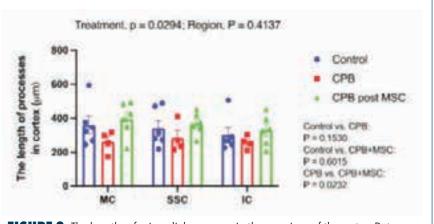
Bone-marrow derived MSCs regulate microglial activation and participate in the phenotypic switch from a pro-inflammatory state to a repair-permissive state.4 In contrast to their ramified morphology under normal conditions, activated microglia undergo structural remodeling and adopt an amoeboid morphology with highly retracted processes, a hallmark of brain inflammation, as shown in the CPB group. Microglia routinely migrate toward and cluster around sites of neuronal degeneration induced by excitotoxic injury.4 In MSC-treated animals, there are significantly fewer amoeboid microglia, with an associated increase in the length in processes and number of branch points to mitigate

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the effects of CPB, indicating attenuated activation of the microglia. MSC delivery during CPB is highly effective and shows translational potential to minimize CPB-induced systemic inflammation and microglial activation in children with CHD.5 In future studies, repeated cell administration as well as different dosages of MSCs should be tested to further optimize MSC treatment for CHD patients.

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**FIGURE 2:** The lengths of microglial processes in three regions of the cortex. Data values are expressed as mean  $\pm$  SEM. P-values were evaluated by two-way ANOVA with Tukey comparison (n=6, 4, 4,).

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# Role of HIV-1 Diversity in Sensitivity to Treatment with Monoclonal Antibodies

Leyn Shakhtour, MSI

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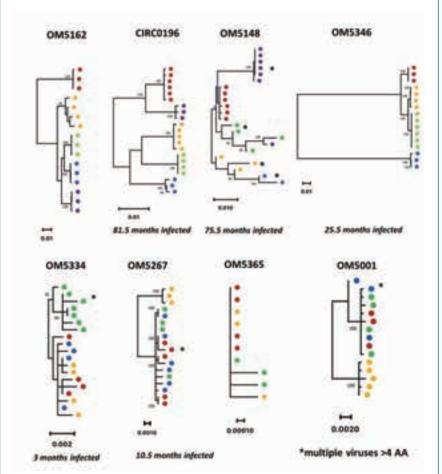
Andrew Wilson,<sup>1</sup> Rebecca Lynch<sup>1</sup>

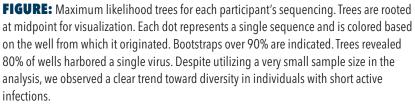


1 Department of Microbiology, Immunology, and Tropical Medicine, George Washington University School of Medicine and Health Sciences

Patients on antiretroviral therapy (ART) must maintain consistent therapy in order to avoid rebound from the latent viral reservoir. More studies are needed to explore the role viral diversity plays in the potential efficacy of treatment with broadly neutralizing antibodies (bNAbs). To do so, we have characterized HIV-1 genetic diversity in individuals with varying lengths of infection, as well as the sensitivity of their inducible virus reservoir to bNAbs.

Peripheral blood mononuclear cells were collected from 8 well-characterized HIV-1+ males on ART with varied lengths of active infection. Resting CD4 T cells were plated at multiple dilutions in replicate and maximally stimulated to induce latent viruses to grow in the supernatants. Cultures were screened for the presence of virus antigen and those that were positive were collected for analysis. 3-5 viral supernatants of virus outgrowth were obtained from each individual. In order to genetically define each person's viral reservoir, the HIV-1 envelope gene (env) was amplified and sequenced from these reservoir-derived outgrowth viruses by single genome amplification (SGS). At least three sequences were obtained





from each well's supernatant. All sequences from an individual were aligned and used to generate a neighborhood-joining tree. If a single virus outgrowth was confirmed phylogenetically in the well, these sequences were then used to generate a well consensus sequence. Consensus sequences were generated and aligned to produce a maximum-likelihood tree displaying all sequences in this study. Wells containing single viruses were then titered and measured for sensitivity to bNAbs in the standard HIV-1 TZM-bl neutralization assay.

Neighbor-joining trees for each participants' sequencing revealed 80% of wells harbored a single virus. Analyzing consensus sequences from

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single virus wells, we observed a wide range of genetic diversity within each individual as measured by average pairwise distance. For individuals with higher levels of viral diversity, no wells had identical viruses and branched separately; however, low-diversity individuals harbored essentially 1-2 different viruses. Despite utilizing a very small sample size in the analysis, we observed a clear trend toward lower diversity in individuals with short active infections. We observed that greater diversity is associated with increased resistance to bNAbs. Overall, our data suggests that average pairwise distance (APD) of HIV-1 env increases with infection length and is associated with greater resistance to bNAbs; however, individuals who start ART early in infection and develop limited virus variation are more likely to be sensitive to bNAb treatment.

# Face Mask Debris: An Analysis of Respirable and Inhalable Particles using Scanning Electron Microscopy and Raman Spectroscopy

Amanda Burns, MSII

**CO-AUTHOR:** Shiori Echizenya<sup>1</sup>

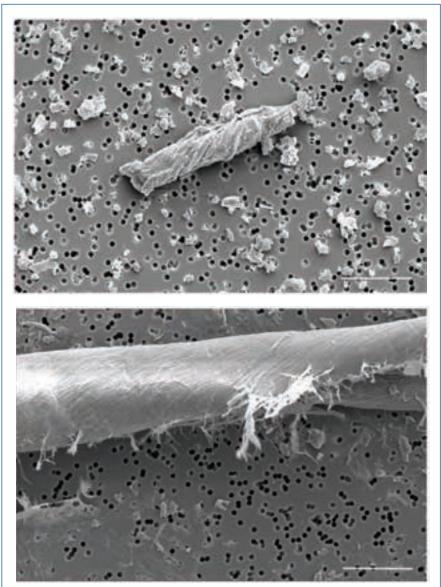
**ADVISOR:** Kent E. Pinkerton, PhD<sup>1</sup>



1 Center for Health and the Environment, University of California, Davis

\*Disclaimer: Masks are essential to lowering the risk of acquiring airborne diseases and exposure to pollution such as wildfires. This project was not created to justify not wearing a mask but to look at the possibility of respirable particles coming from masks.

Face masks have become ubiquitous and a critical protection in daily life for users due to the COVID-19 pandemic as well as to California wildfires. Due to the increased demand and supply shortages, the Centers for Disease Control and Prevention recommends the reuse of approved particulate filtering facepiece respirators or the alternative use of other personal protective face coverings such as surgical masks or fabric masks. These medical face masks, excluding fabric masks, are usually made from three polypropylene layers. This is a petroleum-based plastic and creates concern for the risk of inhalation of microplastics, risk of long-term usage, as well as environmental contamination.1 Some studies have shown masks can release fiber debris, in particular, respirable microplastics and have concluded there can be a microplastic inhalation risk when reusing masks.<sup>2</sup>



**FIGURE:** A. (top panel) SEM image containing particles from a mechanically aged N95 mask with a scale bar of 10  $\mu$ m. B. (bottom panel) SEM image of a particle from a new fabric mask with a scale bar of 10  $\mu$ m.

The objective of this project was to identify the potential respirable particles from new and aged masks (N95, surgical, and fabric).

Sonication with deionized water prefiltered through  $0.4 \mu m$ 

polycarbonate membrane filters was used to maximize the release of debris particles from new and aged masks. Aged masks were created through

Continued on p. 13

metronomically-timed mechanical rubbing at 120 beats per minute. Each mask was individually sonicated with released particle collected on a 0.8µm polycarbonate membrane filter for scanning electron microscopy (SEM) analysis. A 0.8 µm aluminum sputter coated polycarbonate membrane filter was also used for Raman spectroscopy analysis. Particle collection was done for new and aged N95s, surgical masks, and fabric masks along with controls of deionized water preparations. SEM images of non-overlapping fields were acquired for each sample and were used to classify 100 randomized particles within each field based on size and structure. The particle size classes by diameter were  $\leq 2.5 \ \mu m$  which were considered as respirable, 2.5-10 µm which was considered as inhalable, and  $\geq 10 \,\mu\text{m}$  and structure classes were described as fibrous versus non-fibrous. To be considered fibrous, particles had a length-to-width ratio ≥3:1. For determination of elemental composition, some particles were also analyzed using energy-dispersive X-ray. Masks were used for Raman Spectroscopy to create plastic reference spectrums which were matched to samples collected from sonication and filtered through the aluminum sputter-coated polycarbonate membrane filters.

These results demonstrate the possibility of inhalable and respirable particles coming from all three types of face masks. N95 masks released **TABLES 1–3:** Tables display the results of the particle count and classification. All three types of masks for both new and used, over 95% of particles release from sonication were inhalable, over 85% of particles were respirable, and greater than 70% were non-fibrous. For the new mask group, N95 masks had the greatest proportion of respirable particles released, followed by surgical masks, then fabric masks. For the aged mask group, N95 masks demonstrated the release of the greatest proportion of respirable particles, followed by fabric masks, and then surgical masks. Fabric masks released the greatest proportion of fibers within the new masks group and aged group; however, N95 FFR released the greatest proportion of respirable fibers within both mask groups.

New Masks	N95	Surgical	Fabric	Aged Masks	NBS	Surgical	Fabric
<25µm	94.3	92.0	85.0	<2.5 µm	93.7	85.7	90.3
2.5-10 µm	53	5.3	11,3	25-10 µm	5.7	8.7	9.7
>10 µm	0.3	27	37	>10 µm	0.7	21	0.0
respirable	943	92.0	85.0	respirable	91.7	88.7	90.3
infoliative.	897.	107.3	00.2	infuliation	94.3	17.3	300.0
Masks No. Ibran	86.0	05.7	78.5	Masks Non-Abrown	46.0	87.0	713
New	N95	Surgical	Fabric	Aged	N95	Surgical	Fabric
Non-fibrous	86.0	95.7	78.3	Non-fibrous	95.0	87.0	713
Férrus	14.0	43	21.7	Fòrous	5.0	13.0	28.7
iona o mara	Contractor and	-	- CALLER OF	Same		and the second	
Table 3. Pe	rcentage of	respirable vs ir	nhalable fibe	rs. Calculated v	with fibers or	and the second second second second	100000
New Masks	N95	Surgical	Fabric	Aged Masks	N95	Surgical	Fabric
Respirable fiber %	9525	84.8%	60.0%	respirable fiber %	\$3.3%	87.2%	88.4%
Inhalable Iber 15	100.0%	100.0%	63.1%	Inhalable Aber 15	100.0%	100.0%	100.0%

the greatest proportion of respirable particles and fabric masks released the greatest proportion of inhalable particles. Respirable particles were both fibrous and non-fibrous with aerodynamic characteristics to enter the deep lungs and long-term retention in the lungs. However, these particles were released by sonication and thus, the collection process may not replicate the actual breathing patterns of humans to demonstrate the actual numbers of particles released from a mask during respiration.

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# Dexmedetomidine in Alcohol Withdrawal Syndrome: Are We Intubating Less?

Varun Mehta, MSIII, and Sangrag Ganguli, MSIII

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**INTRODUCTION:** About half of the adults in the U.S. consume alcohol regularly, with 10% of this population reporting excessive alcohol usage.1 Roughly three percent of this cohort have reported experiencing alcohol withdrawal symptoms.<sup>2</sup> Symptoms are complex and can often vary from person to person. However, the timeline in which the symptoms occur is well characterized. In the first 6-12 hours after the last drink, patients may present with nausea, dizziness, anxiety, and tremors. After 12 hours, patients begin to experience psychosis in the form of auditory and/or visual hallucinations. By 24-48 hours, these symptoms may be complicated by severe shaking and mild seizures. After 48 hours, patients may experience the most feared complication of alcohol withdrawal: delirium tremens.3 With this condition, elevated heart rate, increased temperature, seizures, hypertension, severe psychosis can greatly increase mortality associated with alcohol withdrawal syndrome (AWS).

The first-line treatment of AWS includes benzodiazepines such as lorazepam, diazepam, and chlordiazepoxide. A more recent addition for AWS treatment is dexmedetomidine, an alpha-2 agonist shown to improve refractory delirium tremens by decreasing the length of active alcohol withdrawal symptoms.4 When used for sedation of non-intubated patients during the treatment of alcohol withdrawal, dexmedetomidine may reduce symptom severity while preventing respiratory depression. The addition of dexmedetomidine to a Clinical Institute Withdrawal Assessment (CIWA) based benzodiazepine treatment strategy, the standard treatment modality for alcohol withdrawal, may

scores greater than 7 between January 2019 and March 2020 were included. We collected demographic and clinical data including CIWA score, benzodiazepine usage, dexmedetomidine usage, and intubation. The primary outcome measure was intubation. Odds ratio (OR) was determined for intubation events based on exposure to dexmedetomidine and benzodiazepine usage.

**RESULTS:** A total of 68 charts were analyzed. The mean patient age was 51, 54 patients were men. 44 patients received standard CIWAbased benzodiazepine therapy without dexmedetomidine, of these 24 (54.5%) were intubated during hospitalization. Twenty-four patients received dexmedetomidine in addition to standard

The addition of dexmedetomidine to a Clinical Institute Withdrawal Assessment (CIWA) based benzodiazepine treatment strategy, the standard treatment modality for alcohol withdrawal, may reduce benzodiazepine usage and ultimately the need for intubation.

reduce benzodiazepine usage and ultimately the need for intubation. We sought to determine whether the addition of dexmedetomidine to a CIWA-based benzodiazepine protocol reduced the risk of intubation for patients admitted to our intensive care units with severe alcohol withdrawal.

**METHODS:** A single center, retrospective cohort study at our urban, academic medical center compared patients receiving dexmedetomidine in addition to the standard CIWA-based benzodiazepine protocol to standard therapy alone. Patients with CIWA therapy; seven of these patients (29.1%) were intubated, with OR = 0.34 [95% CI: 0.12-0.99; p=0.048]. The mean CIWA score was 14.9 for the standard therapy group and 17.4 for the group receiving dexmedetomidine (p=0.21). The mean dose of IV lorazepam given in the 12 hours prior to intubation were 0.9 mg for the standard therapy group and 1.8 mg for the dexmedetomidine group (p=0.65).

**CONCLUSIONS:** In this series of patients with severe alcohol withdrawal

Continued on p. 15

syndrome, the addition of dexmedetomidine to CIWA-based benzodiazepine therapy correlates with a significantly lower frequency of intubation. No significant benzodiazepine-limiting effect was demonstrated. Future prospective analysis is necessary to explore the relationship of these observations.

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# Preoperative Point-of-Care Ultrasound of the Lateral Parapharyngeal Wall Thickness Predicts Difficulty in Mask Ventilation

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**ADVISORS:** Eric Heinz, MD, PhD,<sup>1</sup> Raymond Pla, MD<sup>1</sup>

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Mask ventilation (MV) is one of the key steps in airway management as it is essential for reducing the incidence of hypoxia and hypercarbia during periods of apnea during intubation. Although patient factors such as age, BMI, lack of teeth, presence of a beard, and history of a sleep breathing disorder can increase suspicion for a difficult MV, at present there is no single test that can definitively predict the difficulty of MV. The measurement of the lateral parapharyngeal wall thickness (LPWT) has been shown to correlate with severity of obstructive sleep apnea (OSA), which is a known risk factor for difficult MV.1 This is likely due to a narrower and more collapsible lateral airway in patients with sleepdisordered breathing. Given that OSA is presumed to be a clinical indicator of difficulty in MV, and that the size of the LPW is indicative of presence and



**FIGURE:** Ultrasonographic measurement of LPWT. A. Scanning position to obtain LPWT measurement. With the patient supine, a high-frequency curvilinear probe was placed on the lateral neck in the longitudinal plane. B. Identification of the ICA was assisted with color Doppler imaging, and the lateral wall of the pharynx was visible as a hyperechoic interface (arrows). Distance was measured from the internal border of the ICA to the LPWT.

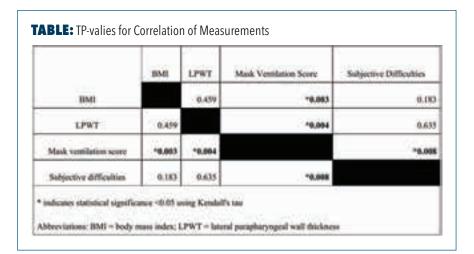
Abbreviations: ICA = internal carotid artery; LPWT = lateral pharyngeal wall thickness

Continued on p. 17

severity of OSA, we hypothesized that the LPW can help predict the difficulty of MV in routine airway management of elective surgical patients. The primary aim of this study was to assess the efficacy of point-of-care ultrasound (POCUS) to measure the LPWT in the preoperative setting to help predict difficulty of MV.

Eighty-eight adult patients who were scheduled for elective surgery requiring general anesthesia were enrolled in the study. In the preoperative arena, the patient was placed in the supine position, and a curvilinear US transducer was placed in the coronal orientation on the lateral neck below the mastoid process (Figure 1). The LPWT was measured as the distance between the inferior border of the internal carotid artery (ICA) and the lateral wall of the pharynx, as described by Chen et al.<sup>2</sup> Standard preoperative measurements including body mass index (BMI), neck circumference, and Mallampati score were also recorded. Following intubation, difficulty of MV was assessed by the attending anesthesiologist and graded according to a standardized MV scale developed by Han et al, in which a score of 1 corresponds to an easy MV and a score of 4 is assigned when the provider is unable to MV.3 The subjective difficulty was also assessed and recorded.

A total of 88 patients were enrolled. Measurements of the LPWT ranged



from 1.52 to 4.43 centimeters. 71% of patients were easy MV (MV score= 1), 18% required oral airway (MV score= 2), 10% required two providers (MV score= 3), and one patient was unable to be mask ventilated (MV score= 4). There was a statistically significant correlation between LPWT and MV score (P = 0.004) (Table 1). Ordinal logistic regression analysis revealed that every 1 cm increase of LPWT was associated with a 3.17 odds of increase in MV score. There was also a statistically significant correlation between BMI and MV score (P = 0.003) as well as between subjective difficulty of MV and standardized MV score (P = 0.008) (Table 1). There was no correlation between LPWT and BMI (P = 0.459) or between LPWT and Mallampati score (P = 0.381).

In addition to confirming that standard preoperative measurements such as BMI are useful in predicting difficult MV, our study also suggests that POCUS measurement of the LPWT is predictive of difficult MV prior to intubation and can be utilized for airway management planning.

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## Lung Nodule Detection via Deep Reinforcement Learning

#### Issa Ali, MSII

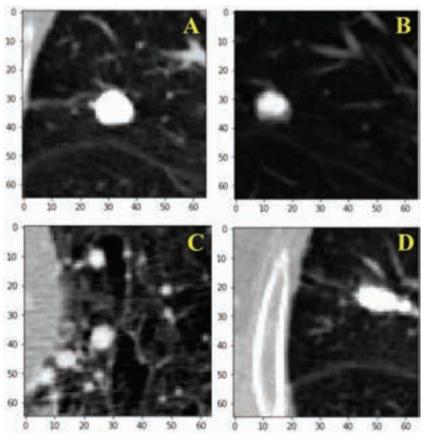
#### **ADVISORS:**

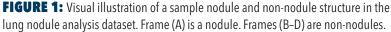
Jun Deng, PhD,<sup>1</sup> Gowthaman Gunabushanam, MD<sup>2</sup>

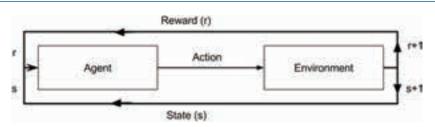


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Lung cancer is the most common cause of cancer-related death globally. As a preventive measure, the United States Preventive Services Task Force (USPSTF) recommends annual screening of high risk individuals with low-dose computed tomography (CT). The resulting volume of CT scans from millions of people will pose a significant challenge for radiologists to interpret. To fill this gap, computer-aided detection (CAD) algorithms may prove to be the most promising solution. A crucial first step in the analysis of lung cancer screening results using CAD is the detection of pulmonary nodules, which may represent early-stage lung cancer. The objective of this work is to develop and validate a reinforcement learning model based on deep artificial neural networks for early detection of lung nodules in thoracic CT images. Inspired by the AlphaGo system, our deep learning algorithm takes a raw CT image as input and views it as a collection of states, and outputs a classification of whether a nodule is present or not. The dataset used to train our model is the LIDC/IDRI database hosted by the lung nodule analysis (LUNA) challenge. In total, there are 888 CT scans with annotations based on agreement from at least three out of four radiologists. As a result, there are 590 individuals having







**FIGURE 2:** A diagram of a reinforcement model. An agent in a given state (s) and reward (r) completes an action in the environment. This results in a change of environment and either an increase/decrease in reward as a result of that action.

one or more nodules, and 298 having none. Our training results yielded an overall accuracy of 99.1% [sensitivity 99.2%, specificity 99.1%, positive predictive value (PPV) 99.1%, negative predictive value (NPV) 99.2%]. In our test, the results yielded an overall accuracy of 64.4% (sensitivity 58.9%, specificity 55.3%, PPV 54.2%, and NPV 60.0%). These early results show promise in solving the major issue of false positives in CT screening of lung nodules, and may help to save unnecessary follow-up tests and expenditures.

## Treatment Trends and Surgical Outcomes of Pituitary Adenoma in the Elderly: A National Cancer Database Analysis

Eric J. Chalif, MSII

**ADVISOR:** Manish K. Aghi, MD PhD<sup>1</sup>

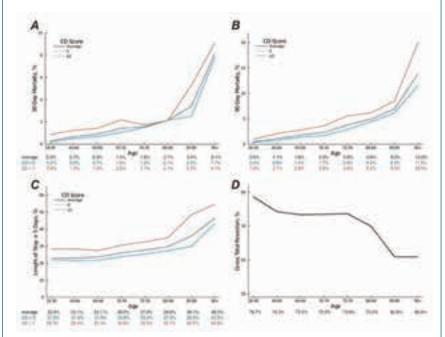


1. University of California, San Francisco, California, Department of Neurological Surgery

The majority of pituitary adenomas (PA) in the elderly ( $\geq 65$  years old) are nonfunctional and treated with surgical intervention when symptomatic. This study involving a large multicenter national registry examined treatment trends and surgical outcomes in this population compared to nonelderly patients (<65 years old)

Our study queried the National Cancer Database (NCDB) for adult patients  $\geq$  18 years old who were diagnosed with pituitary adenoma from 2004 to 2016. Univariate and multivariate logistic regression was used to evaluate the prognostic impact of age and other covariates on 30/90-day post-surgical mortality (30M/90M), length of inpatient stay  $\geq$  5 days (LOS), and extent of resection (EOR). A systematic literature review was performed to compare these real-world outcomes to previous series.

The 96,399 cases met inclusion criteria, of which 25, 464 elderly PA patients were identified. 27.0% of total cases were microadenomas and 73.0% were macroadenomas. 53.3% of elderly PA patients were treated with surgery, 1.9% underwent up-front radiotherapy, and 44.9% were observed without treatment. Elderly patients had increased



**FIGURE 1:** Patient Age by Post-Surgical Outcomes Stratified by Charlson-Deyo Comorbidity Score. 1A: 30 Day Mortality; 1B: 90 Day Mortality; 1C: Length of Stay  $\geq$  5 Days; 1D: Gross Total Resection. Outcomes generally worsen with increasing patient age, which persists in subgroups based on comorbidity status.

**TABLE 1:** Multivariate Analysis of Surgically Treated Elderly Pituitary Patients (n=12,365)

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C.I. = Confidence Interval; CD = Charlson-Deyo Comorbidity Score; LOS = Length of Stay; OR = Odds Ratio; STR = Subtotal Resection.

The OR values are calculated with multivariate logistic regression. \*\* Indicates statistical significance.

Continued on p. 20

rates of 30M: 1.4% vs 0.6%, 90M: 2.8% vs 0.9%, prolonged LOS: 26.1% vs 23.0%, and subtotal resection: 27.2% vs 24.5% (all p≤001) compared to nonelderly PA patients (Figure 1-D). On multivariate analysis, age, tumor size, and Charlson-Deyo comorbidity score (CD score) were independently associated with worse post-surgical mortality (Table 1). High volume facilities (HVF) had significantly better outcomes compared to low-volume facilities (LVF): 30M (0.9% vs 1.8%, p<0.001), 90M (2.0% vs 3.5%, p<0.001), and LOS (21.8% vs 30.0%, p<0.001), but no statistical difference in gross total resection (73.7% vs 71.8%, p=0.083). With increased patient age, the mortality difference between HVF and LVF was greater. A systematic literature review comprised of 22 studies demonstrated an elderly PA mortality rate of 0.7%, which is dramatically lower than real world NCDB outcomes and speaks to substantial selection bias in previously published literature.

In conclusion, our findings confirm that elderly patients with PA are at higher risk of mortality when compared to their younger counterparts. Surgical risk in this age group may have been previously underreported in the literature, and surgical resection at HVF may allow for improved outcomes.

#### **TABLE 2:** Literature Review

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EES = Endoscopic Endonasal Surgery; GTR = Gross Total Resection; HSPA = Hormone Secreting Pituitary Adenoma; LOS = Length of Stay; MTS = Microscopic Transphenoidal Surgery; NFPA = Nonfunctioning Pituitary Adenoma; TC = Transcranial; TS-NOS = Transphenoidal Surgery–Not Otherwise Specified.

\*Represents a median value.

‡ Extracted here is data on the subset of pituitary adenoma patients from a larger series on intracranial tumors in the elderly.

§ Extent of resection defined as "Radical tumor removal".

¶ Extent of resection defined as combined GTR or near total resection (90-100% resection).

#These values are combined with younger PA cohort.

### Percutaneous Cryoablation on an Insulinoma in a Patient with Symptomatic Hypoglycemia Refractory to Bland Microsphere Embolization

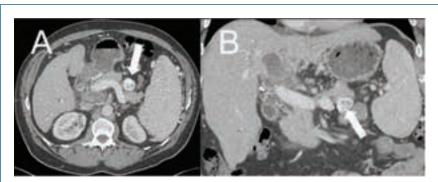
Nima S. Ghorashi, MSII

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We present a 62-year-old male with hepatitis C cirrhosis, portal hypertension and inoperable cholangiocarcinoma undergoing chemotherapy, who was found to have a 1.6 cm enhancing exophytic pancreatic body mass on a computed tomography (CT) done for staging of his cholangiocarcinoma (Fig. 1). Four months after diagnosis of the pancreatic mass, the patient developed symptoms of intractable fasting hypoglycemia requiring three admissions within one month to outside institutions for dextrose infusions. The patient reported no history of diabetes or hypercalcemia and no family history of parathyroid, pituitary, or pancreatic disease. He was initially treated conservatively with diazoxide and achieved euglycemia. However, two months after starting diazoxide, he developed palpitations, requiring its cessation. His hypoglycemia returned and within two weeks he presented to our institution with a fasting glucose level of 14 mg/ dL. A 10% dextrose (D10) intravenous infusion was initiated and surgical consultation was obtained, given the intractable nature of the symptomatic hypoglycemia. Surgical intervention was determined high-risk considering



**FIGURE: 1** A. Axial and B. sagittal contrast enhanced CT images demonstrating an enhancing mass within the ventral body of the pancreas (white arrow).

the patient's underlying cirrhosis and portal hypertension. The patient was referred to interventional radiology and was initially felt that the patient could potentially benefit from bland embolization as previously described.1

Selective bland embolization was performed using 70-150 µm LC Bead LUMI radiopaque microspheres via microcatheter (Fig. 2A). Immediate post-embolization noncontrast CT demonstrated contrast staining of the pancreatic mass compatible with successful LC Bead LUMI microsphere embolization (Fig. 2B). However, the patient's severe hypoglycemia did not improve, requiring continued hospitalization and D10 infusion. Two days post-embolization, it was decided to attempt cryoablation of the insulinoma using CT-guidance. The patient underwent CT-guided placement of two cryoprobes. The freezing protocol consisted of 2 cycles of a 10-minute freeze and 8-minute active thaw. Periodic CT imaging was performed during the procedure to monitor in real-time the "ice ball" that was formed, which completely covered of the targeted mass, including a 5 mm

margin of normal pancreas (Fig. 3). After finishing 2 freeze/thaw cycles, the probes were removed. Within 3 hours of completing the cryoablation, the D10 infusion was tapered and serum glucose levels returned to normal. The patient was discharged post-operative day 2. The patient remains stable clinically 18 months post-cryoablation, with no further hypoglycemic events. The patient underwent CT scans at 2, 6, 12, and 18 months, all demonstrating lack of enhancement within the pancreatic mass. The patient continues to undergo systemic treatment for his inoperable cholangiocarcinoma.

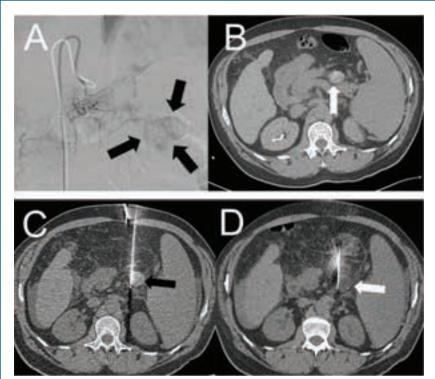
Cryoablation has been used as a palliative treatment modality for locally advanced pancreatic cancer but has not been previously described in the treatment of a pancreatic insulinoma.2,3 Aside from potential thermal injury to the pancreatic parenchyma leading to acute pancreatitis, additional anatomic considerations are necessary to consider, including the risk of injury to the pancreatic duct, common bile duct, duodenum, and adjacent vasculature.

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As the developing ice ball is well visualized on CT during cryoablation, the zone of ablation can be more precisely monitored in comparison to hyperthermic ablation techniques, such as radiofrequency ablation (RFA) and microwave ablation (MWA). In this patient, cryoablation was utilized, as the insulinoma was localized near the splenic vein, inferior mesenteric vein, and duodenum, necessitating precise control of the ablation zone. RFA or MWA would have posed increased risk of thermal injury. To our knowledge, the use of cryoablation to treat symptomatic hypoglycemia from a pancreatic insulinoma has not been previously described.

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**FIGURE 2: A.** Digital subtraction angiography via a microcatheter within the anterior pancreaticoduodenal artery demonstrating a hypervascular mass within the pancreas (black arrow). **B.** A noncontrast CT performed post-embolization demonstrating radiopaque beads within the insulinoma (white arrow). **C.** Axial noncontrast CT image demonstrating the pancreatic mass (black arrow) with a cryoprobe along its medial border. **D.** Axial CT fluoroscopy image demonstrating an ice ball within the targeted insulinoma (white arrow) with cryoprobe medially.

# Clinical Outcomes of Non-Hodgkin Lymphoma Patients on Acalabrutinib Including Off-Label Utilization

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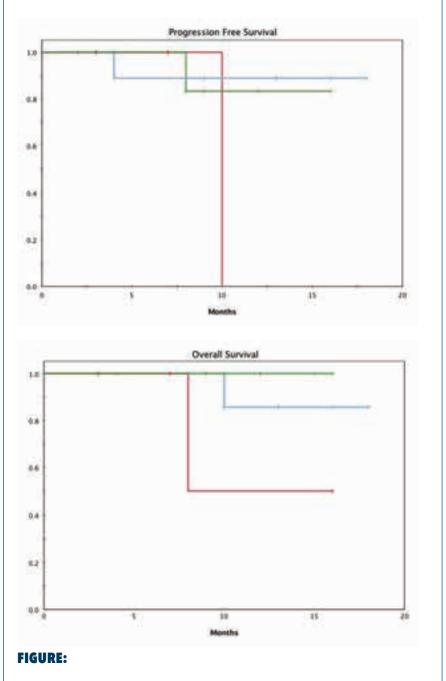


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Acalabrutinib (acala), a Bruton's Tyrosine Kinase inhibitor (BTKi), received accelerated FDA approval for treatment of mantle cell lymphoma (MCL) in 2017. Since approval, there has been limited "real world" data, especially in the setting of off-label utilization. We performed a retrospective analysis of all patients (pts) who had received acala for NHL at the University of Pennsylvania for on- and off-label indications. We examined the safety and efficacy of acala; response assessments were determined by treating physician using standard, diseasespecific criteria. Survival analyses were completed as described by Kaplan and Meier.

We identified 23 pts treated with acala (83% males [n=19]). The majority (65%) of pts received acala 100 mg twice daily, with the rest receiving 100 mg once daily. Diagnoses were chronic lymphocytic leukemia (CLL) (n=10; 44%), MCL (n=9; 39%), and diffuse large B-cell lymphoma (DLBCL) (n=4; 17%). One DLBCL was GCB subtype and three were ABC subtype; two of four DLBCL pts were transformed from



marginal zone lymphoma and two were de novo. The median age at diagnosis was 61 years, median age at acala start was 69 years. Sixteen (70%) of the pts were Ann Arbor/Rai stage III or IV at diagnosis. The median number of prior therapies was three (range 0-12). Of note, the GCB-DLBCL patient had previously undergone both allogeneic (alloSCT) and autologous (autoSCT)

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stem cell transplants and four of the MCL patients (44%) also had prior allo and/or autoSCTs. All CLL pts (n=10; 100%) had at least a partial response (PR), including 1 complete response (CR) by iwCLL criteria. In the MCL cohort of 9 pts, 8 (88%) had at least a PR (including 1 CR), and one patient (11%) had stable disease (SD). One MCL pt achieved a CR and moved to alloSCT. One (25%) of the DLBCL pts had a PR (ABC subtype), and three (75%) had SD (one GCB and two ABC-DLBCL.) At the time of last follow up, two DLBCL pts had SD and remained on acala, one progressed after 10 months, and one died due to disease progression. The 12-month progression free survival (PFS) was 89% for CLL and 83% for MCL; 12 months overall survival (OS) was 89% for CLL and 100% for MCL respectively. (Figure 1).

Of note, 16 pts (70%) had been on ibrutinib previously and all pts discontinued (d/c) ibrutinib due to intolerance. Acala related toxicities included: 26% (n=6) arthralgias/myalgias, 13% (n=3) infection, 13% (n=3) bruising/ bleeding, 9% (n=2) rashes, and 4% (n=1) diarrhea. Ten (43%) of pts tolerated acala without any side effects. Of note, there were 6 pts with a history of atrial fibrillation (afib) or an afib-related toxicity of ibrutinib, and none of our pts experienced new afib while on acala. In total, six pts d/c acala: 1 patient moved to alloSCT, 3 had disease progression, 1 d/c due to toxicity (fatigue/bleeding/ bruising), and 2 pts died. One death was unrelated to lymphoma (renal cancer).

Our "real world" experience with acala demonstrates its efficacy and

tolerability in the setting of NHL, supporting previously published literature.1,2 The response rates in our CLL and MCL cohorts were 100% and 88% respectively and only one patient discontinued acala for intolerance. Our experience supports pilot data showing efficacy and tolerability and thus further research in other B-cell malignancies is warranted, especially in the aggressive/refractory DLBCL population.

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# Database Mining of Cancer Datasets for Roles of P38 MAPK Isoforms Head and Neck Squamous Cell Carcinoma

#### Simran Sandhu, MSII

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As cancer therapy targeting becomes increasingly specific, an area of potential therapeutic targets that remains largely unelucidated includes the p38 family of mitogen-associated protein kinases (MAPK). These protein kinases are implicated in adaptive cellular response to numerous stressful stimuli and also modulate different processes important to tumorigenesis. However, the isoform-specific roles of these MAPKs have largely not been studied in cancers, including head and neck squamous cell carcinoma (HNSCC). Furthermore, it is currently clinically pertinent to stratify HNSCC by whether a patient is positive for human papilloma virus (HPV), and investigation of HPV+ HNSCC versus HPV- HNSCC in relationship to the isoforms has also not been performed.1 We examined correlations of  $p38\alpha$ , p38β, p38γ, and p38δ isoforms (encoded by MAPK14, MAPK11, MAPK12, and MAPK13 genes, respectively) in HNSCC (unstratified and stratified by HPV status) with gene expression, survival, prognosis, immune cell tumor infiltration, and biological pathways.

These analyses were performed on HNSCC datasets from The Cancer Genome Atlas (TCGA) using **TABLE:** Summary of significant results for each MAPK isoform in unstratified, HPV--HNSCC. Row one displays statistically significant changed in each isoformas gene expression in the three groupings of HNSCC tumor analysis with comparison to normal tissue. Row two highlights the variations in overal survival in each group on the basis of high MAPK isoform expression. Row three displays whether overall immune cell infiltration into the tumor was increased, decreased, or mixed on the basis of statistically significant correlations between a protein kinase and a specific immune cell infiltrate. Row four similarly outlines the levels of immune cell biomarkers (increased, decreased, or mixed) on the basis of statistically significant correlations between a protein kinase and the specific immune biomarker.



several web-based bioinformatic tools including GEPIA, LinkedOmics, TIMER and TIMER2.0, as well as GSCA and GSCAlite.

Our results highlighted distinct roles for each of the p38 isoforms in processes important to tumorigenesis in HNSCC which remained largely consistent between HPV- HNSCC and unstratified HNSCC (Table). In HNSCC patients, higher p38β/MAPK11 expression level correlated with improved overall survival, and increased levels of immune biomarkers in the tumor microenvironment. p38y/MAPK12 expression level was higher in HNSCC tumors compared with normal tissue, and was especially high in HPV- relative to HPV+ HNSCC tumors. Immune biomarker levels were both positively and negatively correlated with p38y/ MAPK12 expression in HNSCC and HPV- HNSCC samples, but mostly positively correlated in HPV+ HNSCC samples. p38δ/MAPK13 expression was overwhelmingly negatively correlated with immune biomarker levels; conversely, p38a/MAPK14 expression positively correlated with immune biomarker levels in HNSCC samples.

Given our results, in HNSCC, we postulate a tumor suppressing

role for  $p38\alpha$  and  $p38\beta$ , and a tumor promoting role for p38y and p38ô. Of special interest, p38β/MAPK11 and p38y/MAPK12 are suggested to play larger roles in HNSCC than their counterparts p38α/MAPK14 and p38δ/ MAPK13, which have traditionally been more associated with pathways of tumorigenesis. Furthermore, our analysis did not display large differences in the protein kinases' functions in tumor-related pathways, regardless of stratification of HNSCC by HPV status. Exploration of these results may lead to improved pharmacologic therapy for HNSCC, and our data suggest possible comprehensive applicability of potential therapeutic regimens with regards to HPV+ and HPV- HNSCC patients. Additionally, further investigation of the novel roles of p38β/MAPK11 and p38γ/MAPK12 in HNSCC may be expanded to other cancer types and provide potential therapeutic targets there.

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1 Cancer Genome Atlas Network (2015). Comprehensive genomic characterization of head and neck squamous cell carcinomas. Nature, 517(7536), 576–582. https://doi.org/10.1038/ nature14129

# Transcriptomic Evidence of Distinct Roles for p38 MAPK Isoforms in Cutaneous Melanoma

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Therapeutic treatments for cancers are moving in the direction of personalized medicine, but the data for novel therapeutic targets are limited. One such group of targets includes the p38 family of mitogen-associated protein kinases (MAPK), which are involved in adaptive cellular stress response and varying roles in tumorigenesis. In cutaneous melanoma (SKCM), isoform-specific roles of these MAPKs have largely not been elucidated. Additionally, these isoforms have not been investigated in context of clinically important driver mutations, BRAF and NRAS.1 We examined correlations of  $p38\alpha$ ,  $p38\beta$ ,  $p38\gamma$ , and p38 $\delta$  isoforms (encoded by MAPK14, MAPK11, MAPK12, and MAPK13 genes, respectively) with gene expression, survival, prognosis, immune cell tumor infiltration, and biological pathways in SKCM.

These analyses were performed on SKCM datasets from The Cancer Genome Atlas (TCGA). This SKCM dataset was analyzed as a whole (unstratified SKCM) as well as divided into BRAF-mutated and NRASmutated SKCM. Aforementioned analyses were conducted using several web-based bioinformatic tools: GEPIA, **TABLE 1:** Summary of signidificant results for each MAPK isoform in unstratified, BRAD-mustated, and NRAS-mutated SKCM. Row one displaces statistically significant changes in each isoforms gene expression in the three groupings of SKCM tumors with comparison to normal tissue. Row two ighlights the increase in disease-free survival assiociated with increased p288/MAPK13 expression. Row three displays whether overall immune cell infiltration into the tumore microenvironment was increased, decreased, or mixed on the basis of statistically significant corrolations between a protein kinase and a specific immune cell infiltrate. Row four similarly outlines the levels of immune cell biomarkers (increased, decreased, or mixed) on the basis of statistically significant correlations between a protein kinase and the specific immune biomarker.

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LinkedOmics, TIMER and TIMER2.0, as well as GSCA, GSCAlite, and cBioPortal. Further BRAF- and NRASmutated immune cell infiltration and immune biomarker expression analyses were performed manually using GraphPad Prism.

Our results highlighted distinct roles for each of the p38 MAPKs in SKCM, and even identified differences for the isoforms based off driver mutation stratification.

Table 1 provides

a summary of gene expression, disease free survival, immune cell infiltration, and immune cell biomarker expression for each of the four isoforms in the three SKCM groups. In SKCM data,  $p38\beta/MAPK11$  expression level was increased specifically in BRAF-mutated tumors, but correlated with increased levels of immune biomarkers in the tumor microenvironment for both BRAF- and NRAS- mutated tumors. High  $p38\gamma/MAPK12$  expression in unstratified, BRAF- mutated, and NRAS- mutated tumors correlated with decreased levels of immune infiltration and immune biomarkers, and  $p38\alpha/MAPK14$  expression was correlated with a mixed response: positively correlating with specific

In BRAF-mutated SKCM, our results suggest a tumor promoting role for all isoforms; in NRASmutated SKCM, p388/MAPK13 and p38a/ MAPK14 displayed tumor suppressing roles.

> biomarkers and negatively correlating with others. p38δ/MAPK13 expression was increased in BRAF-mutated SKCM, and positively correlated with immune biomarker levels, but in unstratified and NRAS-mutated SKCM, expression was decreased, although the same correlation with immune biomarker levels remained. Of note, in unstratified SKCM, high levels

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of MAPK13 associated with improved disease-free survival.

Given these summarized results, as well as identification of pathway specific functions of the isoforms and specific identities of the over- and underrepresented immune cell biomarkers, we suggest differing tumor promoting and tumor suppressive roles for the p38 isoforms in SKCM (Table 2). In BRAF-mutated SKCM, our results suggest a tumor promoting role for all isoforms; in NRAS-mutated SKCM, p38 $\delta$ / MAPK13 and p38 $\alpha$ /MAPK14 displayed tumor suppressing roles. Unstratified data points to a tumor promoting role for p38 $\gamma$ /MAPK12, a suppressive role **TABLE 2:** Summary of postulated tumor promoting and tumor suppressive roles for p38/MAPK isoforms in unstratified, BRAF-mustated, and NRAS-mutated SKCM.



for p38 $\delta$ , and a mixed suppressive and promoting role for p38 $\alpha$ .

Our analysis demonstrated unique roles for the isoforms in SKCM, with functional differences particularly emphasized in the driver mutations for SKCM. Further investigation of these relationships raises the possibility of pharmacologic targeting for a more individually-specialized medical approach in treatment of SKCM.

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# Antisynthetase Syndrome-Associated Cardiomyopathy

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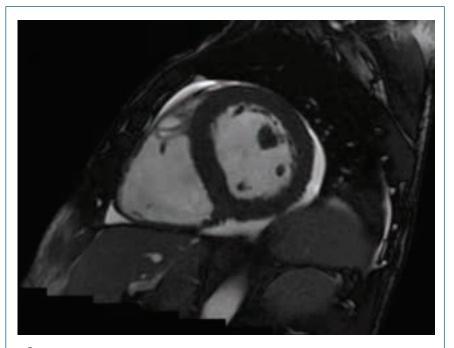
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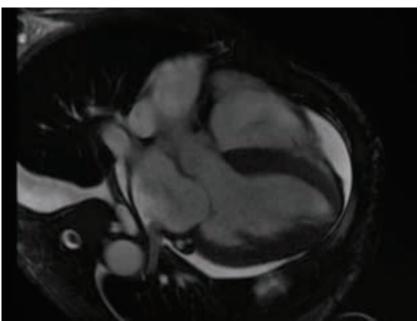
**INTRODUCTION:** Antisynthetase syndrome (aSS) is an autoimmune myopathy characterized by interstitial lung disease, myositis including dermatomyositis or polymyositis, Raynaud's phenomenon, and arthritis of anti-tRNA synthetase antibodies.<sup>1</sup> Antisynthetase syndrome seldom presents with cardiac involvement, as one study reported a frequency of only 3.4%. Here we present a case of antisynthetase syndrome with induced cardiomyopathy.<sup>2</sup>

CASE: A 59-year-old man with a history of cardiomyopathy, left ventricular systolic dysfunction, and interstitial lung disease, presented to the emergency department (ED) with shortness of breath, muscle weakness, and weight loss. Prior cardiac history includes biventricular heart failure with 20-25% ejection fraction. Upon presentation, the patient underwent a cardiac MRI which revealed severely dilated cardiomyopathy, right moderate circumferential pericardial effusion with no focal or diffuse areas late gadolinium enhancement (Figure). A previous diagnosis of aSS was made from the presence of antibodies against EJ, aminoacyl tRNA synthetase, and Ro60+.

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a.



### b.

**FIGURE:** Cardiac MRI showing moderate to severe concentric left ventricular hypertrophy, left ventricular dilation with left ventricular end diastolic volume of 217 ml, severe right ventricle dilation with right ventricular end diastolic volume of 263 ml as well as moderate circumferential pericardial effusion. a. Short axis diastole. b. Long axis diastole.

Electromyography of right vastus lateralis, right deltoid, and right sternocleidomastoid muscles were all consistent with inflammatory myositis. Prior to presentation at the ED, the patient was on immunosuppressants, but had a history of non-compliance. In the ED, labs were consistent with profound electrolyte disturbances including a potassium of 1.6, magnesium of 0.04, corrected serum calcium of 4.9, as well as BNP of 15,000, and troponin of 0.04. A CT scan was consistent with cardiomegaly, enlarged pulmonary artery and lower lobe predominant interstitial fibrotic changes. An EKG revealed left anterior fascicular block. Left heart catheterization was negative for ischemic disease, while right heart catheterization was compatible with mild pre-capillary pulmonary hypertension. The treatment plan for this patient was multifaceted given the complex nature of the case. For heart failure, the patient was treated with spironolactone, carvedilol, Sacubitril/Valsartan, as well as a maintenance diuretic. For aSS the patient was given IVIG for 5 days. Follow-up echocardiogram prior to discharge indicated anEF of 35-40%. The patient was eventually discharged with close outpatient follow-up.

**DISCUSSION:** Given the patient's initial presentation, different etiologies were ruled out including parasitic,

ischemic, as well as infiltrative diseases. In this case, the patient tested positive for anti-aminoacyl tRNA synthetase antibodies, which are pathognomonic for aSS.<sup>3</sup> Amongst all presentations for cardiac antisynthetase syndrome, cardiac involvement with histologic evidence of myocarditis has been well documented in the literature; although in clinical practice the diagnosis is typically based on less invasive tests such as MRI, EKG, and troponin levels.<sup>4</sup> Myocarditis as the etiology of dilated, as in this case, cardiomyopathy occurs in 30% of cases. A systematic review in patients with active myopathies suggested that the most common ECG findings include conduction abnormalities leading to premature ventricular contractions, left anterior hemiblock, and AV block. The gold standard for myocarditis remains endomyocardial biopsy; however, in this case, biopsy was deferred given the clinical evidence of active myositis secondary to anti-synthetase syndrome and successful treatment with corticosteroids and IVIG. Elsewhere in the literature, cases of aSS cardiomyopathies have been successful managed with adjuvant medications such as azathioprine, cyclophosphamide, and rituximab.5

**CONCLUSION:** aSS is a rare syndrome that is not typically associated with cardiac involvement. In cases where there is an association, patients commonly present with histological evidence of myocarditis, and less commonly with dilated cardiomyopathy and features of heart failure. Therapies are not well studied, and medical management varies from case to case. Directed guideline-medical therapy, IVIG and steroid use in antisynthetase syndrome provided clinical benefit in this case.

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# Long-Term Arrhythmia Outcomes in Adults with Repaired Tetralogy of Fallot

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**BACKGROUND:** Tetralogy of Fallot (TOF) is among the most common cyanotic congenital heart diseases in adults, accounting for up to 10% cases.<sup>1,2</sup> While 30–40-year survival is excellent at 85%-90%, patients are at risk of arrhythmias and sudden cardiac death (SCD) after repair.<sup>3,4</sup> The objective was to determine the frequency of various arrhythmias and assess therapies used to treat each type.

**METHODS:** A retrospective review was conducted of all adults with repaired TOF (n=242) from the Washington Adult Congenital Heart Program at Children's National Hospital. Data were extracted from patient charts and analyzed in R, Version 4.1. We used a Chi-squared Goodness of Fit test to compare frequency of any arrhythmia with the 43% reported by Khairy et al.<sup>5</sup>

**RESULTS:** With a mean age of 38.1 years (55% female, 64% white), and mean follow-up duration of 30.2 years, 29.8% of the cohort (n=72) developed at least one arrhythmia, significantly lower than the 43% previously reported (X2=17.3; p < 0.0001). The most frequent was ventricular tachycardia

Arrhythmia Type	Response to medical therapy	Response to ablation	PM implant	ICD Implant	ICD Therapies
Sick sinus syndrome (n=1)	0	0	- F	0	0
3rd degree AV block (#=8)	0	0	8	0	0
Atrial tachycardia (n=22)	9	3	0	0	0
AVNRT (n=1)	0	1	0	0	0
Atrial flutter (n=25)	5	9	0	0	0
IART (#=5)	2	3	0	0	0
Atrial fibrillation (n=9)	3	1	0	0	0
PVC's (n=7)	5	1	0	0	0
Ventricular tachycardia (n=37)	6	2	0	28	12

(n=37). Medical therapy had a 41.6% success rate; ablation (n=27) carried a 74.1% success rate. Devices (pace-maker=9; ICD=28) were implanted in 37 patients (ICD, 67.8% primary prevention). Twelve patients with ICDs had shocks (three inappropriate), nine had antitachycardia pacing, and six had both. In our series, there were no cases of SCD.

**CONCLUSION:** The frequency of arrhythmias in adults with repaired TOF approximates 30% in our cohort, less than what has been reported previously. Catheter ablation was effective for those who failed medical therapy. Future investigation will aim to identify risk factors associated with the development of various arrhythmias.

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# Evaluation of a Screening Protocol for Implantable Cardioverter-Defibrillator Related Anxiety and the Impact of COVID–19

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Two to five years following implantable cardioverter-defibrillators (ICD) implantation, clinical studies suggest that up to 20% of ICD recipients are at high risk for the development of severe anxiety-related disorders such as posttraumatic stress disorder (PTSD) or generalized anxiety disorder (GAD), while in the era of COVID-19, this number may be greater.<sup>1</sup> Therefore, the main objective of our study was to implement a web-based self-report questionnaire to evaluate the impact of COVID-19 on the psychosocial distress of ICD patients within the GW ICD clinic community.

All ICD patients reporting to the George Washington University Cardiology ICD clinic for routine follow-up care from March 2020 to September 2021 were asked if they would like to volunteer to complete an electronic tablet-based (Survey Monkey<sup>™</sup>) self-report questionnaire. An informed consent letter was offered and read to the participants. To assess ICD-induced anxiety, depression, and exacerbated psychosocial distress from COVID-19, we adapted the Florida Shock Anxiety Scale (FSAS), Patient Health Questionnaire-2 (PHQ2), GAD-2, Diagnostic and Statistical Manual of Mental Disorders(DSM-5) panic attack scale, and the Coronavirus Anxiety Scale (CAS).<sup>2-4</sup> This protocol was adapted from a similar study from the cardiac screening program at the University of California, Los Angeles.<sup>5</sup> Survey completers were included in the analysis for positive screens across the total cohort. Statistical analysis for comparisons

included a twosample t-test for continuous variables and Fisher's exact test.

A total of 104 (58 male and 46 female) ICD recipients within the

last 5 years completed the questionnaire. Within this population, 21% screened positive for generalized anxiety (GAD-2) while 16% for PTSD / panic symptoms (DSM-5 Panic).Of these subjects, 28% reported receiving a shock from their device. No statistically significant differences in positive screens were determined for male and female subject comparisons. Positive screens for males vs. females respectively were (3.5% vs. 8.7% FSAS), (15.5% vs. 8.7% PHQ2), (20.7 % vs. 13% GAD-2), and (8.6% vs.19.6% PTSD). Contrary to our hypothesis regarding COVID19, no subjects satisfied the cutoff score for the CAS.

These findings support previous research in identifying anxiety and

PTSD-like symptoms in 16%–21% of ICD recipients, while psychosocial distress from COVID-19 was not evident. Given the impact of anxiety related dis-orders on adverse cardiovascular outcomes, this at-risk population may benefit from a mental health service screen and referral program.

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Given the impact of anxiety related dis-orders on adverse cardiovascular outcomes, this at-risk population may benefit from a mental health service screen and referral program.

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# Cresting Mortality: Defining a Plateau in Ongoing Massive Transfusion

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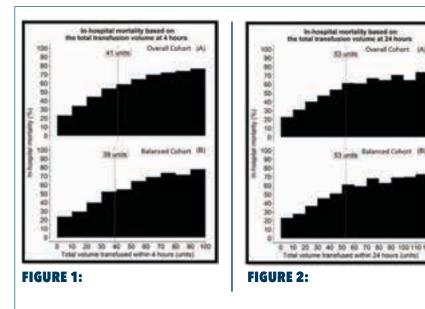
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Blood-based balanced resuscitation is the standard of care in massively bleeding trauma patients, but there is no data as to when this therapy no longer significantly improves mortality. We sought to determine if there is a threshold beyond which further massive transfusion will not improve in-hospital mortality.

The Trauma Quality Improvement database was queried for all adult patients registered between 2013 and 2017 who received at least one unit of blood (PRBC) within four hours of arrival. In-hospital mortality was evaluated based on the total transfusion volume (TTV) at four and 24 hours in the overall cohort (OC) and in a balanced transfusion cohort (BC), composed of patients who received a transfusion at a ratio of 1:1 – 2:1 PRBC:plasma. A bootstrapping method



in combination with multivariable Poisson regression (MVR) was used to find a cutoff after which additional transfusion of blood products no longer affected in-hospital mortality.

MVR was used to control for age, sex, race, highest abbreviated injury score in each body region, comorbidities, advanced directives limiting care, and the primary type of surgery performed for hemorrhage control.

The OC consisted of 99,042 patients of which 28,891 and 30,768 received a balanced transfusion during the first four and 24 hours, respectively. The mortality rate plateaued after a TTV of 41 (95% CI, 40-41) units in the OC at 4 hours and after a TTV of 53 (95% CI, 52-53) units at 24 hours following admission. In the BC, mortality plateaued at a TTV of 39 (95% CI, 36-41) units and 53 (95% CI, 41-42) units at four and 24 hours following admission, respectively (figures 1, 2).

These [total transfusion volumes] can be used as markers for resuscitative timeouts in order to assess the plan of care moving forward.

> Transfusion thresholds exist beyond which ongoing transfusion is not associated with any clinically significant change in mortality. These TTVs can be used as markers for resuscitative timeouts in order to assess the plan of care moving forward.

# Endotracheal Tube Surveillance: Can Point of Care Ultrasound Replace Chest Radiographs?

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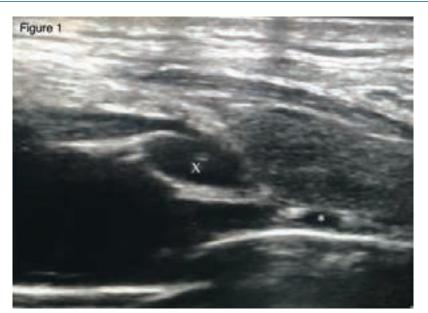
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There are many potential complications associated with endotracheal tube (ETT) malpositioning in critical care settings, such as accidental extubation, bronchial migration or vocal cord herniation.<sup>1,2,3</sup> These events can prolong patient recovery and lengthen ICU stays.<sup>4</sup> The goal of this study is to demonstrate that point of care ultrasound (POCUS) is noninferior to chest X-ray (CXR) in identifying proper ETT depth.

The high specificity and NPV values suggest that if ETT position appears within normal limits on POCUS (tip of ETT between 3–7 tracheal rings), ETT position is likely adequately positioned even when performed by novices.

We conducted an observational cohort study of intubated patients across four multidisciplinary ICUs at an urban academic hospital. Each patient



**FIGURE:** The image is a photo from a POCUS assessment. A linear transducer is placed superficial to the cricoid cartilage in the sagittal plane. The X demonstrates the cricoid cartilage and \* marks the 1st tracheal ring. The hyperechoic lines are the ETT, which runs beyond the 1st tracheal ring in this image.

underwent daily POCUS assessment of ETT positioning by novice sonographers (medical students). ICU/ED

> physicians led four hourlong informal training sessions to teach medical students POCUS technique. Subjects were excluded if they were COVID positive, had c-spine precautions, had recent neck surgery, or planned to be extubated within 24 hours. Patient ETT position was measured using POCUS assessment (balloon cuffborder ending between 3–7 tracheal rings) and compared to daily CXR

landmarks (5 cm +/- 2 cm above carina). Recommendations based on sonographic and radiographic landmarks were compared to assess sensitivity and specificity of POCUS to evaluate need for ETT repositioning. Statistical significance was assessed using the Clopper-Pearson binomial confidence interval.

Twenty patients were enrolled for a total of 62 ventilator-days. The cohort was majority female (55%), Black/ African American (75%) and mean age 55 +/- 18 years. In 58 instances (93.5%), both sonographic and radiographic landmarks agreed on maintenance of ETT position. In one instance (1.6%), sonographers recommended ETT repositioning while radiographic landmarks did not. In three instances (4.8%), ETTs appeared in place by sonographic but not radiographic landmarks. The data yields a specificity of 98.31% CI [90.91,99.96] for proper ETT

Continued on p. 34

placement with a negative likelihood ratio of 1.02 CI [.98, 1.05] and negative predictive value (NPV) of 95.08% CI [94.92,95.24].

The high specificity and NPV values suggest that if ETT position appears within normal limits on POCUS (tip of ETT between 3–7 tracheal rings), ETT position is likely adequately positioned even when performed by novices. Further studies should investigate the use of POCUS as a monitoring alternative and as a reliable tool postintubation to confirm ETT depth.

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# Decision Support Alerts for Delays in Trauma Resuscitations

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Children's National Hospital is a Level-1 pediatric trauma center serving the District of Columbia metropolitan area. About 600 children are treated through the trauma department each

The introduction of the IV slider decreased the percentage of premature checkoffs, leading to fewer missed alerts in task completion delays.

year, with each case video recorded for quality, safety, and research review. During pediatric trauma resuscitations, a senior resident or fellow uses a digital checklist based on the Advanced Trauma Life Support (ATLS) protocol,1 indicating completion of tasks while junior surgical residents, nurses, and respiratory therapists provide handson care. Prior work showed that the "Confirm intravenous (IV)/intraosseous (IO) access has been established" task was often checked-off before completion.<sup>2,3</sup> Discrepancies between the state of resuscitation and information recorded on the ATLS checklist regarding IV access is problematic,

hindering both team communication and decision support.<sup>4</sup> To address this discrepancy and support delay alerts, we implemented a progress slider. Unlike other tasks in the protocol, the process of establishing IV access requires multiple steps. While the checkbox only supports a binary outcome, the progress bar allows the leader to indicate if the task is not started, in progress, or complete. After releasing this feature on the checklist, we evaluated the accuracy of documentation before and after its introduction.

A Python script was used to parse 140 pediatric resuscitations from April 2018-May 2019 and determined that the median time from patient arrival to IV access confirmation was seven

> minutes. Delay alerts were implemented based upon this time or after the secondary survey, whichever came first.<sup>5</sup> The IV task slider was implemented in November 2020; 218 pediatric resuscitations from June 2020 to May 2021 were video reviewed for IV access confirma-

tion and compared to alert triggers to determine the accuracy of alerts. Alert accuracy was defined as false alert, missed alert, true alert, or true non-alert. The number of false and missed alerts were then analyzed with the IV slider implementation at three intervals: checkbox only, checkbox and slider, and slider alone.

Statistical analysis identified no significant differences in the number of delays between each cohort. The percentage of missed alerts decreased with the introduction of the IV slider and the elimination of the checkbox design (76.7% vs. 40.0% vs. 10%; p < 0.001). The percentage of false alerts increased with

the same progression (14.3% vs. 23.7% vs. 36.6%; p=0.02).

**CONCLUSIONS:** The introduction of the IV slider decreased the percentage of premature checkoffs, leading to fewer missed alerts in task completion delays. The same feature, however, increased the rate of cases with false alarms. Further modifications to the checklist will be necessary to minimize false alerts.

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# Examining the Association of Sleep Disturbances with Older Adult Age in Atopic Dermatitis Patients

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Atopic dermatitis is a chronic, inflammatory skin disease associated with sleep disturbance. When caring for geriatric patients, several factors such as sleep disturbance, polypharmacy, cognition, social support, and mobility should be considered. Our study investigated the association of older adult age with atopic dermatitis severity and sleep disturbances.

This was a cross-sectional, dermatology practice-based study of adults (≥18 years) with atopic dermatitis diagnosed by Hanifin-Rajka criteria. Patients were serially recruited from the eczema clinic at an academic medical center between 2014–19. Patients underwent full body skin exam and completed electronic questionnaires. Atopic dermatitis severity was assessed using Eczema Area and Severity Index, SCORing Atopic Dermatitis total and itch subscores, Investigator's Global Assessment, Patient-reported Global

Assessment of atopic dermatitis severity, and Patient-Oriented Eczema Measure. Frequency of sleep disturbances was assessed, including difficulty falling asleep and staying asleep.

Older adult age

 $(\geq 65 \text{ years})$  was not associated with AD severity in the following measures (adjusted odds ratio [95% confidence interval] for Eczema Area and Severity Index: 1.47 [0.68-3.18]; total SCORing Atopic Dermatitis: 1.10 [0.52-2.34] and itch subscore: 1.00 [0.55-1.81]; Investigator's Global Assessment: 1.87 [0.98-3.56]; Patient-reported Global Assessment of atopic dermatitis severity:

0.80 [0.45-1.41]; Patient-Oriented Eczema Measure: 0.55 [0.29-1.06]). However, older adult age was associated with increased number of nights of sleep disturbance from atopic dermatitis (2.14 [1.16-3.92]). Older adult age was also associated with increased fatigue (1.81 [1.05-3.09]), trouble sleeping (1.98 [1.16-3.36]), and trouble staying asleep

When caring for geriatric patients [with Atopic dermatitis], several factors such as sleep disturbance, polypharmacy, cognition, social support, and mobility should be considered.

(2.26 [1.32-3.89]), but not with difficulty falling asleep (1.16 [0.66-2.03]), in atopic dermatitis patients.

While older adult patients with atopic dermatitis had similar disease severity compared to younger adults with atopic dermatitis, they had more profound sleep disturbances than younger adults, particularly trouble staying asleep.

# Evaluating Provider Perceptions and Attitudes About the Unique Needs of Older Adult Patients in Dermatology Clinics

## Jaya Manjunath, MSII

**ADVISOR:** Adam Friedman, MD<sup>1</sup>



perceptions and attitudes about the unique needs of older adult patients in dermatology. 169 health care practitioners completed the survey. 92.9% of the survey respondents were dermatologists, and 6.5% were dermatology advanced practice providers.

The following barriers to care in older adult patients were identified by dermatology providers (%): hearing problems (82.9%), lack of a social support system (82.8%), immobility (74.4%), ability of the patient to communicate clearly (69.5%), transportation (77.5%), financial limitations (72.2%), Medicare limitations (66.9%), poor psychosocial functioning (77.5%) and telehealth due to the COVID-19 pandemic (71.2%). Additionally, providers identified the following barriers to treatment in the older adult population: poor psychosocial functioning (89.9%), polypharmacy (87.8%), lack of social support system (88.5%), poor adherence to medications (81.1%), and lack of a primary care physician (72.3%).

Overall, practitioners selected lack of social support system, difficulty in comprehending treatment plans, and limited financial means as the three most pressing issues affecting the care of older adult patients. Additional research is warranted to develop interventions to reduce barriers to care and treatment for older adult patients in dermatology clinics.

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Previous literature has identified important principles of geriatrics to consider in older adult dermatology patients, including cognition, polypharmacy, mobility, and social support. We aimed to assess provider

# Evaluation of Cannabis and Cannabinoid Product Use, Knowledge and Attitudes in the Eczema Community

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**ADVISOR:** Adam Friedman, MD<sup>2</sup>

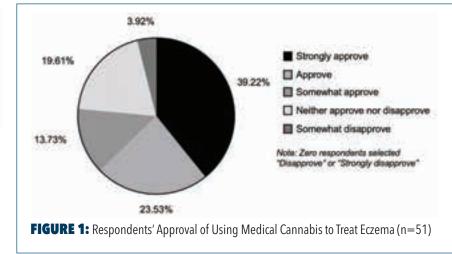


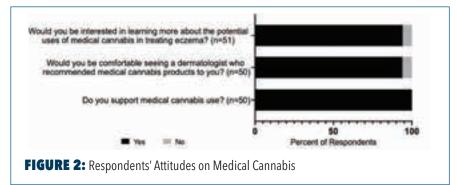
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Current data supports the potential for targeting the cutaneous endocannabinoid system to treat eczematous dermatoses.<sup>1-3</sup> However, our understanding of patient knowledge and utilization of cannabis/cannabis-derived products as treatments for eczema is limited, highlighting both a gap and opportunity to engage with the eczema community.

An online survey was used to assess the use, knowledge, and attitudes of a broad scope of cannabis product types was advertised by the National Eczema Association (NEA) via social media and NEA network dissemination.

Of the 76 respondents to the survey, 69 (88.46%) were individuals diagnosed with eczema and seven (8.97%) were primary caregivers of a dependent diagnosed with eczema. Respondents most frequently used OTC products purchased without recommendation from a dermatologist (22 [36.07%], n=61) and least frequently used medical cannabis recommended by a dermatologist (2 [3.12%], n=64). Most respondents held favorable attitudes on the usage of medical cannabis to treat eczema ("strongly approve," 20 [39.22%], and "approve," 12 [23.53%], n=51) (Figure 1).





All respondents supported medical cannabis use (50 [100%], n=50) and most respondents (47 [94%], n=50) would be comfortable seeing a dermatologist who recommended medical cannabis (Figure 2). 94% of respondents (47, n=50) would be interested in learning about using medical cannabis for treatment of eczema, but most had never discussed this topic with their health care provider (54 [93.10%], n=58). 46.67% of respondents (28, n=60) were unsure if OTC cannabis-derived products were regulated by the FDA.

Eczema patients are open to learning about cannabinoids and many are already using OTC products. As both consumer interest/use and the cannabis industry continue to outpace medical research and guidelines, dermatologists need to be prepared to counsel patients on cannabinoid applications in dermatology.

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# Identifying Factors Associated with Multi-Biologic Use at an Academic Center

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Though biologic agents have shown excellent efficacy in treating many patients with moderate to severe plaque psoriasis, a subset of these patients are refractory to treatment with multiple biologic agents.1 Certain variables such as demographics, degree of disease severity, genetics, and prior experience with biologic therapy have been shown to influence response to single biologic therapy in patients with plaque psoriasis.<sup>2</sup> We examined clinical data from 222 psoriasis patients at UCSF; 171 reported use of only a single biologic agent and 51 reported prior use of three or more biologics at enrollment from 2006 to 2020. We analyzed demographic features, clinical features, and co-morbidities associated with use of three or more biologics. On multivariate analysis, use of three or more biologics was associated with greater duration of psoriasis (22.9 vs. 19.3 years [p = .01]), initial presentation of psoriasis on the gluteal cleft (15.7% vs 4.7% [p=0.05]), less family history of psoriasis (43.1% vs 54.7% [p = .01]), and lower prevalence

of high cholesterol (19.6% vs 22.8% [p=0.008]). Erythrodermic type psoriasis (13.7% vs 2.9% [p=0.06] trended towards significance with use of three or more biologics). These results may suggest certain subsets of patients with psoriasis are harder to treat with biologics. In the next phase of this project, patient data (demographics, disease severity, treatment history, etc.) will be collected using a novel, physician crowd-sourced database that will allow physicians to contribute cases of psoriasis patients who have failed multiple biologics or cases who have responded to a single biologic.

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# Single Cell Transcriptomic Analysis of Cutaneous T-cells in Psoriasis

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 Amgen Research Department of Inflammation and Oncology Psoriasis is an immune-mediated disease characterized by skin and systemic inflammation that affects 125 million people worldwide. However, the underlying pathways contributing to psoriasis pathogenesis have not been fully elucidated. This project utilizes single-cell transcriptomes of T-cells and other immune cell types from healthy and psoriatic skin in an effort to identify key biomarkers and pathways of psoriasis. T-cells were clustered into subtypes and differential gene expression analysis was performed between lesional and healthy skin to identify psoriatic marker genes in each T-cell

subtype. Regulatory CD4+ T-cells in psoriasis lesional skin were found to upregulate cytokines such as IL-32, as well as genes in the interferon-gammamediated signaling, NF-kB signaling, and putrescine catabolic pathways. As a result, psoriatic Tregs may amplify several of the pathways behind psoriasis and drive inflammation via IL-32, which has been previously found to be significantly upregulated in plaque psoriasis. Ongoing work includes using stratification by HLA type, VDJ analysis to more closely investigate psoriatic TCR abnormalities, and incorporation of more patient data.

# Clinical Translational Research: Emergency Medicine

# RNA Biomarkers of Host Immune Activation in Suspected Abdominal Infections: More Advanced Diagnostics for Abdominal Infections with RNA (MADAIR)

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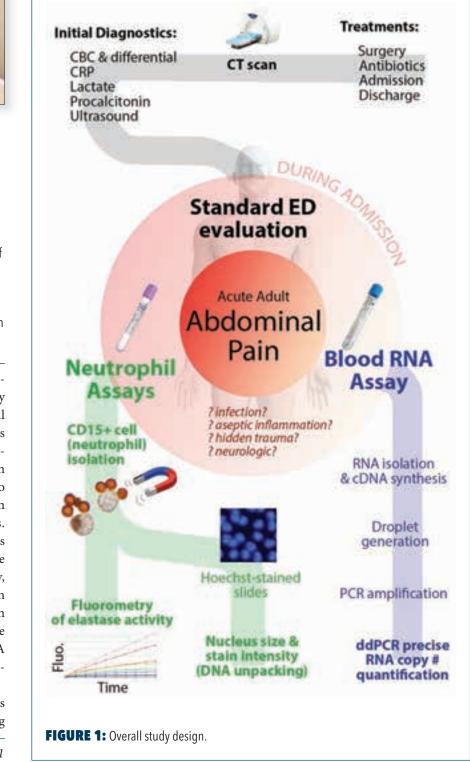


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Abdominal pain is a common presentation in United States Emergency Departments (EDs).<sup>1</sup> Intra-abdominal infections (IAIs), such as appendicitis and diverticulitis, contribute to a significant proportion of abdominal pain cases,<sup>2</sup> but it can be challenging to distinguish them from abdominal pain arising from non-infectious causes. Computerized tomography (CT) is the most specific and sensitive in the diagnosis of most IAIs but is costly, carries a risk of malignancy, and can prolong length of stay in the ED.<sup>3,4</sup> In our prospective observational study, we tested the diagnostic utility of mRNA biomarkers from circulating neutrophils in blood (RNAv).

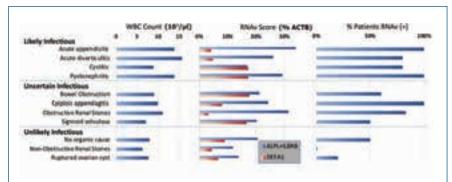
**METHODS:** A cohort of 542 patients at the GW Hospital ED presenting



Continued on p. 41

with abdominal pain were screened for inclusion and exclusion criteria to obtain 100 patients, all of whom provided informed consent. All subjects enrolled in the study were clinically diagnosed through CT imaging and conventional laboratory tests. Whole blood was collected, from which RNA was isolated. Additionally, CD15+ cells, buffy coat cells, and platelets were isolated from a subset of subjects. Droplet digital PCR (ddPCR) was performed to quantify neutrophil activation transcripts neutrophil defensin 1a (DEFA1), alkaline phosphatase (ALPL), and interleukin 8 receptor ß (IL8RB/ CXCR2). Transcript abundance was calculated as a percentage of Actin B (ACTB) transcript. Neutrophil elastase activity of isolated CD15+ cells was measured through a fluorometric and colorimetric assay (Figure 1).

**RESULTS:** Based on a previous study, we established cutoffs for the presence of an IAI, considered to be RNAv positive (+), as  $\geq 20$  %ACTB for ALPL + IL8RB and/or ≥10 %ACTB for DEFA1.5 When clinical outcomes were grouped based on probability of infectious etiology, RNAv exhibited high sensitivity in diagnosing likely infections: appendicitis (10/10), diverticulitis (5/6), cystitis (3/3), peritonitis (1/1), pyelonephritis (5/5), and tubo-ovarian abscess (1/1) (Figure 2). Among 34 cases with a clinically unlikely IAI, RNAv detected immune activation in 12 cases that included a clinical diagnosis of fibroids, gastritis, or ruptured ovarian cyst. In the Unlikely Infectious group, RNAv was positive for nine of the 18 with no organic cause of abdominal pain, which suggests that conventional diagnostics can miss up to 50% of IAIs in the ED. When compared with



**FIGURE 2:** RNA Biomarkers relative to clinical diagnosis in patients with abdominal pain. The subject groupings were classified based on their final diagnosis of conditions that are "Likely", "Uncertain", or "Unlikely" infectious. For each final diagnosis, the mean white blood cell count (WBC) (left graph), mean RNAv Score (middle graph), and percentage of patients with abnormal RNAv score (right graph) are shown.

the Unlikely Infectious group, it was found that the Likely Infectious group had higher white blood cell count (OR=24.89, p<0.003), neutrophil to lymphocyte ratio (OR=6.82, p<0.020), and %ALPL+%IL8RB (OR=9.38, p<0.000). When assessing correlations between the RNAv test and conventional laboratory tests, the absolute neutrophil count has a moderate to strong positive correlation with RNAv scores except DEFA1 which is consistent with previous work: %ALPL (r=0.70), %DEFA1 (r=0.14), %IL8RB (r=0.40), combined %ALPL and %IL8RB (r=0.58). In a subset of 15 patients from which CD15+ cells were isolated, neutrophil elastase activity was also positively correlated with RNAv score (r=0.65).

**CONCLUSION:** The RNAv test is highly sensitive in detecting likely infectious causes of abdominal pain. If further confirmed, it may provide valuable clinical utility by assisting in ruling out infectious causes of abdominal pain before the use of imaging, invasive surgical procedures, or antibiotics. The positive association between RNAv and neutrophil elastase activity suggests that both tests can detect neutrophil activation in response to infection.

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# In Emergency Department Patients with Biliary Colic, Hospital Admission is Associated with Higher Costs but Not with Better One-Year Outcomes in Analysis of a Statewide Database

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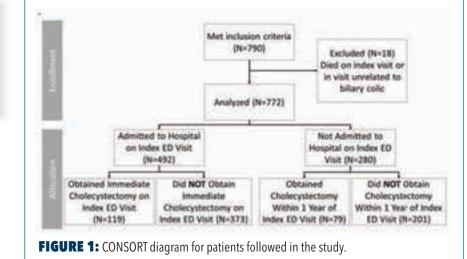


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**STUDY OBJECTIVES:** Although approximately 335,000 cases of biliary colic present to emergency departments (EDs) in the US annually, minimal data exists on the benefits of hospital admission for these patients.1 While there is limited evidence that ED readmissions contribute to increased patient costs for these patients, there is wide variability in the assessed need for hospital admission and/or surgical intervention.2,3 Our objective was to compare one-year surgery rates, ED visits, complications, readmissions, and costs in ED patients with uncomplicated biliary colic who were admitted versus those that were discharged.

**METHODS:** Using the State ED Database (SEDD) from the Maryland Healthcare Cost and Utilization Project (HCUP), a census of all ED visits in the state, we identified patients with a primary diagnosis of uncomplicated biliary colic seen between 2016 and 2018. We divided patients into those initially admitted and initially discharged. With unique identifiers from



ambulatory surgery, inpatient, and SEDD databases, we followed selected patients for one-year outcomes. We used Medicare Relative Value Units (RVUs) and HCUP cost-charge ratio files to estimate direct costs of care, and then performed a multivariate logistic regression analysis comparing groups.

**RESULTS:** Of the 772 patients eligible for the study, 64% (N=492) were admitted to the hospital while 36% (N=280) were discharged. Admitted patients had significantly higher repeat hospitalizations per patient (0.037  $\pm$  $0.018 \text{ vs } 0.007 \pm 0.010)$  and one-year costs (\$9542 ± \$571 vs \$1035 ± \$87) than those discharged on initial visit. There was no significant difference in recurrent ED visits rates, deaths, or new-onset complications of biliary colic (i.e., acute cholecystitis, cholangitis, gallstone pancreatitis, etc.) between admitted and non-admitted patients. Logistic regression analysis (accuracy = 72%) showed that hospital admission was associated with obesity (OR = 1.46; 95% CI 1.25 - 1.67) and mood

disorders (OR=1.36; 95% CI 1.16-1.56) but no association was observed between admission and race, gender, and insurance status. Of note, there was a statistically significant covariant relationship between obesity and mood disorders (p < 10-74).

We then analyzed outcomes for patients who received a cholecystectomy versus those who did not in the admitted and discharged groups. Of those admitted, 24% obtained cholecystectomy during the initial hospital stay, and immediate cholecystectomy was associated with fewer repeat hospitalizations (0.000 vs 0.049 ± 0.023), fewer recurrent ED visits (0.000 vs 0.027  $\pm$  0.017), and higher costs (\$11757  $\pm$  $1232 \text{ vs } 8848 \pm 617$ ) than patients who were admitted but did not obtain an immediate cholecystectomy on initial visit. Of those discharged, 28% obtained cholecystectomy within one year, and cholecystectomy was associated with more repeat hospitalizations

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 $(0.027 \pm 0.036 \text{ vs} 0.000)$ , more recurrent ED visits (0.080  $\pm$  0.072 vs 0.005), and higher incurred costs (\$1597  $\pm$  \$179 vs \$817  $\pm$  \$80).

**CONCLUSIONS:** In our analysis of ED patients with uncomplicated biliary colic from a single state, repeat visits were extremely low (less than 0.04 visits per patient) for both discharged and admitted groups of patients and

were therefore not significant drivers of the cost of care. Consequently, oneyear costs of care were almost ten-fold higher ( $$9542 \pm $571 vs $1035 \pm $87$ ) for patients that obtained an initial hospital admission on their index ED visit, and immediate cholecystectomy was not associated with lower costs.

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# In Emergency Department Patients with Appendicitis, Surgical Management Reduces Readmissions, Length of Stay

#### Michael Makutonin, MSII

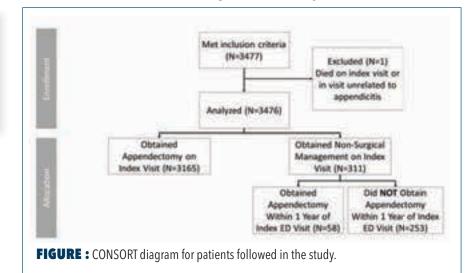
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**STUDY OBJECTIVES:** There are approximately 300,000 cases of acute appendicitis in the US annually.<sup>1</sup> Laparoscopic appendectomy is currently the preferred method for management for these patients,<sup>2</sup> but nonoperative management has been cited as a viable alternative to surgery,<sup>3</sup> though the literature comparing these treatments has been conflicting. The primary objective of this study was to compare ED patients with acute appendicitis who receive immediate appendectomy versus those who receive



non-operative management in initial visit for the following one-year outcomes: total costs, repeat ED visit, hospital length of stay (LOS), and repeat hospital admissions.

**METHODS:** Using the State ED Database (SEDD) from the Healthcare Cost and Utilization Project (HCUP) for the state of Maryland, patients with the ICD-10 codes for a primary diagnosis of uncomplicated appendicitis (K35.30, K35.80, and K35.890) who were seen in an ED between 2016 and 2018 were identified. Patients who received appendectomy on initial visit were compared to patients who obtained non-surgical management. Identified patients were then followed for one year by means of unique identifiers in the SEDD, the State Ambulatory Surgery Database, and the State Inpatient Database. Costs were estimated using Medicare Relative Value Units and HCUP Cost-Charge Ratio files, and a multivariate logistic regression analysis was performed to compare the two groups.

**RESULTS:** Of the 3476 patients analyzed in this study, 91% (N=3165) obtained an appendectomy on initial visit, while 9% (N=311) received

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non-surgical management. Patients who obtained an immediate appendectomy had lower repeat hospitalizations per patient (0.0 vs  $0.115 \pm 0.038$ ), lower recurrent ED visits ( $0.003 \pm 0.002$  vs  $0.074 \pm 0.030$ ), lower combined length of stay (2.3026  $\pm$  0.0823 vs 3.8581  $\pm$ 0.4823 days), and lower one-year costs (\$5631 ± \$204 vs \$7425 ± \$1132) than patients who obtained non-surgical management on initial visit. Nonsurgical management on initial visit was associated with appendicolith/ bowel obstruction (OR = 1.23; 95% CI 1.15 - 1.31), increasing age (OR = 1.19, 95% CI 1.07 - 1.31), and ischemic heart disease (OR=1.21; 95% CI 1.02-1.21) but no association was observed between

management type and race, gender, insurance status, CMDF CCI score (a measure of medical comorbidity)4, or pregnancy.

**CONCLUSIONS:** Operative treatment of patients presenting to the ED with uncomplicated appendicitis was associated with significantly lower one-year costs, combined LOS, hospital readmissions, and repeat ED visits than non-operative treatment. This study suggests that initial surgical intervention may not only be the most clinically effective choice, but also the most cost-effective choice when compared to nonsurgical alternatives.

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# Clinical Epidemiology and Outcomes of Candidemia in Hospitalized Children

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**PURPOSE:** Candidemia is the most common invasive fungal infection in hospitalized children, and the third most common cause of pediatric nosocomial bloodstream infections.<sup>1-3</sup> The distribution of species of Candida causing bloodstream infections in hospitalized children has shifted over time, as have the resistance patterns to antifungal drugs. The objective of this study is to investigate the epidemiology, the species distribution, patient outcomes, and the species' time to positivity (TTP) for Candida bloodstream infections.

**METHODS:** This retrospective cohort study analyzed all patients <21 years of age with a positive blood culture for Candida admitted to Children's National Hospital between January 1, 2010, and December 31, 2020. Demographic features, baseline clinical characteristics, clinical outcomes including complications, Candida species and susceptibilities, duration of fungemia, and TTP for yeast were collected from the electronic health records through structured chart review.

**RESULTS:** One-hundred episodes of Candida (94 patients) were included in this study. The mean age of patients

**TABLE:** Baseline Characteristics of Patients with Candida Bloodstream Infection SD: standard deviation; IQR: interquartile range; PICU: pediatric intensive care unit; NICU: neonatal intensive care unit; BMT: bone marrow transplant; CICU: cardiac intensive care unit; NSU: neurosurgical unit; SCU: surgical care unit; CLABSI: central-line associated bloodstream infection

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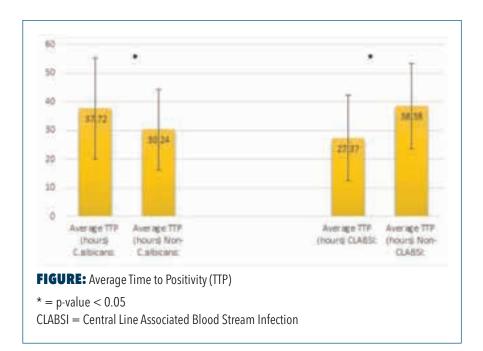
	Episodes (N = 100)	Mean ± SD	Median (IQR)
Age Range		$5.81 \pm 6.51$ years	2.62 (9.68) years
0-1month	14	$12.36 \pm 5.47$ days	11.5 (7.5) days
1 month -< 1 year	19	$5.60 \pm 3.38$ months	5.82 (6.12) months
1 year - <5 years	29	$2.53 \pm 1.06$ years	2.48 (1.95) years
5 years - <12 years	15	7.95 ± 1.99 years	8.18 (2.74) years
12 years +	23	$16.5 \pm 1.97$ years	16.86(2.46) years
Duration (days) of Hospital Stay:		57.15 ± 64.69	34.5 (44.75)
Duration (days) of admission post- positive blood culture:		38.54±41.44	22(29.5)
Hospital Acquired Infection	62		
Where in the hospital			
General Hospitalist Service	19		
PICU	19		
NICU	17		
Heme/Oncology/BMT	16		
Intestinal Rehabilitation Unit	12		
CICU	10		
NSU/SCU	3		
Other	4		
Central Line			
Central Line	89		
CLABSI	52		
Unknown if CLABSI or not	31		
Not a CLABSI	6		
Total Removed Central Line	70		
Total CLABSI Removed Central Line	49		

in the cohort was  $5.81 \pm 6.51$  years (Table). The mean duration of admission was 57.15 days  $\pm$  64.69. Further,

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46% of episodes were admitted to critical care units, while 16% were admitted to the hematology/oncology/ bone marrow transplant unit, and 12% were admitted to the intestinal rehabilitation unit. Sixty-two percent of episodes were hospital-acquired and 52% of episodes were deemed a central-line associated bloodstream infection (CLASBI). C. parapsilosis/ guilliermondii was the most identified pathogen (44), followed by C. albicans (38), C. lusitaniae (8), C. tropicalis (7), C. krusei (2), C. famata (1), C. glabrata (1). Ninety-four percent of isolates showed susceptibility to fluconazole, with two episodes of C. krusei, one episode of C. glabrata, one episode of C. parapsilosis/guilliermondii, one episode of C. tropicalis, and one episode of C. albicans demonstrating resistance to fluconazole. The mean TTP for C. albicans was 37.72±17.56 and non-C. albicans was 30.24±14.07 (p=0.031). The mean TTP for CLABSIs was 27.37  $\pm$  14.90 and non-CLABSIs was 38.38  $\pm$ 15.05 (p=0.003) (Figure).

**CONCLUSION:** Candida bloodstream infections occurred most frequently in critically ill children admitted in the intensive care unit,



and more than half were determined to be CLABSIs. The time to positivity was significantly longer for CLABSIs than non-CLABSIs and for C. albicans vs. non-C. albicans species. The vast majority of isolates were susceptible to fluconazole.

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# Imaging Findings in COVID-19: Relationship Between Initial Chest Imaging, ICU Admission and Mortality

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The novel SARS-CoV-2 virus, commonly known as COVID-19, was declared a pandemic by the World Health Organization in March 2020. COVID-19 causes a wide spectrum of clinical conditions, ranging from mild anosmia to life-threatening acute respiratory distress syndrome (ARDS).1,2,3,4,5 Fever and dyspnea are common symptoms upon hospital admission,<sup>2</sup> but there is no strong consensus on which symptoms are indicative of severe COVID-19. It remains difficult to predict which patients are at increased risk for severe disease that necessitates ICU admission and/or intubation.

Given that many patients initially present with respiratory symptoms, patients generally receive chest imaging upon admission and repeatedly during hospitalization. The American College of Radiology issued guidelines in March 2020 regarding the appropriate use of chest radiography and computerized tomography (CT) scans in patients with suspected or confirmed COVID-19 disease. It is currently recommended that chest CT not be used as first-line imaging, and portable chest radiography may be recommended when radiography is necessary due to the need for careful infection control.<sup>3</sup>

Common findings on chest radiography include patchy, hazy, reticular, and widespread opacities, while

chest CT findings common in patients with COVID-19 include ground glass opacities, reticular pattern, and crazy paving.<sup>4</sup> These findings, though, are nonspecific and indicate the need for careful exami-

nation of chest imaging of known COVID-19 positive patients to identify any commonalities.

The purpose of this study is to determine whether there is an association between initial chest imaging findings, ICU admission, and mortality in COVID-19 positive patients, which may potentially be used to identify patients at risk for adverse outcomes.

A retrospective chart review of COVID-19 positive inpatients at a tertiary care facility between March 1, 2020, and May 31, 2020 was conducted. Initial chest imaging reports were reviewed for keywords. EMR was reviewed for data on ICU admission and mortality. Statistical analyses utilized were Mann-Whitney U, Fisher's exact, and chi-squared tests. Included were 365 patients with an average age of 61.4 years (range: 20-105; SD 17.8). Initially 335/365 (91.78%) patients received a chest radiograph and abnormalities were present on 273/335 (81.49%).

A statistically significant relationship was found between ICU admissions and a chest radiograph revealing opacities (P<0.04), in a diffuse distribution (P<0.04) or bilateral distribution (P<0.04). However, the Mann-Whitney U test revealed

Patients with diffuse or bilateral opacities, or pleural effusion on initial imaging should be considered high risk for ICU admission and mortality.

no statistically significant difference (P=0.21) in severity scores for ICU admission. A statistically significant relationship was also found between the presence of diffuse (P<0.001) or bilateral (P<0.007) opacities; pleural effusion (P<0.031); or underlying pulmonary conditions (P<0.048) on initial chest radiograph and mortality. The one-sided Mann-Whitney U test indicated that the patients who died had a statistically significantly larger severity score (P=0.00004) than patients who survived.

Our results identify initial chest imaging findings that may portend poor prognosis. Patients with diffuse or bilateral opacities, or pleural

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effusion on initial imaging should be considered high risk for ICU admission and mortality. Underlying pulmonary pathology present on initial imaging increases risk of ICU admission and mortality, confirming findings established by prior research. Initial radiographic findings can be used to stratify patients at increased risk for mortality and efficiently allocate hospital resources.

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# The Effects of Parenting Stress Between Poverty and Language Outcomes at One and Two Years



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**BACKGROUND:** Poverty and parenting stress are associated with well-established impairments on language devel-

Socioeconomic adversity at birth and parenting stress did not predict language outcomes at age 1. However, by age 2, higher socioeconomic adversity composites at birth (p=.005) predicted worse overall language ability.

opment, which predicts academic success throughout school.<sup>1</sup> The Family Stress Model has been proposed as a mechanism linking socioeconomic adversities to early language skills, with parenting stress moderating this relationship.<sup>2,3</sup> However, most prior studies sample school-age children and are not enriched for low-income families, potentially underestimating the effects of poverty on emerging language skills in infancy. It remains unclear how poverty and parenting stress may affect child language learning in the earliest stages of development.

**SAMPLE:** A cross-sectional cohort was recruited to form well-characterized groups of 1-year-olds (n=129) and 2-year-olds (n=139). Healthy term-born (>36 weeks gestation) 1-year-olds were recruited from the Early Life Adversity and Biological Embedding study, which oversampled urban St. Louis families in poverty through the March of Dimes 1000 Women Cohort. Two-year-olds were recruited from the Washington University Neonatal Developmental Research study. Groups were similar in social diversity, socioeconomic disadvantage, and delivery hospital.

METHODS: At birth,

maternal demographic stressor indices (race, age, and education) were calculated as a proxy for family-level poverty, as systemic inequalities disproportionately impose financial hardships on African Americans, teenagers, and mothers who did not graduate high school. The Area Deprivation Index (ADI) quantified community-level poverty,

which aggregates local family incomes, housing quality, and employment opportunities into national percentiles of neighborhood disadvantage.<sup>4</sup> Principal component analysis (PCA) computed composites of socioeconomic adversity. At subsequent 1- and 2-year assessments, mothers reported general parenting stress (Parenting Stress Index, 3rd Edition) and child receptive, expressive, and overall language abilities were assessed (Bayley Scales of Infant and Toddler Development, 3rd Edition). Stepwise linear regression models assessed the independent and interactive effects of poverty and parenting stress on children's language outcomes at ages 1- and 2- years after adjustment for child sex, preterm birth, and infant temperament.

**RESULTS:** Socioeconomic adversity at birth and parenting stress did not predict language outcomes at age 1. However, by age 2, higher socioeconomic adversity composites at birth (p=.005) predicted worse overall language ability. Receptive language skills were most impacted, as communitylevel poverty (p=.002), family-level poverty (p=.01), and parenting stress (p=.04) had significant main effects. Interaction terms with socioeconomic adversity composites (p=.02) and community-level poverty (p=.02) revealed significant moderating effects of parenting stress between socioeconomic adversity and receptive language skills at age 2. As shown in the figure, high parenting stress ( $\geq$  85th percentile) predicted impaired receptive language irrespective of disadvantage. Low/ normal parenting stress was not a significant buffer against the effects of poverty on language development.

**DISCUSSION:** This study suggests that socioeconomic adversity at birth, particularly living in a disadvantaged neighborhood, is a significant risk factor for impaired language development by age 2. General parenting stress is also of concern, but only regarding

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receptive language. It may be too early to observe these effects at age 1, as language is less typically developed at this stage. By identifying disadvantaged mothers at birth, interventionalists may narrow persisting achievement gaps by helping socially disadvantaged infants master emerging language skills before the effects of poverty set in.

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# The POMS "Crater" Profile as seen in College Students

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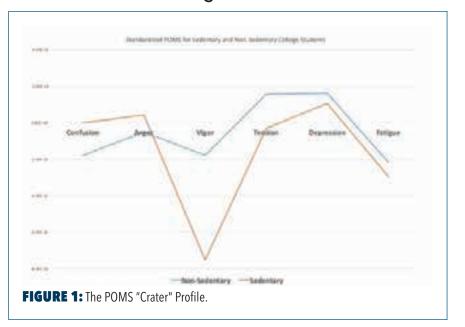
There are two critical phenomena occurring in college students across America: Students are becoming increasingly sedentary, and students' levels of negative emotional states continue to deteriorate.<sup>1</sup>

There is a wealth of studies that have examined the correlation between activity and mental health. The most famous of these studies is referred to as the Profile of Mood States (POMS) Iceberg profile, which indicates six subscales of emotional state: confusion,

# This study could highlight how widespread the rising emotional crisis among college students is.

anger, vigor, and tension. <sup>2,3</sup> This study demonstrated that elite athletes who exercised more often than the general population were expected to have lower levels of confusion, anger, tension, depression, and fatigue, but much higher levels of vigor.<sup>2</sup> When these two groups were graphed on a comparison chart, a very large and singular spike was seen on the vigor scale.<sup>2</sup> This spike in vigor is what coined the phrase "Iceberg."<sup>2</sup>

Although the relationship between exercise quantity and emotional state



has been well-studied and documented, little research exists to show the relationship between sedentary time and emotional state.

To help understand the mood state profile of college students who are

sedentary, a cross-sectional study was performed, consisting of 62 University of Utah kinesiology undergraduate participants — 25 male, 37 female. These participants each completed a self-report questionnaire describing their

demographics, minutes of sedentary behavior per day, and also completed a Profile of Mood States questionnaire. The participants were grouped into two categories based on their responses, more sedentary (>8 hr/day) or less sedentary (<7 hr/day). The grouping numbers were chosen because of the standard American 9 a.m.–5 p.m. work schedule.<sup>1</sup> This placed 27 students in the less sedentary group, and 35 in the more sedentary group. Once the data and the participants were grouped, the POMS subscale scores were standardized and

graphed on a comparison chart. Data was standardized using the "standardize" function in excel, which is analyzed using the sum, mean, and standard deviation of the raw data. The process was performed for both groups, and the standardized data was used to make the conclusions. It was originally theorized that results would be similar to the POMS Iceberg Profile study, with the less sedentary group showing a large spike on the vigor subscale. However, the results show no statistical significance between the two groups in confusion, anger, tension, depression, or fatigue subscales. There was, however, a significant drop in the vigor score of the more sedentary group. This drop led to what we now call a POMS "Crater" Profile, a direct reversal of the POMS Iceberg Profile.

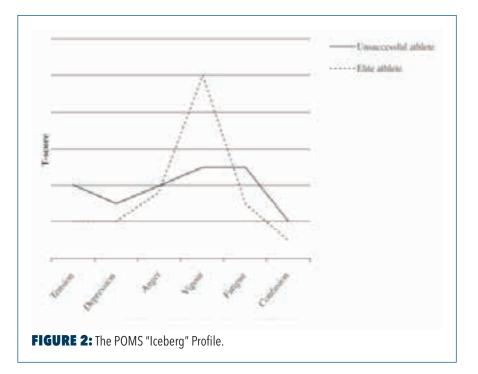
The implications of this study are notable for the emotional well-being of college students, as college students across the United States are spending on average 76% of their waking hours performing sedentary activity.<sup>1</sup> With

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a minimum of 12 waking hr/day, this puts the average college student being sedentary for 9 hr/day minimum, well over the 8 hr/day threshold as defined by this study. This study could highlight how widespread the rising emotional crisis among college students is. Universities should take action to help students be more successful and have more vigor, and they should ensure policies that allow students more time to be standing or active throughout the day, especially during rigorous class schedules.

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# Neuropsychological Assessment of Patients in a Newly Established Multidisciplinary Turner Syndrome Clinic.

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Turner syndrome (TS) is a rare genetic condition caused by a partial or completely missing second X-chromosome in a phenotypic female. TS is characterized by short stature, primary ovarian insufficiency, congenital heart

Turner syndrome (TS) is a rare genetic condition caused by a partial or completely missing second X-chromosome in a phenotypic female.

and renal defects, skeletal anomalies, lymphedema, hearing loss, metabolic syndrome, and cognitive difficulties.<sup>1</sup> While patients typically exhibit normal intelligence and strong verbal abilities, impairment in mathematics, executive function, visuospatial ability, as well as diagnoses of autism, attention deficit disorders and anxiety are common.<sup>2,3</sup> Guidelines recommend

Scores	Median Interquartile T-scores Range		N (%) clinically elevated, (definition)	
BRIEF Global executive composite, (N=20)	58.5	53.5-67.8	3/20 (15%), (>70)	
CBCLTotal Problems (N=21)	57	52-64	6/21 (29%), (> 63)	
CBCL Internalizing Problems (N=20)	59	55.5-65.8	7/20 (35%), (>63)	
CBCL Externalizing Problems (N=20)	55.5	48.2-62.2	4/20 (20%), (>63)	
CBCL Anxious/Depressed (N=20)	58	51.8-63.5	2/20 (10%), (>70)	
CBCLDSM-5 Anxiety Problems (N=20)	61.5	53.5-69.8	5/20 (25%), (>70)	

**TABLE:** Parent reported behavioral and cognitive problems on standardized

routine neuropsychological (NP) screening at developmental transitions for all patients with TS.<sup>1</sup> Our objective was to characterize the spectrum of cognitive impairment in patients with TS referred from the newly established

multidisciplinary TS specialty clinic at Children's National Hospital.

**METHODS:** The study protocol was deemed exempt by the institutional review board. We retrospectively reviewed data from all completed neuropsychology (NP) assessments between 1/1/2019 and 5/31/2021 along with

karyotype, age at diagnosis, and age at estrogen start. Descriptive analyses of parent reports, impairments based on the evaluator's interpretation of scores as stated in the NP summary report, and Spearman correlation with clinical factors (SAS V9.4) are presented.

**RESULTS:** Of 75 patients, 23 (31%) had completed NP assessment, with median age 11.4y (2.3-20.2), 48%

were of 45,X karyotype and 30% were diagnosed in the pre/perinatal period. Parent-reported T-scores (mean 50, SD 10) on BRIEF (Behavior Rating Inventory of Executive function v1 or v2) and CBCL (Child Behavior Checklist) are shown in Table. In the summarized NP report, 5/23 (22%) had autism; 7/23 (30%) attention deficit disorder, 9/23 (39%) developmental delays, 14/23 (61%) impaired academic function, 13/23 (57%) social difficulties, 11/23 (48%) memory problems, 12/23 (52%) impairment in math, 13/23 (57%) impaired visual-spatial abilities, 16/23 (70%) impairment in executive functioning, and 12/23 (52%) anxiety disorder. In 11 patients with data on treatment of primary ovarian insufficiency, the age at estrogen start was positively correlated with memory impairment (p=0.009), but other correlations were not significant.

**CONCLUSIONS:** Our data confirm the high prevalence of NP impairment in TS affecting multiple domains, in

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excess of parental reports. One limitation is a potentially biased sample since the pandemic led several families to delay the assessment, and those that were completed may reflect patients with a greater degree of impairment. Future studies are necessary to assess barriers to following through with NP testing after referral, optimal tools for assessing areas of deficit in TS, frequency of testing, and the impact of test results on treatment planning.

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# Mixed Method Examination of the Brain Health of Former NCAA Division I Football Athletes and Former NFL Athletes

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**BACKGROUND:** The purpose of this study was to examine the concerns of brain health and wellness of former NCAA Division I (DI) football athletes compared to former National Football League (NFL) athletes. This study aimed to understand (1) How post-concussion symptoms, measured using the Neurobehavioral Symptom Inventory (NSI), compare between former NCAA DI football athletes and former NFL athletes, and (2) How these groups of former athletes describe the role that playing football had on their brain health.

**METHODS:** We utilized a mixed methods design incorporating a survey of former NFL athletes and former NCAA DI football athletes (N = 131) **TABLE:** Means, standard deviations, and independent t-tests for former NFL and Division I College Football Athletes

	Former NFL Players		Former Division 1 College Football Athletes				
Variable	М	SD	М	SD	U	Estimated p-value	
Total Number of Concussions Sustained	8.995	9.068	4.72	6.426	735	0.01	
Worry	5.011	2.254	5.92	2.06	849	0.233	
NSI Score	11.94	13.517	10.52	7.875	1179	0.651	

and subsequent semi-structured interviews (N = 19). Survey data was analyzed using descriptive and inferential statistics; analysis of the interviews was descriptive.

**RESULTS:** Several themes were captured from the interviews, including (1) concerns about living with the consequences of sport concussions, (2) concerns for developing long-term sequelae from sport concussions and chronic traumatic encephalopathy (CTE), (3) expressing concerns for long-term effects or symptoms, (4) difficulties differentiating between normal aging and long-term effects of sport concussions, and (5) concerns for the long-term sequelae from sport concussions in current and former athletes at all levels of football. There was a significant difference in the number of concussions sustained between former NCAA DI football athletes and former NFL athletes, but no significant difference in the NSI scores or self-reported worry about future brain health, measured on a scale from 1-8 (Table).

**CONCLUSIONS:** No significant difference exists in concern about brain health between former NFL and former NCAA DI football athletes despite former NCAA DI football athletes having significantly fewer self-reported sport concussions and less total playing time. This is significant for current and future health care professionals to recognize that worry about sequelae from sport concussions is individual to each patient. Athletes' concerns about brain health in relation to multiple concussions will be important to address in future research.

# Rehabilitation Aspects of Acquired Wernicke-Korsakoff Syndrome from Hyperemesis Gravidarum-Induced Nutritional Thiamine Deficiency



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**CASE DIAGNOSIS:** A patient with acquired Wernicke-Korsakoff Syndrome (WKS) due to hyperemesis gravidarum induced nutritional thiamine deficiency.

**CASE DESCRIPTION:** We present the case of a previously healthy,

non-alcohol drinking, 26 year old female who suffered hyperemesis gravidarum and spontaneous abortion during a pregnancy. Two weeks after pregnancy loss, the patient developed severe memory impairment, ataxia, nystagmus, and polyneuropathy. Laboratory results revealed a vitamin B1 level of less than 20.0 (undetectable) and neuro-imaging revealed hyperintensities in her mammillary bodies. Intravenous thiamine replacement was initiated and she was discharged to an acute inpatient rehabilitation facility (IRF). In the (IRF), she had an admission total self-care GG0130 score of 29 and an admission mobility GG0170 score of 34. Her total self care goal score was 42 while her mobility goal score was 64. On discharge, 10 days after admission, she reached a total self care goal of 42 and a mobility score of 79. Based on clinical notes and scores from occupational and physical therapy, the patient demonstrated continued improvement and significant

recoveries in functional impairment from physical rehabilitation.

**DISCUSSION:** This patient, a young, non-alcoholic woman, does not fit the classic demographic of WKS, which typically presents as an older alcoholic male. Due to this rare presentation, we believe that she exhibited an extremely positive response to the acute inpatient rehabilitation. In just 10 days, she was able to exceed discharge goals and regain significant function. As such, for patients of this demographic, it may be helpful to refer them to the acute inpatient rehabilitation for improvement and optimization of their functionality.

**CONCLUSIONS:** This young female with Wernicke-Korsakoff secondary to acquired thiamine deficiency was an atypical presentation for her diagnosis. Her quick progression with acute inpatient rehabilitation services can inform goals for similar patients in the future.

# How High Should You Go? Buprenorphine Dosing in the ANCHOR Investigation

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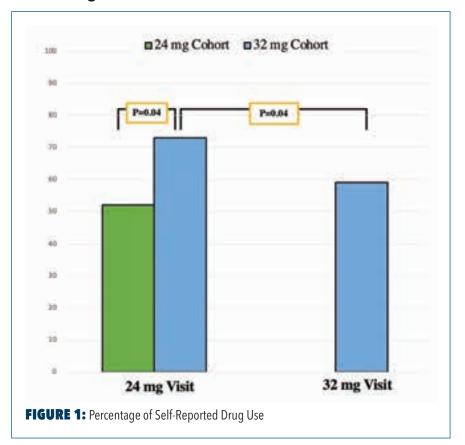
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**BACKGROUND:** In people who use drugs (PWUD) with opioid use disorder (OUD), buprenorphine is a vital treatment to decrease opioid use and overdose. FDA prescribing information for buprenorphine advises dosing up to 24mg/day, however doses of buprenorphine up to 32mg have been shown to be safe and effective.1 Further, treatment retention increases linearly with higher doses of buprenorphine up to 32mg<sup>2</sup> and doses over 16mg are associated with decreased opioid use.3 However, 32mg dosing is not recommended in SAMHSA guidelines and is often not supported by insurance. We aimed to understand the outcomes associated with buprenorphine dosing of 32mg/day relative to 24mg/day.

**METHODS:** ANCHOR is a single center study of PWUD with HCV, OUD, and opioid misuse within three months, who were treated for HCV and offered buprenorphine. Patients initiating buprenorphine were induced



on 16mg/day and up-titrated to 32mg/ day as needed. Patient-endorsed drug use, mode of drug use and urine drug screens (UDS) were collected at first visit post-dosage increase, and after two weeks on increased dose. For analysis, the cohort was divided into individuals stabilized on 24mg (24mg-cohort) and 32mg (32mg-cohort). Comparisons were made looking at drug use factors of both cohorts at 24mg dosing, and within the 32mg-cohort alone, comparing visits on 24mg to visits on 32mg. Fisher's exact test was used for statistical analysis.

**RESULTS:** Seventy three participants initiated buprenorphine treatment. Patients were predominantly male (54,74%) and Black (71,96%), injected daily (46,63%), and had a mean

OUD-DSM5 score of 9.4. The average age at which opioid use was initiated was 21.4 years.

Over the course of median 64 weeks of buprenorphine treatment (IQR197-785), one (1.3%) patient remained on 16mg, 18 (25%) patients stabilized on 24mg (24mg-cohort), and 54 (74%) patients stabilized on 32mg (32mgcohort). Stabilizing on 32mg was not significantly associated with housing status, baseline IDU frequency, previous MOUD treatment, hazardous alcohol use, comorbid mental illness, or age of opioid initiation (p> 0.05 for all).

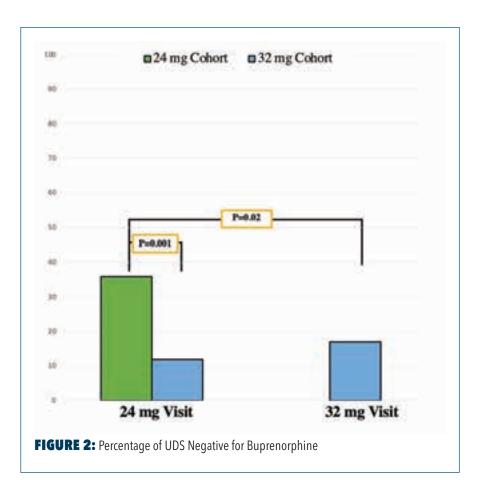
When comparing 24mg and 32mgcohort patients at visits receiving 24mg/ day, 32mg-cohort patients were more

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likely to endorse drug use (p=0.04), despite also being more likely to have buprenorphine present in UDS (p=0.004). There was no statistically significant association between mode of drug use (p=0.44), or UDS positive for opioids (p=0.20).

When looking only at the 32mgcohort patients, and comparing factors at visits while on 32mg vs 24mg, patients were less likely to endorse prior week drug use (p=0.04) or being triggered to use by cravings (p=0.017) or withdrawal (p=0.017) while on 32mg. There was no significant association between dose strength and presence of buprenorphine in UDS (p=0.31) or UDS positive for opioids (p=0.65).

**CONCLUSION:** Higher buprenorphine doses have been associated with better retention and outcomes.1.3 In our cohort, patients who stabilized on 32mg were more likely to endorse drug use while on 24mg compared to those stabilized on 24mg. After increasing to 32mg dosing, these patients were less likely to endorse drug use, triggers of craving, and withdrawal. These data indicate that there are some patients who benefit from 32mg/day of buprenorphine. Consideration should be given to modifying treatment guidelines and insurance policies to facilitate higher dosing in these patients.



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# Tranexamic Acid for the Prevention of Postpartum Hemorrhage: A Cost-Effectiveness Analysis



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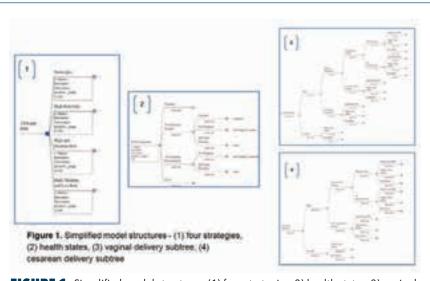
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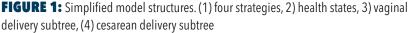
**OBJECTIVES:** To estimate the costeffectiveness of alternative risk-dictated strategies utilizing prophylactic tranexamic acid for the prevention of postpartum hemorrhage.

**METHODS:** We constructed a microsimulation-based Markov decision-analytic model estimating the cost-effectiveness of three alternative

Our findings suggest that routine prophylaxis with tranexamic acid would likely result in substantial cost-savings and reductions in adverse maternal outcomes in this context.

risk-dictated strategies for tranexamic acid prophylaxis versus no prophylaxis in a cohort of 3.8 million pregnant women delivering in the United States: tranexamic acid in high hemorrhage risk patients only, tranexamic acid in high and medium hemorrhage risk patients, and tranexamic acid in all





patients irrespective of hemorrhage risk. Each strategy differentially modified risk-specific hemorrhage probabilities by estimates of tranexamic acid's prophylactic efficacy. Outcome

> measures included incremental costs, quality-adjusted lifeyears, and outcomes averted. Costs and benefits were considered from the health care system and societal perspectives over a lifetime time horizon and were discounted at an annual rate of 3%.

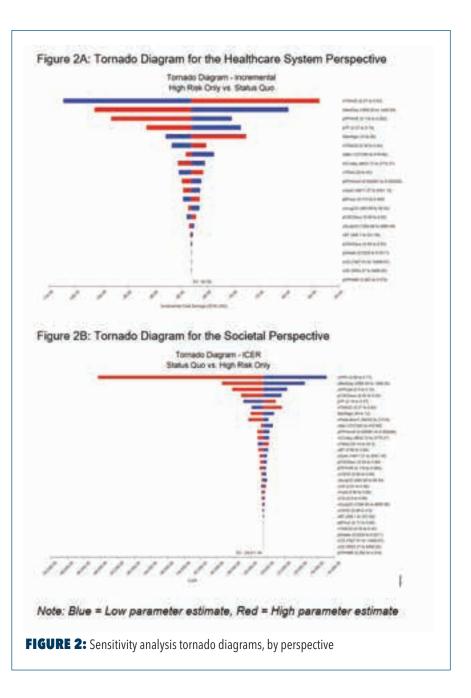
One-way deterministic Monte Carlo probabilistic sensitivity analyses were performed to assess parameter uncertainty across a wide range of literaturesupported estimates.

**RESULTS:** All intervention strategies were dominant versus no

prophylaxis, implying that they were simultaneously more effective and cost-saving. Prophylaxing delivering women irrespective of hemorrhage risk produced the most favorable results overall, with estimated cost savings greater than \$690 million and up to 149,505 PPH cases, 2,933 hysterectomies, and 70 maternal deaths averted, per annual cohort. Threshold analysis suggested that tranexamic acid is likely to be cost-saving for health systems at costs below \$190 per gram.

**CONCLUSIONS:** Our findings suggest that routine prophylaxis with tranexamic acid would likely result in substantial cost-savings and reductions in adverse maternal outcomes in this context.

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# A Survey on Management of Pediatric Vulvoperineal and Perianal Lichen Sclerosus in Individuals Assigned Female Sex at Birth

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Lichen sclerosus (LS) is a chronic condition which can result in anogenital scarring and vulvar squamous cell carcinoma (SCC) if not treated appropriately. In pediatric patients, the risk of developing long-term complications related to scarring is unknown.<sup>1</sup> Although LS often symptomatically improves at puberty, active disease can persist through adulthood.<sup>1</sup> The goal of this survey is to identify variations in methods of diagnosis, treatment regimens and long-term management of PVPLS in individuals assigned female at birth.

We administered a 35-question survey on diagnosis and management of PVPLS through the North American Society for Pediatric and Adolescent Gynecology and Pediatric Dermatology Research Alliance. Survey responses were collected electronically between July 13 and Aug. 30, 2021.

There were 102 responders. The majority were attending physicians (n=95, 93%) consisting of 44 (46%) pediatric and adolescent gynecologists, 38 (40%) pediatric dermatologists. More than half (n= 55, 55%) treated only two patients with PVPLS per month. Only 23 (23%) of the responders were completely confident in diagnosing PVPLS. There was not a statistically significant

difference in confidence in diagnosis between specialties (p=0.39). Sixty-six (65%) used clinical features (history and physical) alone for diagnosis. There was a statistically significant difference in the use bacterial/ fungal cultures (p = .01), parasite testing (p = .01, STI testing (p = .04 and

the use of a Wood's lamp (p=.03) for diagnosis between specialties. Only 12 (12%) reported use of biopsy for diagnosis and the difference between the specialties was not statistically different (p=.63). Vitiligo was identified as the most difficult diagnosis to differentiate from PVPLS (n=54, 53%). Less than half (n=48, 47%) were aware of published guidelines for the management of PVPLS and 86% (n=42 of 49 respondents) desired additional guidelines. Ninety-eight (96%) prescribed high or super high topical steroids for initial treatment. Maintenance therapy was recommended by 66 (65%). There was a statistically significant difference between the specialties with a greater number of pediatric dermatologists recommending maintenance therapy

(p < .001). Only 41 (42%) recommended lifelong follow-up. There was not a statistically significant difference in recommendation for long-term follow-up between the specialties (p =.66).

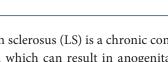
Initial treatment was similar among various specialties, likely reflecting the presence of guidelines and uniformity in training for newly diagnosed PVPLS. However, there was considerable variation in maintenance therapy and longterm follow-up despite the risk of persistence of PVPLS into adulthood.<sup>2</sup> This potentially reflects a lack of confidence

Lichen sclerosus (LS) is a chronic condition which can result in anogenital scarring and vulvar squamous cell carcinoma (SCC) if not treated appropriately.

> because of limited exposure and /or lack of guidelines for the long-term management of PVPLS.<sup>3</sup> Further studies are needed to elucidate the natural history of PVPLS and to identify optimal longterm management.

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# Vulvar Disorders Encountered at a Multidisciplinary Pediatric Clinic: A Retrospective Chart Review

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Vulvar dermatology is a field in which many pediatricians, gynecologists, and dermatologists may lack sufficient comfort and training, leading to delays in diagnosis and treatment.<sup>1</sup> Anogenital vitiligo and lichen sclerosus (LS) can be difficult to distinguish, especially in skin of color, in part because depigmentation in LS can persist after symptom resolution and because vitiligo can coexist with symptomatic dermatoses.<sup>2</sup> Proper diagnosis is essential because undertreated LS is associated with long-term sequelae including scarring and squamous cell carcinoma.<sup>3</sup>

Time from symptom onset to LS diagnosis (months)

**TABLE:** African American (AA) patients with LS experienced the longest time from

symptom onset to diagnosis (18.76 months vs 10.6 months in other races, P=0.024).

Data were extracted from 180 patients seen over a 3.5 year period in a joint dermatology-gynecology clinic at an academic children's hospital. Descriptive statistics were used to analyze data on diagnosis, symptom onset to time of diagnosis, and misdiagnosis by race.

LS (58.59%), vulvovaginitis (18.18%), and vitiligo (17.17%) were the most common diagnoses. Vitiligo was most frequently initially misdiagnosed (50%) as another disease and most frequently diagnosed in patients with darker skin tones. LS and vitiligo were most frequently misdiagnosed as each other. African American (AA) patients with LS experienced the longest time from symptom onset to diagnosis (18.76 months vs 10.6 months in other races, P=0.024; table). LS and vitiligo may present more similarly to each other in darker skin tones.4 Further research is needed to elucidate disease presentation in skin of color with the aim of developing criteria to distinguish LS and anogenital vitiligo.

Other

races

10.6

P-value

0.024

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African American

18.76

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# Practices of Sickle Cell Disease Genetic Screening and Testing in the Prenatal Population

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Genetic screening and testing has only recently become an accessible assessment for genetic risk. Unfortunately, these technologies have been underutilized in minority populations despite their usefulness for predicting diseases like sickle cell disease (SCD), often found in African American and Black and Hispanic populations. We surveyed prenatal patients to understand current choices, beliefs and experiences surrounding genetic screening and testing, specifically for sickle cell disease.

In this cross-sectional survey, we collected information from 322 women

during prenatal visits from July 2019 through May 2021. Responses to questions about pregnancy screening and testing practices were analyzed for trends to identify barriers to care and education about testing and screening for sickle cell disease. Patients were asked to rate whether they agree or disagree with statements regarding sickle cell health behaviors. We used  $\chi 2$  tests

to compare categorical variables by self-reported race. Binary logistic regression was used to determine the odds ratios and confidence intervals for each outcome.

Women were a mean (SD) age of 33.3 (6.1). 42.9% of patients self-identified as White while 41.3 of patients self-

identified as African American/Black. Screening questions were adjusted for differences in race, insurance, and education levels to show significant differences in responses between African Americans/Blacks and Whites for screening for SCD (p=0.047, OR 95% CI= 0.455 [0.210-0.989]) and plans to meet with genetic counselors (p=0.049, OR 95% CI = 0.299 [0.090-0.993]). Regarding sickle cell health behaviors, only the responses to the statements about if sickle cell is not in their family, then it is likely not in themselves or their children, and partners' opinions about genetic screening remained significant (p=0.011 and p=0.081, respectively).

Our findings suggest gaps in screening, testing, and educational

Our findings suggest gaps in screening, testing, and educational efforts between African American/Black and White patients, as well as differences in opinions regarding pregnancy management with a family history or gestational diagnosis of sickle cell disease.

> efforts between African American/ Black and White patients, as well as differences in opinions regarding pregnancy management with a family history or gestational diagnosis of sickle cell disease. Future research should focus on decreasing these health care gaps and improving education that address concerns about SCD for relevant populations.

# Intraocular Pressure Response in the Untreated Contralateral Eye After Selective Laser Trabeculoplasty

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**PURPOSE:** Selective laser trabeculoplasty (SLT) is a procedure commonly used as a primary or adjunctive therapy in glaucoma to lower intraocular pressure (IOP). Currently, there is no consensus on whether SLT causes a decrease in IOP in the untreated contralateral eye.<sup>1,2,3</sup> Our study investigates the pre- vs post-operative change in IOP and the number of medications used in a patient's untreated contralateral eye within 12 months after receiving SLT.

**DESIGN:** A retrospective observational study was conducted on patients who visited the George Washington University Department of Ophthalmology between January 1st, 2008 and January 1st, 2020 with primary open-angle, pseudoexfoliation, pigmentary, or normal-tension glaucoma and who received 360 degrees SLT. Patients were excluded if they had laser or glaucoma surgery either prior to or within 12 months after SLT, if they had other glaucoma types, or if they used steroid medications. Demographics were collected and the pre- vs post-SLT IOP and number of **TABLE:** Mean IOP values in the untreated contralateral eye within 12 months following SLT.

	Number Observed	Mean	Std. Dev	Std. Error		nfidence rival	Trailue	P-value
pre-op	125	15.21	3.55	0.32	14.59	15.84		
veeks	125	14.29	3.50	0.31	13.67	14.91	3.33	0.0006
months	125	14.22	3.61	0.32	13.58	14.86	3.09	0.0025
post-op 12 months	125	14.74	3.53	0.32	14.12	15.36	1.59	0.1149

medications were analyzed using a paired samples t-test and ANOVA.

**RESULTS:** A total of 125 patients were included in this study. Mean IOPs for the untreated eyes at baseline, 6-week post-operation, 6-month post-operation,

and 12-month post-operation were 15.21  $\pm$  3.55 mmHg, 14.29  $\pm$ 3.5 mmHg (P < 0.05), 14.22  $\pm$  3.61 mmHg (P < 0.05), and 14.74  $\pm$  3.53 mmHg (P > 0.05), respectively. For

the same time points, the mean number of medications were  $1.73 \pm 1.29$ ,  $1.68 \pm 1.31$  (P < 0.05),  $1.68 \pm 1.30$  (P < 0.05),  $1.68 \pm 1.29$  (P > 0.05), respectively.

**DISCUSSION:** The mean pre-op IOP and number of medications in the untreated eye had a statistically significant reduction at 6 weeks and 6 months post-SLT but not at 12 months post-SLT. This study differs from previous research in showing a statistically significant reduction in the mean number of medications in the untreated eye post-SLT.<sup>3</sup> This study's population also improves on the previous study's external validity. There were 125 patients (previously 291, 432, 323) with diverse backgrounds

First-time SLT glaucoma patients have a statistically significant decrease in IOP and medications used in the untreated contralateral eye at 6 weeks and 6 months after treatment.

(African American (57.6%), Caucasian (31.2%), Asian (5.6%), Hispanic/Latino (4%), not reported (1.6%) - previously unreported2 or homogenous3) and no history of laser treatments (previously included patients with prior laser treatments<sup>2,3</sup>).

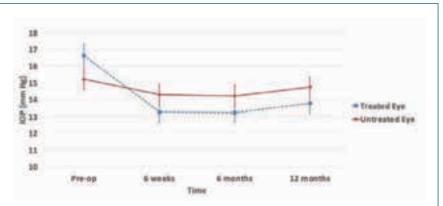
**CONCLUSION:** First-time SLT glaucoma patients have a statistically significant decrease in IOP and

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medications used in the untreated contralateral eye at 6 weeks and 6 months after treatment.

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**FIGURE:** Mean IOP in the treated and untreated eye within 12 months following SLT with 95% confidence intervals.

# Paraspinal Muscle Health is Related to Fibrogenic, Adipogenic, and Myogenic Gene Expression in Patients with Lumbar Spine Pathology

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The aim of this study was to investigate the relationships between groups of genes within the atrophic, myogenic, fibrogenic, adipogenic/metabolic, and inflammatory pathways and multifidus muscle health in individuals undergoing surgery for lumbar spine pathology.

Lumbar spine pathology is a common feature of lower back and/or lower extremity pain and is associated with observable degenerative changes in the lumbar paraspinal muscles that are associated with poor clinical prognosis.<sup>1</sup> The multifidus muscle is of particular interest due to its role in stabilizing the lumbar spine. Degenerative changes visualized on magnetic resonance imaging (MRI) (Figure 1) typically include the accumulation of fat (white) and the deposition of fibrotic tissues within the muscle compartment (grey) with worsening degree of degeneration (left to right).<sup>2</sup> Despite how commonly this degenerative phenotype is observed in this patient population,

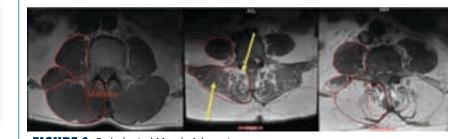


FIGURE 1: Pathological Muscle Adaptations

the underlying molecular mechanisms are not well understood. Prior work has demonstrated relationships to individual genes,<sup>3</sup> however this is thought to oversimplify complex underlying physiology. To our knowledge only one prior study has cumulatively looked at

gene expression among multiple pathways associated with muscle health in individuals with LSP,<sup>4</sup> yet did not examine gene expression levels alongside objective measures of muscle health.

Multifidus

muscle biopsies

were obtained from patients (n=59) undergoing surgery for lumbar spine pathology to analyze 42 genes from atrophic, myogenic, fibrogenic, adipogenic/metabolic, and inflammatory gene pathways using quantitative polymerase chain reaction. Multifidus muscle morphology was examined preoperatively at the level and side of biopsy using T2-weighted MRI to determine whole muscle compartment, lean muscle, fat cross-sectional areas, and proportion of fat within the muscle compartment. These measures were used to investigate the relationships between gene expression patterns and muscle size and quality.

Relationships between gene expression and imaging (Figure 2) revealed associations between (a) lower expres-

Lumbar spine pathology is a common feature of lower back and/or lower extremity pain and is associated with observable degenerative changes in the lumbar paraspinal muscles that are associated with poor clinical prognosis.<sup>1</sup>

sion of adipogenic/metabolic gene (PPARD), and (b) higher expression of fibrogenic gene (COL3A1) and lower fat fraction on MRI (r=-0.346, p=0.018, and r=0.386, p=0.047 respectively). Additionally, (c) lower expression of myogenic gene (mTOR) was related to greater lean muscle cross-sectional area (r=0.388, p=0.045).

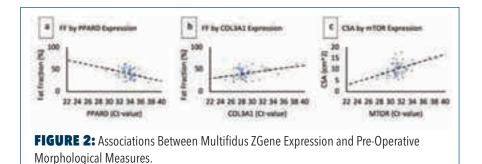
Fibrogenic and adipogenic/metabolic genes were related to pre-operative

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muscle quality, and myogenic genes were related to pre-operative muscle size. These findings provide insight into important molecular pathways associated with muscle health in the presence of lumbar spine pathology, establishing a foundation for future research that addresses how these changes impact outcomes in this patient population.

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# The Role of Antiretroviral Therapy in the Development of Osteonecrosis in HIV Patients

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**INTRODUCTION:** With modern antiretroviral therapy (ART), human immunodeficiency virus (HIV) infection has become a chronic condition. Patients diagnosed with HIV now live longer but with more medical comorbidities than the general population.1-4 Patients with HIV also face certain medical conditions more often than patients without HIV, including osteonecrosis (ON).3,4 ON has a 3-100 times higher incidence in patients with HIV not on ART when compared to the general population (0.135%).<sup>3-5</sup> HIV is shown to be a risk factor for ON, and early literature suggests that antiretroviral therapy (ART) may be an additional, independent risk factor.<sup>3,4</sup> Our study aimed to assess to what extent ART increases the odds of developing ON in the HIV+ population.

**METHODS:** Utilizing an insurance database (PearlDiver Technologies) from 2010–20, we selected patients using the international classification of disease (ICD) for ART, HIV, and **TABLE 1:** Multivariate analysis results reported as odds ratios, 95% confidence intervals, and p-values.

CATEGORY	HIV+/ART+ vs HIV+/ART					
	OR	95% CI	p-value			
TOTAL ON	1.401	1.384 - 1.419	<.001			
ON of Hip	1.405	1.384 - 1.426	<.001			
ON of Knee	2.56	2.393 - 2.738	<.001			
ON of Shoulder	1.054	1.010 - 1.100	0.016			

ON. Our comparison groups were HIV on ART with ON (HIV+/ART+) and HIV not receiving ART with ON (HIV+/ART-). Subcategorization, via ICD codes, was also used to identify which joints were affected by ON (hip, knee, shoulder). Chi-squared univariant analysis compared incidence rates as well as age, gender, long-term

steroid use, sickle cell disease, hyperlipidemia, and elixhauser comorbidity criteria for statistical significance (p<0.2). Significant criteria were controlled for in multivariate analysis as inde-

pendent variables. Statistically significant ON of any joint and sub-analysis of individual joints (p<0.05) were used as dependent variables for multivariate analysis.

**RESULTS:** In total, 219,853 patients were found to have HIV between 2010-2020. Of those patients, 123,710 had a history of ART, while 96,143 did not. Univariate analysis was significant for age, gender, and all comorbidities, except coagulopathy (p=0.365), metastatic cancer (p=0.404), and nonmetastatic cancer (p=0.642) (Table 2). ON of any joint, including each individually, was also significant and included in the multivariate analysis. Multivariate analysis found that patients in the HIV+/ART+ cohort had higher odds of developing ON when compared to the HIV+/ARTcohort in any joint (OR=1.401; 95% CI:1.384-1.419; p<0.001), hip (OR:1.405;

This retrospective case-control study found that patients who are HIV+ and on ART have a higher risk of developing ON than HIV+ patients who are not on ART.

> 95% CI:1.384-1.426; p<0.001), knee (OR:2.56; 95% CI:2.393-2.738; p<0.001) and shoulder (OR:1.054; 95% CI: 1.010-1.100; p=0.016) (Table 1).

> **CONCLUSION:** This retrospective case-control study found that patients who are HIV+ and on ART have a higher risk of developing ON than HIV+ patients who are not on ART. This difference remained significant when stratifying by joint. However, ART remains the gold standard for

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the treatment of HIV and, due to the well-known dangers of untreated HIV, we do not recommend discontinuing ART to decrease the risk of ON. Further studies are warranted to determine if the increased risk of ON is modifiable or if the risk associated with individual antiretroviral medications differs in a clinically meaningful way. Physicians should be aware of the risks ART may pose to HIV+ patients and monitor them closely to mitigate potential complications of ON.

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**TABLE 2:** Demographic and comorbidity univariate results. P-value <0.2 was considered significant and included in multivariate analysis. P-value bolded if NOT significant.

	Total	HIV+/ART+	HIV+/ART	P-value
	219853	123,710	96,143	<.001
AGE				
Avg.		44.61	46.32	< 0.001
Std. Dev.		12.13	15.77	
GENDER				
Female	84968	37,974	46,994	<.001
Male	136882	87,736	49,146	
COMORBIDITIES				
Alcohol abuse	5232	2,574	2,658	<.001
Anemia, Blood Loss	5730	2,196	3,534	<.001
Anemia, Nutritional	25207	11,295	13,912	<.001
Arrhythmias	38892	20,719	18,173	<.001
Chronic Kidney Disease	22768	13,619	9,149	<.001
Chronic Pulmonary Disease	48598	26,642	21,956	<.001
Coagulopathy	13129	7,389	5,740	0.365
Depression	54170	32,548	21,622	<.001
Diabetes Mellitus	44893	19,272	25,621	<.001
Drug abuse	35863	20,981	14,882	<.001
Fluid/Electrolyte Disorders	46106	26,951	19,155	<.001
Heart Failure	18035	8,785	9,250	<.001
Hyperlipidemia	73554	38,193	35,361	<.001
Hypertension	64605	34,307	30,298	<.001
Hypothyroidism	24303	8,272	16,031	<.001
Leukopenia	10216	6,860	3,356	<.001
Liver Disease	39118	20,522	18,596	<.001
Long-term Steroid Use	4733	2,488	2,245	<.001
Lymphoma	3636	2,493	1,143	<.001
Metastatic Cancer	4581	2,567	2,014	0.404
Nonmetastatic Cancer	15070	8,567	6,503	0.642
Obesity	25561	11,952	13,609	<.001
Other Neurological Disorders	15984	8,540	7,444	<.001
Paralysis	4895	2,649	2,246	<.001
Peptic Ulcer Disease	2157	1,092	1,065	<.001
Perivascular Disease	23289	13,105	10,184	<.001
Psychoses	16396	8,606	7,790	<.001
Pulmonary Circulatory Disorders	7290	3,971	3,319	<.001
Rheumatoid Arthritis/Collagen Vascular Disease	13452	4,811	8,641	<.001
Sickle Cell Disease	2201	1,006	1,195	<.001
Smoking	49961	29,938	20,023	<.001
Valvular Disease	18293	9,069	9,224	<.001

# Different Arthroplasty Procedures of the Knee for Osteoarthritis from 2010 to 2019: Trends in Overall and Robotic-Assisted Utilization

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BACKGROUND: Total knee arthroplasty (TKA) is the gold-standard for surgical knee replacement.<sup>1</sup> However, there has been a recent trend to use less invasive procedures for knee arthroplasties that can preserve more function, such as unicompartmental arthroplasties (UKA's) - medial or lateral compartment, patellofemoral arthroplasties (PFA's), and bicompartmental arthroplasties (BKA's). Early studies with UKA's and BKA's showed poor patient outcomes leading to limited usage, but recent literature has shown improved outcomes.<sup>2,3</sup> There has also been a movement towards using robotic-assisted surgeries in many procedures, with multiple studies showing an increase in utilization in robotic-assisted knee arthroplasties from 2009 to 2014.4,5 There is limited literature examining the recent trends in utilization for each knee arthroplasty

modality. The aims of the study were: (1) compare the trends in utilization of PFA's, UKA's, BKA's, and TKA's and (2) stratify the trends for robotic-assisted and non-robotic-assisted PFA's, UKA's, BKA's, and TKA's.

**METHODS:** A retrospective cohort analysis was conducted using data collected from the PearlDiver database from 2010 to 2019. Patients who underwent PFA, UKA, BKA, and

TKA for an indication of osteoarthritis were identified using Current Procedural Terminology (CPT) codes. CPT codes for robotic-assisted procedures was included to analyze trends of robotic-assisted for each arthroplasty type. Trends analysis was done using the PearlDiver "BREAKDOWN" function to determine the number of PFA, UKA, BKA, and TKA procedures performed

each year from 2010 to 2019 for total procedures, robotic-assisted procedures, and non-robotic-assisted procedures.

**RESULTS:** 1,243,677 patients underwent an arthroplasty procedure for OA of the knee, composed of 4,111 (0.33%) PFA's, 87,028 (7.00%) UKA's, 1,109 BKA's (0.09%), and 1,151,429 TKA's (92.58%). There was a significant decrease in the utilization of PFA (Compound annual growth rate [CAGR]: -5.73%; p=0.011) and BKA (CAGR: -10.49%; p=0.013) from 2010 to 2019 but no significant difference in that of UKA (p=0.224) and TKA (p=0.421). Of the PFA, UKA, BKA, and TKA procedures performed, 6.88%, 8.83%, 17.49%, and 7.41% were performed under robotic assistance, respectively. For both UKA (CAGR: +19.81%; p=0.002) and TKA (CAGR: +3.90%; p=0.038) there was a significant increase in the utilization of robotic

As the use of robotic-assisted procedures becomes more popular, other arthroplasty procedures may become less favorable and decline in their prevalence. The results from this study contribute to the scarce body of research for robotic-assisted knee arthroplasties and adds data on each of the arthroplasty modalities.

assistance from 2010 to 2019, but no significant difference in that for PFA (p=0.724) and BKA (p=0.951).

**CONCLUSIONS:** TKA is still the most used arthroplasty procedure for OA (92.58% utilization rate). While outcomes have improved from earlier studies with PFA's, UKA's, and BKA's, this has not corresponded with a change in utilization in these procedures, but rather a decrease in PFA and

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BKA utilization. Our analysis suggests that the decrease in PFA and BKA utilization may be attributed to the transition to more innovative surgical techniques employing robotic assistance. As the use of robotic-assisted procedures becomes more popular, other arthroplasty procedures may become less favorable and decline in their prevalence. The results from this study contribute to the scarce body of research for robotic-assisted knee arthroplasties and adds data on each of the arthroplasty modalities. Future studies should investigate outcomes following robotic-assisted and nonrobotic-assisted arthroplasties to provide evidence-based recommendations that physicians can refer to when discussing arthroplasty procedures with their patients.

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## Impact of Human Immunodeficiency Virus on 2-Year Revision Rates Following Lumbar Fusion for Degenerative Spinal Conditions: a Retrospective Cohort Study

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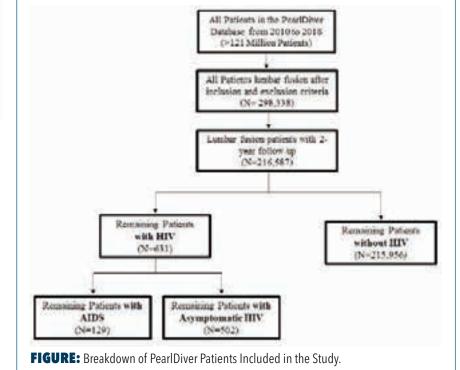


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The average age for individuals living with human immunodeficiency virus (HIV) is increasing with the development of highly effective treatment options.1 With the population continuing to age, and more cases of degenerative spinal conditions arising, surgeons are performing lumbar arthrodesis on older patients.2-4 Thus, the demand for lumbar fusions continues to increase in seropositive patients with HIV,<sup>5</sup> so analysis of the relationship between HIV and complications/outcomes following lumbar fusion is imperative. However, no studies exist that evaluate the impact of HIV on long-term revision rates following lumbar fusion. This study aims to understand how HIV impacts 2-year revision rates and 90-day postoperative complication rates following primary lumbar fusion for degenerative spine conditions.

Data collection was done using PearlDiver Patient Records Database,



a national insurance database from 2010-2019. Patients who underwent primary lumbar fusion for degenerative diseases were identified and divided into a cohort of patients that are HIV positive (HIV), have asymptomatic HIV (AHIV), acquired immune deficiency syndrome (AIDS), and HIV-negative patients. Univariate and multivariable regression analyses were performed to determine rates of revision surgery, surgical site infection (SSI), neurological complications, sensory deficits, bowel/bladder dysfunction, and myelopathies within two years of surgery as well as 90-day postoperative complications.

In total, 216,587 patients who underwent primary lumbar fusions for degenerative spinal conditions were included in this study (Figure 1). Of these, 631 patients (0.29%) had a diagnosis of HIV at the time of their procedure, including 502 patients (0.23%) with a diagnosis of asymptomatic HIV and 129 patients (0.06%) with a diagnosis of AIDS at the time of lumbar fusion (Figure 1). Relative to the control cohort, patients diagnosed with HIV had no difference in odds of two-year revision surgery, surgical site infection (SSI), neurological complications, sensory deficits, bowel/ bladder dysfunction, and myelopathies. However, patients with HIV did have increased odds of postoperative pneumonia (OR 1.592; 95% CI 1.048-2.314; p=0.021) (Table 1). In terms

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		ALL HIV	Patients			Asympto	matic HIV			A	DS	
Multivariate	Odds Ratio	25%	75%	P-value†	Odds Ratio	25%	75%	P-value†	Odds Ratio	25%	75%	P-value†
NEUROLOGICAL COMPLICATIONS	0.127	0.007	0.560	0.039	5.32E- 06	1.95E- 33	2.31E- 34	0.908	-	-	-	-
BOWEL BLADDER												
DYSFUNCTION	0.646	0.441	0.911	0.018	0.568	0.358	0.854	0.011	-	-	-	-
MYELOPATHIES			-	-		-	-	-	-	-	-	-
OSTEOPOROSIS	-	-	-	-	0.223	0.013	0.988	0.134	2.765	0.673	7.488	0.087
RENAL FAILURE	1.251	0.827	1.821	0.265	-	-	-	-	2.912	1.521	5.213	0.001
ANEMIA	0.934	0.718	1.197	0.601	0.866	0.638	1.152	0.340	-	-	-	-
ARRHYTHMIA WITH AFIB	-	-	-	-	0.641	0.418	0.939	0.030	-	-	-	-
ARRHYTHMIA WITHOUT AFIB									1.323	0.650	2.463	0.406
HEART FAILURE	0.633	0.323	1.109	0.142	0.632	0.276	1.265	0.231	-	-	-	-
BLOOD TRANSFUSION	-	-	-	-	-	-	-	-	0.605	0.185	1.451	0.327
PULMONARY EMBOLISM	-	-	-	-	-	-	-	-	-	-	-	-
CELLULITIS									1.656	0.693	3.337	0.202
PNEUMONIA	1.592	1.048	2.314	0.021	-	-	-	-	3.564	1.883	6.207	0.001
RESPIRATORY COMPLICATIONS	1.326	0.767	2.127	0.275	-	-	-		2.585	1.075	5.264	0.017
SEPSIS	1.202	0.668	1.982	0.505	-	-	-	-	2.702	1.122	5.514	0.013

**TABLE:** Multivariate Analysis of 2-Year Complications and 90-Day Medical Complications Following Lumbar Fusion

*†Pearson's chi-squared test Bolding equals significance p<0.05* 

#### Continued from p. 72

of 90-day medical complications, AIDS patients had greater odds of respiratory complications (OR 2.585; CI 95% 1.075-5.264; p=0.017) and septic complications (OR 2.702; 95% CI 1.122-5.514; p=0.013) (Table 1).

Our results indicate that HIVpositive status does not affect 2-year revision rates following lumbar fusion. If appropriate prophylaxis strategies are taken before and after the procedure, HIV-positive patients may be successful lumbar fusion candidates, especially with a well-controlled HIV viral load. As the number of HIV positive patients undergoing elective surgery increases, it is imperative that surgeons carefully weigh the risks and benefits of operating on patients with a diagnosis of HIV and monitor their patients closely postoperatively to mitigate potential complications.

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## No Significant Differences in Postoperative Complications Between Outpatient and Inpatient Single-Level or Multiple-Level Cervical Disc Replacement

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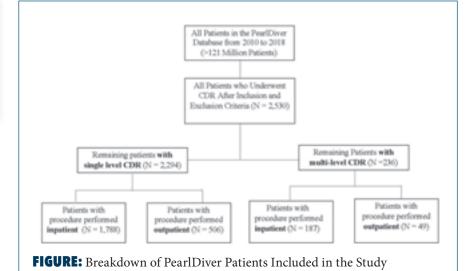
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Cervical disc replacement (CDR) has gained greater popularity in the past decade and is gaining traction as an option for operative management for patients with neck pain due to cervical degenerative disc disease (CDDD). CDR, in comparison to traditional anterior cervical discectomy and fusion (ACDF), has become a more desirable option for treating CDDD due to its ability to preserve motor function, restore the biomechanical properties of the intact cervical spine,1-3 prevent adjacent segment degeneration (ASD),<sup>4,5</sup> and be performed in the outpatient setting. Outpatient CDR has been an increasing trend in recent years because it increases patient satisfaction and reduces hospital-related costs. Current literature investigating outpatient versus inpatient CDR has shown a similar safety profile among the two cohorts. However, most of these studies have relatively small sample sizes with



short-term follow-up. Our study aimed to investigate the safety profile of outpatient versus inpatient single-level and multi-level CDR by analyzing shortterm and long-term outcomes using an extensive patient database.

A retrospective cohort study was done using the PearlDiver patient database between 2010 and 2019. Patients who underwent single-level and multi-level CDR with a follow-up of at least two years were identified. Patients within

each procedure cohort were subdivided into an outpatient and an inpatient group. Univariate and multivariable analyses were performed to identify 1-year and 2-year surgical complications, including anterior revision, posterior revision, incision and drainage, decompression laminectomy, and dural tear, as well as 90-day postoperative complications.

There were 2,294 patients who underwent single-level CDR, and 236 patients underwent multi-level CDR

[I]t is imperative that surgeons carefully weigh the risks and benefits of operating on patients in an outpatient setting and monitor their patients closely postoperatively to mitigate potential complications.

> (Figure 1). Of the patients who underwent single-level CDR, 506 patients underwent outpatient CDR, and 1788 underwent inpatient CDR (Figure 1). Of the patients who underwent multi-level CDR, 49 patients underwent outpatient

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CDR, and 187 underwent inpatient CDR (Figure 1). In the single-level CDR cohort, patients undergoing outpatient CDR were found to have lesser odds of a decompressive laminectomy at 1-year following the initial procedure (OR: 0.471; CI: 0.205 to 0.945; p=0.05) (Table 1). No other significant differences in 1-year or 2-year surgical or 90-day medical complications were found for the single-level CDR cohort. In addition, no significant differences in 1-year and 2-year surgical complications and 90-day postoperative complications were found on multivariable analysis of outpatient versus inpatient multilevel CDR.

As more patients undergo CDR, performing the procedure in an outpatient setting is gaining traction to reduce costs and improve patient satisfaction. Our study found that performing single-level and multi-level CDR on an outpatient basis has a similar safety profile to performing these procedures in an inpatient setting. Additionally, there is no statistical difference in longterm outcomes for outpatient multiplelevel CDR compared to inpatient. The outpatient setting for a single-level CDR was found to have lesser odds of **TABLE:** Multivariable Analysis of Surgical Outcomes and Complications following

 Single-Level Outpatient Cervical Disc Replacement compared to Single-Level Inpatient

 Cervical Disc Replacement

	Single-Level CDR Outpatient					
	Odds Ratio	95% Confidence Interval (Lower)	95% Confidence Interval (Upper)	P-value		
Total						
1-year Decompression Laminectomy	0.471	0.205	0.945	0.050		

1-year decompression laminectomy. If appropriate strategies are taken, performing a single-level CDR in the outpatient setting could lead to better long-term surgical outcomes for patients. However, it is imperative that surgeons carefully weigh the risks and benefits of operating on patients in an outpatient setting and monitor their patients closely postoperatively to mitigate potential complications.

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# The Effect of Obesity on Complications Following Isolated Posterior Cruciate Ligament Reconstruction

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Posterior cruciate ligament (PCL) injuries most commonly occur due to sports or motor vehicle accidents.1 PCL reconstruction has a relatively high complication rate of up to 20.1%, <sup>2</sup> therefore, it is imperative to assess preoperative risk factors that may impact the complication rate. Obesity is a known risk factor for post-surgical complications across various orthopedic procedures, including different arthroscopic surgeries.<sup>3-5</sup> Obesity has been associated with a higher cost of care related to managing comorbidities, increased operative time, and longer hospital stays after surgical procedures. Therefore, when selecting patients for surgery, especially procedures with a high complication rate like PCL reconstruction, it is crucial to consider the potential increased risk of postsurgical complications in patients with an elevated BMI.

**TABLE 1:** Demographics and Clinical Characteristics Among Patients Undergoing PCL

 Reconstruction

Demographics	Non-Obese	Obese	p-value
Total patients, n	258	156	
Sex, n (%)			0.595
Female	57 (22.1)	38 (24.4)	
Male	201 (77.9)	118 (75.6)	
Ethnicity, n (%)			0.446
Caucasian	133 (73.5)	92 (70.8)	
Black or African American	17 (9.4)	14 (10.8)	
Hispanic	17 (9.4)	19 (14.6)	
American Indian or Alaska Native	1 (0.6)	1 (0.8)	
Asian	9 (5.0)	2 (1.5)	
Native Hawaiian or Pacific Islander	4 (2.2)	2 (1.5)	
ASA, n (%)			< 0.001
l or ll	255 (98.8)	140 (89.7)	
III or IV	3 (1.2)	16 (10.3)	
Smoker, n (%)	50 (19.4)	33 (21.2)	0.662
Dependent Functional Status, n (%)	2 (0.8)	3 (1.9)	0.293
Mean age, yrs (SD)	30.91 (10.97)	35.88 (12.18)	< 0.001*
Mean BMI (SD)	25.43 (3.09)	35.08 (5.60)	< 0.001*

Pearson's chi-squared test \*\*Analysis of variance Bolding equals significance p<0.05

The literature is limited when examining the impact of elevated BMI on postoperative outcomes in patients undergoing PCL reconstruction. In order to understand what risk factors contribute to the high complication rate associated with PCL reconstruction 4 and adverse surgical outcomes, it is important to assess complication risks for isolated PCL injuries. In addition, most PCL reconstruction surgeries occur in the outpatient setting, and the need for whether or not patients require postoperative hospital admission after surgery is important for surgical planning. The purpose of this study was to utilize an extensive database to assess the risk of 30-day complications for obese patients, defined as a BMI > 30.0 kg/m2, undergoing isolated PCL reconstruction. We hypothesized that obese patients would have an increased risk of postoperative complications

From the years 2006 to 2019, the

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National Surgical Quality Improvement Program database was queried for patients undergoing isolated PCL reconstruction. Two patient cohorts were defined in this study: patients who were obese (BMI > 30.0 kg/m2) and non-obese patients (BMI < 30 kg/ m2). Patients' baseline demographics and medical comorbidities were collected and compared between the two groups. Postoperative outcomes were also assessed with the use of bivariate and multivariate analyses.

Of 414 patients who underwent PCL reconstruction, 258 patients (62.3%) were non-obese, whereas 156 patients (37.7%) were obese. Obese patients were more likely to be older, have a higher American Society of Anesthesiologists classification, and have hypertension compared to non-obese patients (p<0.05 for all) (Table 1). Following adjustment on multivariate analyses, relative to patients without obesity, those with obesity had an increased risk of admission to the hospital overnight (OR 1.66; p=0.048) (Table 2).

Our results and the heterogeneity in the literature indicate that obesity has a significant impact on the rates **TABLE 2:** Multivariate Analysis of Postoperative Complications of Patients Following

 PCL Reconstruction

Obese (versus Non-Obese) O	Odds Ratio	95%	6 CI	P Value
Postoperative Admission	1.661	1.004	2.749	0.048

Bolding equals significance p<0.05 PCL, posterior cruciate ligament; Cl, confidence interval

of hospital admission following PCL reconstruction. Though no studies have examined whether weight loss before PCL surgery improves outcomes, having patients lose weight prior to the procedure has the potential to reduce costs. Additionally, it merits consideration of refraining from performing isolated PCL injuries on obese patients in stand-alone surgery centers as there is an increased complication of unintended hospitalization. Overall, it is important for surgeons to carefully weigh the risks and benefits of operating on obese patients and to plan surgery settings accordingly, as obese patients may require postoperative hospital admission. This study indicates that patients with BMI > 30 are at increased risk of requiring postoperative hospital admission after PCL reconstruction.

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## Decreased 5-Year Anterior and Posterior Revisions Following Single-Level Cervical Disc Replacement When Compared to Single-Level Anterior Cervical Discectomy and Fusion in Patients with Cervical Radiculopathy

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Surgical approaches for diseases of the cervical spine have evolved considerably since the early 20th century. Anterior cervical discectomy and fusion (ACDF) was first implemented in the 1950s as an alternative to the posterior approach for easier access to the intervertebral disc space.<sup>1</sup> Several long-term studies support ACDF as an effective treatment option for patients with cervical myelopathy, radiculopathy, and cervical degenerative disc disease (CDDD).<sup>2</sup> However, ACDF does not preserve the natural segmental motion of the spine, resulting in reduced range of motion and increased risk of developing adjacent segment disease (ASD).3 Cervical disc replacement (CDR) was initially described in 1966 by Fernstrom et al who aimed to maintain segmental motion in all three rotational planes of the spine by using a ball and socket prosthesis.<sup>4</sup> In the past decade, CDR has gained traction as an alternative treatment option for radiculopathy, myelopathy, displacement of cervical intervertebral

**TABLE 1:** Cox Proportional Hazard Regression Models of 5-Year Surgical Outcomes

 Following Cervical Disc Replacement Compared to Anterior Cervical Discotemy Fusion.

		CDR				
	Hazard Ratio	95% Confidence Interval (Lower)	95% Confidence Interval (Upper)	P-value		
Total						
Anterior Revision	0.348	0.242	0.498	< 0.001		
Posterior Revision	0.568	0.434	0.744	<0.001		
Decompression Laminectomy	0.680	0.523	0.884	< 0.001		

discs without myelopathy, and CDDD.<sup>5</sup> However, as more patients undergo CDR, questions remain regarding the safety and effectiveness of this procedure. The aims of this study were to evaluate 5-year surgical outcomes as well as 90-day medical outcomes between patients who underwent CDR and those

who underwent ACDF.

A retrospective study was performed using patient data collected from the PearlDiver database between 2010 to 2020. Patients who underwent single-level CDR or ACDF with a follow-up of at least five years were identified and included in this study.

Univariate and multivariable analyses were performed to determine the rate of 5-year surgical outcomes as well as 90-day postoperative complications among the CDR and ACDF cohorts.

In total, 53,139 patients were included in this study, of which 1,324 patients (2.5%) underwent single-level CDR and 51,815 (97.5%) underwent single-level ACDF. Relative to the ACDF cohort, patients in the CDR cohort had a significantly lower risk of anterior revision surgery (Hazard Regression (HR): 0.35; 95% Confidence Interval (CI): 0.24-0.50; p<0.001), posterior revision surgery (HR: 0.57; 95%

Our study showed that CDR has a lower incidence of anterior and posterior revision surgery compared to ACDF, supporting the results of prior randomized control studies and international database studies.

CI: 0.43-0.74; p<0.001), and decompression laminectomy (HR: 0.68; 95% CI: 0.52-0.84; p<0.001) within 5-years of index surgery (Table 1). Additionally, patients who underwent CDR had lower odds of hematoma, respiratory failure, and stroke within 90-days of index

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surgery when compared to the ACDF cohort (Table 2).

CDR and ACDF are often recommended as treatment options for similar pathologies. Our study showed that CDR has a lower incidence of anterior and posterior revision surgery compared to ACDF, supporting the results of prior randomized control studies and international database studies. As surgeons gain greater experience with this relatively novel technique, CDR may become the gold standard for treating cervical radiculopathy and other cervical pathologies resulting from degenerative processes.

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**TABLE 2:** Multivariable Regression of 90-Day Complications Following Cervical Disc Replacement Compared to Anterior Cervical Discectomy Fusion.

	CDR					
	Odds Ratio	95% Confidence Interval (Lower)	95% Confidence Interval (Upper)	P-value		
Total						
Hematoma	0.547	0.371	0.774	0.001		
Pneumonia	0.556	0.287	0.962	0.055		
Respiratory Failure	0.119	0.020	0.371	0.003		
Sepsis	0.436	0.108	1.147	0.154		
Stroke	0.235	0.059	0.943	0.041		
Blood Transfusion	0.316	0.018	1.419	0.252		
Deep Vein Thrombosis	0.649	0.256	1.334	0.297		
Readmission	0.9	0.699	1.139	0.396		

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# Overweight BMI and Its Impact on Lumbar Fusion Complications in the Elderly U.S. Population

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As the percentage of the United States population above age 65 has grown, so too has the proportion of individuals who are elderly and overweight.1 In a 2019 report, 39% of men and 32% of women aged 65 to 74 years were overweight, with these percentages increasing to 47% and 35%, respectively, in those 75 years and older.<sup>2</sup> The rise in BMI and the aging population have coupled with an increase in lumbar spondylosis and spondylolisthesis diagnoses.<sup>3,4</sup> The rise in these spinal pathologies has led to a vast increase in lumbar fusion operations, which is an established treatment option to stabilize painful vertebral segments.<sup>3,4</sup> From 2004 to 2012, the volume of lumbar fusion operations increased 62.3% with the greatest increases seen in the population 65 years and older.<sup>4</sup> Although previous research has identified complication rates in elderly obese patients following lumbar fusion, elderly overweight patients are poorly studied despite comprising a large portion of the U.S. population.<sup>5</sup> The primary purpose of this study is to examine complication and readmission rates in overweight individuals following anterior, posterior, or transforaminal interbody lumbar fusion operations in an elderly population.

**TABLE 1:** Bivariate Analysis of Postoperative Complications of Patients Following Lumbar Fusion.

Complications	Normal Weight (BMI ≥ 18.5 & ≤ 24.9)	Overweight (BMI ≥ 25.0 & ≤ 29.9)	p-value <sup>4</sup>
Total patients, n	6,171	12,697	
Major complication, n (%)**	179 (2.9)	344 (2.7)	0.453
Minor complication, n (%)††	1,145 (18.6)	2,070 (16.3)	<0.001
Superficial Surgical Site infection, n (%)	42 (0.7)	85 (0.7)	0.930
Deep Surgical Site Infection, n %)	28 (0.5)	59 (0.5)	0.917
Wound Dehiscence, n (%)	16 (0.3)	32 (0.3)	0.926
Pneumonia, n (%)	80 (1.3)	124 (1.0)	0.046
Renal Insufficiency, n (%)	11 (0.2)	15 (0.1)	0.296
Palmonary Embolism, n (%)	37 (0.6)	84 (0.7)	0.617
Urinary Tract Infection, n (%)	130 (2.1)	266 (2.1)	0.958
Stroke, n (%)	18 (0.3)	33 (0.3)	0.693
Transfusion Requirement, n (%)	948 (15.4)	1,647 (13.0)	< 0.001
Deep Vein Thrombosis, n (%)	46 (0.7)	116 (0.9)	0.240
Myocardial Infarction, n (%)	39 (0.6)	82 (0.6)	0.911
Sepsis, n (%)	41 (0.7)	80 (0.6)	0.782
Death, n (%)	34 (0.6)	39 (0.3)	0.011
Extended Length of Stay, n (%)	1,140 (18.5)	2,140 (16.9)	0.006
Readmission, n (%)	367 (7.5)	707 (7.1)	0.292
Reoperation, n (%)	182 (2.9)	411 (3.2)	0.288

'Pearson' s chi-squared test

Bolding equals significance p<0.05

\*\*Includes deep surgical site infection, renal insufficiency, pulmonary embolism, stroke, myocardial infarction, sepsis, or mortality.

††Includes superficial surgical site infection, wound dehiscence, urinary tract infection, transfusion requirement, deep venous thrombosis, or pneumonia.

The National Surgical Quality Improvement Program database, a national registry that includes patient data from numerous medical centers nationwide, was used for this study. It was queried for patients aged 65 years or older undergoing lumbar fusion from 2005 to 2019. Two patient cohorts were defined: patients who were normal weight (BMI > 18.5 kg/ m2 and < 24.9 kg/m2) and patients who were overweight (BMI > 25.0 kg/ m2 and < 29.9 kg/m2). In this analysis, demographics, medical comorbidities, and postoperative complications were compared between the two different

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cohorts using bivariate and multivariable regression analyses.

Of 18,868 geriatric patients with a BMI < 30 kg/m2 undergoing lumbar fusion, 6,171 patients (32.7%) had a normal weight whereas 12,697 patients (67.3%) were overweight. Bivariate analyses revealed that when compared to overweight patients, patients who were normal weight were at increased risk of minor complications, pneumonia, transfusion requirement, mortality, and extended length of stay (p<0.05 for all). Following adjustment with multivariable analysis to control for patients' demographics and comorbidities, there were no differences in any postoperative complications between the normal weight and overweight groups.

Given the lack of research in the overweight population, defined as BMI 25-29.9 kg/m2, this study sought to determine thirty-day complication rates in the elderly and overweight population following lumbar fusion operations. While the initial bivariate analysis indicated that lumbar fusion patients with normal BMI had a higher rate of postoperative complications, the small differences between the groups were likely not clinically meaningful and did not hold up on the multivariable analysis. Despite increased BMI, **TABLE 2:** Multivariate Analysis of Postoperative Complications of Patients Following Lumbar Fusion.

Overweight (versus Normal Weight)	Odds Ratio	Odds Ratio 95% CI		P-Value.
Minor Complication ††	0.981	0.845	1.139	0.797
Pneumonia	1.058	0.619	1.808	0.838
Transfusion Requirement	0.917	0,780	1.079	0.297
Death	1.324	0.548	3.198	0.533
Extended Length of Stay	0.973	0.837	1.131	0.721

†Hincludes superficial surgical site infection, would dehiscence, urinary tract infection, transfusior requirement, deep venous thrombosis, or pneumonia

CI, confidence interval

the results after multivariate adjustment demonstrated that there are no differences in thirty-day postoperative complication rates following lumbar fusion operations between normal weight and overweight elderly patients. Further research should be conducted to determine potential longer-term complications in the overweight and elderly population. Additionally, future studies could also evaluate at which specific point does a change in BMI have an impact on complications. Including more relevant weight classes, such as obese and morbidly obese, for this patient population may add more information to the existing literature and may be the basis for future research studies.

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# LRP5 Variants Associated with Bone Quality Measures In Young Adults

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Osteoporosis, a musculoskeletal disorder characterized by low bone mineral density (BMD) and reduced bone quality, causes more than 8.9 million fractures each year globally.1 Prior studies have demonstrated that lossof-function mutations in low-density lipoprotein receptor-related protein 5 (LRP5), found in the Wnt/ $\beta$ -catenin pathway, can cause low BMD, while gain of function mutations can result in high BMD.<sup>2</sup> The purpose of this study was to expand our understanding of the impact of LRP5 variants on bone quality phenotypes in cohorts of Caucasian and African American young adults.

**COHORTS:** The Assessing Inherited Markers of Metabolic Syndrome in the Young (AIMMY) cohort consisted of (i) healthy African American young adults (n=166, 47 male, 119 female, 18-25 ages) from Howard University (HU) and (ii) healthy Caucasian young adults (n=117, 58 male, 59 female, 18-35 ages) from the University of Calgary (UC) recruited for a study aiming to identify genotypes associated with risk factors for metabolic syndrome. The Functional Single Nucleotide Polymorphism Associated

with Human Muscle Size and Strength (FAMuSS) cohort consisted of healthy Caucasian young adults (n=438, 170 male, 268 female, 17-40 ages) who participated in a non-dominant arm strengthening program for three months.

#### **GENOTYPING:**

DNA samples in AIMMY and FAMuSS cohorts were genotyped with TaqManTM Alleleic

Discrimination Assays (Applied Biosystems) and QuantStudioTM Flex Real-Time PCR System.

SNPs were evaluated for Hardy Weinberg Equilibrium. Genotype associations were explored using analysis of covariance (ANCOVA) additive models with covariates of age and/or weight. Post hoc pair-wise comparisons were conducted, and p-values were adjusted using the Sidak method. Statistical analysis confirmed Hardy Weinberg Equilibrium of (i) rs4988300 in the FAMuSS and AIMMY HU cohorts and (ii) in rs634008 FAMuSS, AIMMY HU, and AIMMY UC cohorts (p> 0.05). **AIMMY:** Caucasian males with rs634008 CT genotype were found to have increased total BMD in comparison to those with TT genotype (p=0.0326), while rs4988300 was not associated with total BMD. African American females with rs634008 CT genotype were found to have decreased weight in comparison to those with CC genotype (p=0370).

FAMuSS: Females with rs634008 CT genotype were found to have decreased non-dominant arm baseline

This study explored the association of TT genotype with BMD and found reduced total BMD in a population of Caucasian males in the AIMMY cohort. This finding which exhibits sexual dimorphism may have implications for long-term fracture risk.

> whole arm volume in comparison to those with CC genotype (p=0.0229). Males with rs634008 TT genotype were found to have increased dominant arm post-strengthening one-repetition maximum strength in comparison to those with CC genotype (p=0.0350).

> Wang et al. linked rs634008 TT genotype with reduced total hip and femoral neck BMD in cohorts of Han ethnicity.<sup>3</sup> This study explored the association of TT genotype with BMD and found reduced total BMD in a population of Caucasian males in the AIMMY cohort. This finding which

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exhibits sexual dimorphism may have implications for long-term fracture risk. Here we demonstrate the association of rs634008 CT with reduced body weight in African American females from the AIMMY cohort. Prior studies have reported both positive and negative associations of total body weight and bone health. While increased mechanical loading in individuals with high body weight benefits BMD, studies have indicated that metabolic changes associated with obesity increase pro-inflammatory cytokines which negatively impact bone.<sup>5</sup> This study demonstrated additional associations suggesting that variants in LRP5 may impact muscle phenotypes, indicating the need for further investigation. This study is limited by the absence of BMD measurements for African American young adults in the AIMMY and FAMuSS cohorts.

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**IRB:** Approved by Children's National Hospital Institutional Review Board

## Sexually Transmitted Infections and Treatment Adherence Among Adolescents in the Emergency Department: A Mobile Health Pilot Intervention

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Although adolescents and young adults represent only 25% of the sexually active population, they account for nearly 50% of all newly diagnosed sexually transmitted infections (STI) annually.<sup>1,2</sup> Failure to diagnosis and treat STIs in a timely manner can lead to worse health outcomes, including pelvic inflammatory disease. Adolescents often receive sexual and reproductive health services in the emergency department (ED). However, when adolescents are prescribed outpatient treatment for STIs in the ED, less than 60% of prescriptions are filled.<sup>3</sup> Lack of STI treatment adherence can further perpetuate the STI epidemic among this high risk group. The objective of this study was to evaluate the impact of a mobile health (mHealth)/text messaging intervention on prescription fill rates and treatment adherence following STI diagnosis in the ED.

From June 1, 2021 to Sept. 10, 2021, patients age 15–21 years were approached for study enrollment in person or by phone following their ED

visit if they were tested for gonorrhea/ chlamydia in the ED, prescribed outpatient STI treatment, and had a cell phone with text messaging (TM) capabilities. Enrolled patients received daily TM reminders to fill their prescription and barrier support for up to seven days. Once patients reported filling their prescription, they received daily TM reminders to take their medicine twice

a day. Research team helped address any identified barriers to prescription filling or treatment through TM. Study participants responded to a survey via text or phone after completion of their treatment on the usefulness of the reminders and TM support. Primary outcomes were prescription filling and

self-reported STI treatment adherence (finishing medication), and the secondary outcome was attitudes toward text messaging. Prescription filling data were abstracted from the electronic health record via SureScripts, an informatics network that collects data about prescription filling from participating pharmacies and insurance plans. Descriptive statistics were used to summarize the data.

There were a total of 60 patients eligible to participate in the study. Of those, 12 (20.0%) refused, and 15 (25.0%) were not able to be reached, and 33 (55.0%) were enrolled in the mHealth intervention. Participants were predominantly Non-Hispanic Black (81.8%), female (72.7%), and publicly insured (56.3%), with a mean age of 17.8 years. Of the enrolled patients, 20 (60.6%) completed the mHealth intervention, 4 (12.1%) opted out, 5 (15.2%) were lost to follow-up, and 4 (12.1%) are currently active as this is an ongoing study. Nearly all enrolled participants (93.9%) filled their prescription and 18 (90%) of those who completed the study reported finishing their medication. The majority of participants found the texts to be helpful reminders to fill their prescriptions (95%) and to take their medications (100%).

Text messaging can be an effective tool to address treatment adherence in adolescent ED patients, an at-risk population who may otherwise be difficult to reach.

> Text messaging can be an effective tool to address treatment adherence in adolescent ED patients, an at-risk population who may otherwise be difficult to reach. mHealth provides additional support to patients following their ED visit, which can help increase treatment adherence and reduce the spread of STIs, which is key for the broader management of public health.

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# Analysis of Routine Intensive Care Unit Admission Following Palatoplasty in Patients With Robin Sequence

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Management of neonatal upper airway obstruction (UAO) in patients with Robin Sequence (RS) may impact the need for intensive care unit (ICU) care following primary palatoplasty (PP) later in life. The current study investigated the necessity for ICU admission after PP in patients with RS, based upon prior upper airway management.

We conducted a review of patients with RS who underwent PP between 2006-2020. Patient demographics, perioperative characteristics, ICU admission, and postoperative airway and non-airway complications were compared, based on prior airway management, as determined by multidisciplinary team evaluation and consensus.

Fifty-eight patients were included. Median [IQR] age at PP was 12.9 [10.8,15.6] months. Three groups were compared: Conservative (n=30), tongue-lip adhesion (TLA) (n=14) and mandibular distraction osteogenesis

<b>TABLE 1:</b> Comparison of airway and non-airway outcomes between the study groups.								
Complications	Overall (N= 58)	Conservative (N= 30)	TLA (N= 14)	MDO (N= 14)	P value			
Non-airway complications, n (%)	13 (22.4)	8 (26.7)	1 (7.1)	4 (28.6)	0.320			
<ul> <li>Prolonged time to feeding (&gt;24 hours)</li> </ul>	7 (12.1)	4 (13.3)	1 (7.1)	2 (14.3)	0.999			
<ul> <li>–Unexpected gavage feeding</li> </ul>	1 (1.7)	1 (3.3)	0 (0.0)	0 (0.0)	0.999			
-Transfusion	1(1.7)	1 (3.3)	0 (0.0)	0 (0.0)	0.999			
–Fistula	2 (3.4)	2 (6.7)	0 (0.0)	0 (0.0)	0.999			
-Readmission	4 (6.9)	2 (6.7)	0 (0.0)	2 (14.3)	0.531			
Airway complications, n (%)	25 (43.1)	8 (26.7)	9 (64.3)	8 (57.1)	0.034			
<ul> <li>Prolonged intubation</li> <li>(&gt;4 hours)</li> </ul>	3 (5.2)	1 (3.3)	2 (14.3)	0 (0.0)	0.283			
-Reintubation	4 (6.9)	2 (6.7)	1 (7.1)	1 (7.1)	0.999			
-Mechanical ventilation	5 (8.6)	2 (6.7)	1 (7.1)	2 (14.3)	0.826			
-Supplementary oxygen via nonbreathable mask, nasal cannula, aerosol mask, previous	12 (20.7)	4 (13.3)	4 (28.6)	4 (28.6)	0.338			
tracheostomy -Length of stay > 2 days	18 (31.0)	6 (20.0)	6 (42.9)	6 (42.9)	0.161			

(MDO) (n=14). While ICU admission (conservative, 33.3%; TLA, 78.6%; MDO, 78.6%; p=0.002) and overall airway-related complications were significantly higher in patients with prior TLA and MDO (conservative, 26.7%; TLA, 64.3%; MDO, 57.1%; p=0.034), rates of major post-PP airway events (prolonged intubation >4h, unexpected ventilatory support via pre-existing tracheostomy, or reintubation) that would have required ICU care were low and insignificant between groups (0-14.3%; p>0.05); post-hoc analysis documented significant differences only in overall airway events between

TLA vs. conservative airway groups (64.3% vs. 26.7%; p=0.02).

ICU care after PP in patients with RS may not be necessary in infants who had appropriate management of neonatal UAO, potentially preserving resources for patients with greater need. Special attention may be prudent for post-PP patients who underwent neonatal TLA.

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**TABLE 2:** Comparison of airway and non-airway outcomes between the study groups stratified by major and minor events.

Outcomes	Overall (N= 58)	Conservative (N= 30)	TLA (N= 14)	MDO (N= 14)	P value			
Non-airway complications, n (%)								
–Minor event	12 (20.7)	7 (23.3)	1 (7.1)	4 (28.6)	0.516			
–Major event	1 (1.7)	1 (3.3)	0 (0.0)	0 (0.0)				
Airway complications, n (%)								
–Minor event	19 (32.8)	6 (20.0)	7 (50.0)	6 (42.9)	0.135			
–Major event	6 (10.3)	2 (6.7)	2 (14.3)	2 (14.3)				

\*P values were obtained from Fisher's exact test

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# Trends in Natural Decannulation in Patients with Robin Sequence: A 25-Year Retrospective Review

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Robin sequence (RS) is defined by micrognathia and glossoptosis that result in upper airway obstruction (UAO). In RS patients who undergo tracheostomy, long-term goals include decannulation without further surgical intervention (natural decannulation). The objective of this study was to identify long-term trends in rate and length of time to natural decannulation.

A retrospective chart review was performed on 151 RS patients treated at a large pediatric tertiary center from 1995 to 2020. Patients with UAO treated with tracheostomy were grouped by year of tracheostomy: 1995-2004, 2005-14, and 2015-20. Demographic data, UAO management, postoperative care, complications, and time to decannulation were recorded.

Thirty-six patients (n=36) met the inclusion criteria (50% syndromic RS). Median UAO treatment age was 9.5 [0 to 571] days of age. Nearly 53% (n=19) of patients were naturally decannulated. Overall median time to decannulation was 5.5 years. Natural decannulation rate was higher in the non-syndromic

RS patients (78% non syndromic vs. 28% syndromic; p = 0.003) and during the first study period (1995-2004: 73%, 2005-2014: 36%, and 2015-2020: 43%; p<0.05). Pre-operative capillary blood gas max-CO2 was higher in patients with syndromic RS (80 mEq/L vs. 67 mEq/L; p = 0.036). Univariate and multivariate regression analyses failed to demonstrate significant factors associated with barriers in getting decannulated. Rate of tracheostomy-specific complications was 54%, with an overall mortality rate of 3%. Lastly, median follow-up time after tracheostomy was 5.88 [2.15 to 10.32] years.

Syndromic RS and higher pre-op max-CO2 were associated with longterm tracheostomy dependency. Decannulation rates were higher in the 1995-2004 patient subgroup, likely because tracheostomy is now only used in the most severe cases at our institution and mandibular distraction osteogenesis has become accepted primary surgical treatment in severe RS upper airway obstruction.

# Efficacy of Ethanol Ablation as a Treatment of Benign Head and Neck Cystic Lesions

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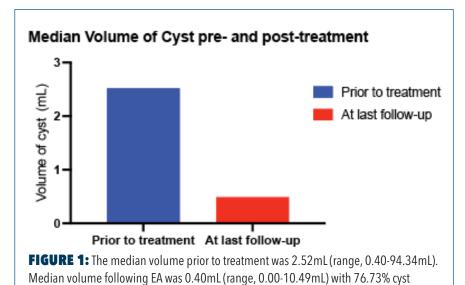
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Sclerotherapy, or ethanol ablation (EA) has been shown to be a safe, cost-effective, and minimally invasive alternative to surgical intervention for the treatment of a range of head and neck cysts.<sup>1</sup> This study aims to describe the use of ultrasound-guided EA in the treatment of benign cystic lesions of the head and neck within the otolaryngology clinic setting, reducing the need for external referrals and streamlining the treatment by a single provider.

This study further aims to assess the efficacy and safety profile of EA for the treatment of various cystic lesions of the head and neck. A total of 25 patients who received ethanol ablation (EA) of head and neck cystic lesions by an otolaryngologist at a single institution between October 2017 and October 2020 were identified. Patient demographics, clinical characteristics, treatment details, and treatment outcomes at follow up visits were obtained by retrospective review of electronic medical records. For the descriptive



statistical analysis, the categorical variables were expressed as numbers and percentages, and the continuous variables were expressed as medians and ranges. The volume of cyst prior to

reduction by volume (range, 37.50-100.00%) (p=0.002).

treatment and volume of the cyst at last follow-up were compared using Wilcoxon signed-rank test. Statistical significance was declared at p<0.05. The statistical analyses were performed using the SPSS software version 27.0 (SPSS Inc., Chicago, IL).

Twenty-five patients who underwent ethanol

ablation of head and neck cystic lesions were included, with a median age of 52 years old (range,19-81 years) and 12 males (47.0%). The most common cysts treated with EA were thyroglossal duct cysts (n=8, 32.0%) and lymphoepithelial parotid cysts (n=7, 28.0%). The median volume prior to treatment was 2.52mL (range, 0.40-94.34mL). Median volume following EA was 0.40mL (range, 0.00-10.49mL) with 76.73% cyst reduction by volume (range, 37.50-100.00%) (p=0.002). The median time to the last follow-up was one month (range, 0.5-18

Sclerotherapy, or ethanol ablation (EA) has been shown to be a safe, cost-effective, and minimally invasive alternative to surgical intervention for the treatment of a range of head and neck cysts.<sup>1</sup>

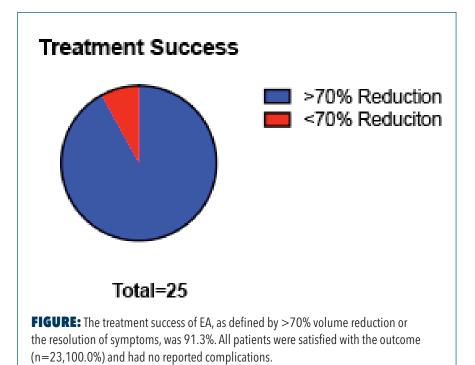
> months). One patient received surgery despite treatment success to obtain a definitive diagnosis of the mass. No other patients received further surgical management. The treatment success of EA, as defined by >70% volume reduction or the resolution of symptoms, was

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91.3%. All patients were satisfied with the outcome (n=23,100.0%) and had no reported complications. In conclusion, EA is an effective and safe alternative to surgery for the treatment of head and neck cystic lesions that can be performed in an outpatient setting by an otolaryngologist.

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# **Comparison of Auditory Brainstem Responses at Different Medical Centers**

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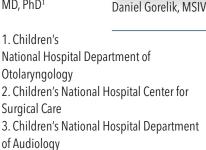
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Newborn hearing screenings have become a universal practice in order to limit delays in childhood development. At present, the diagnosis of hearing loss is accomplished by testing otoacoustic emissions (OAE) and auditory brainstem response (ABR). In recent years, ABRs have grown in use and as they can be conducted in children and infants unable to undergo traditional hearing tests due to age or disability. This noninvasive test measures electrical activity along the auditory pathway in response to auditory stimuli including clicks, tonebursts, and chirps.1

Current Early Hearing Detection and Intervention (EHDI) guidelines recommend a hearing screen by one month of age, diagnosis of hearing loss

by three months of age, and enrollment in early intervention programs by six months of age. Previous reports identify that adherence to these guidelines is significantly associated with better vocabulary, language abilities, and speech intelligibility.<sup>2,3</sup>

To date, the use of ABR testing and its relationship to the EHDI guidelines has not been studied despite its role in early hearing loss detection. The primary purpose of this study is to evaluate for discrepancies in diagnostic ABRs between Children's National Hospital (Children's National), a pediatric medical center, and outside facilities (OSH) that referred patients to Children's National for confirmatory evaluation. Such discrepancies could impact EHDI timelines.

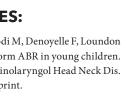
Retrospective chart review from an internal database of patients who underwent diagnostic ABR from 2017-21. Only patients with ABR results from both Children's National and OSH were analyzed. Demographic data, external and internal test results, and intervention data were obtained. Hearing loss severity was graded on a scale of 0-9 (0 = normal, 1 = normal to mild, 2 = mild, 3 = mild to moderate, 4 =moderate, 5 =moderate to severe, 6 = severe, 7 = severe to profound, 8 =profound, 9 = could not be determined). Each patient's score was the average between the left and right ear.

Forty-eight patients met the inclusion criteria. The average age was 138.9 days and bilateral hearing loss was noted in 37 patients at Children's National and 35 patients at OSH (p = 0.637). Median hearing loss severity at Children's National was 3.0 (mild to moderate) compared to 4.0 (moderate) at OSH (p = 0.002). Of note, 26 of 48 (54%) went on to ultimately receive a hearing amplification device: 18 (69%) were fitted for hearing aids while remaining eight (31%) got cochlear implants. ABR results from Children's National and OSH differed in 20 of these patients; six (30%) had worse hearing loss on Children's National ABR and 14 (70%) had worse hearing loss on OSH ABR.

Our results showed statistical significance in median severity of hearing loss between Children's National and OSH. A substantial proportion (77%) of children in our dataset who had received a cochlear implant or hearing aids had ABR discrepancies between Children's National and OSH. These findings have implications with regards to appropriate usage of health care resources and maintaining Early Hearing Detection and Intervention timelines.

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# Apparent Diffusion Coefficient and T2 Signal in MRI's of Clinically Significant Prostate Cancers

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Over the last decade, standard of care has shifted towards evaluation of men with elevated prostate specific antigen (PSA) with prostate MRI, for identification of suspicious lesions and targeted MRI-ultrasound fusion guided biopsy.1 Correlation of MRI imaging features with prostate cancer Gleason grade (GG) is critical for the diagnosis of clinically significant prostate cancer (csPCA), defined as GG of greater than or equal to 3. The purpose of this study is to calculate the apparent diffusion coefficient (ADC) and T2 signal of csPCA and determine if it correlates with GG.

Methods: Patients who had a preoperative MRI and prostatectomy at GW Hospital between January 2015 and December 2019 were identified using electronic medical records. Out of 148 initially screened patients, 41 were included in the study. Patients were included if the index cancer, defined as the highest GG cancer on surgical pathology, could be confidently localized on MRI using the pathology report and 3 Tesla MRI scan was performed. Patients were excluded if prostatectomy was performed for benign prostatic hypertrophy, 1.5 Tesla MRI exam was performed, or MRI artifact obscured the index cancer. Surgical pathology reports were reviewed and correlated with pre-operative MRI to identify

FIGURE: Axial T2 and ADC map, prostate with tracing (ROI) around the index cancer.

the index cancer on imaging. Region of interests (ROIs) were drawn around the index cancer on axial T2 and ADC sequence. Mean and 95% confidence intervals for T2 and ADC signal were calculated for low-grade (GG1 and 2) and csPCA (GG3, 4, and 5) and compared with T-tests.

**Results:** Mean T2 and ADC signals as well as frequency for each GG can be found in the included table. For T2 imaging, the mean signal value for low-grade was 225.78 (95% CI 189.49-262.08) and 236.87 for csPCA (95% CI 210.81-262.93). The mean ADC signal

value for low-grade was 1075.89 (95% CI 991.57-1160.20) and 982.04 for csPCA (95% CI 914.50-1049.58). There was no statistically significant difference in T2 signal (p = 0.615) and ADC signal (p = 0.097) between low-grade and csPCA, although ADC signal was approaching significance.

**Conclusion:** Based on existing studies, it was expected for ADC signal to negatively correlate with GG.<sup>2,3</sup>

However, ADC was only shown to approach significance in this analysis. The absence of correlation may be due to the small study population. The large size of the prostate cancers included in this study and intra-tumoral heterogeneity may also account for lack

The large size of the prostate cancers included in this study and intra-tumoral heterogeneity may also account for lack of correlation: the index cancer may be a small portion of the overall ROI selected on imaging.

> of correlation: the index cancer may be a small portion of the overall ROI selected on imaging. Further study with a larger sample size that has more GG4 and GG5 could illustrate the expected trend of more aggressive cancers having lower T2 and ADC signal values.

> It was also found that 49% of patients had discordance between their pre-operative biopsy and surgical

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pathology GG; biopsy GG was lower in 15 patients, higher in 5 patients. Given this high discordance between biopsy and pathology, it would be helpful if MRI could predict the GG of lesions identified on MRI. On a similar note, imaging data from this study can be used to train and test machine learning algorithms in identifying csPCA and predicting their GG.

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	N =	T2 Signal	ADC Signal
GG1/2:	13	225.78	1075.89
GG3:	16	238.92	987.04
GG4:	3	224.00	1129.20
GG5:	9	237.51	924.11

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# Aspiration Needle Design for Intracerebral Hematoma Surgical Evacuation

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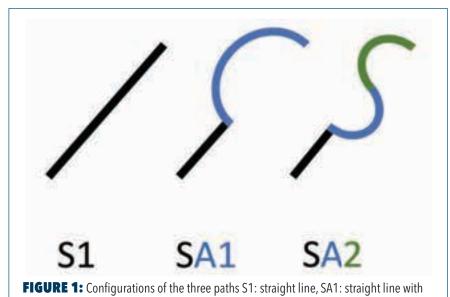
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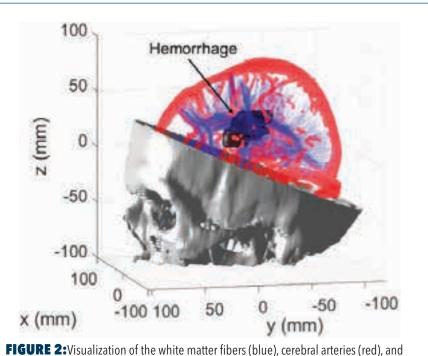
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Hemorrhage from ruptured intracranial vessels displaces brain parenchyma creating an intracranial hematoma (ICH). Despite the high mortality rate reported in the acute phase, surgical evacuation still fails to show improvement over medical treatment of ICH.<sup>1,2</sup> Proposed reasons include lack of intraoperative visualization of the hematoma and iatrogenic damage to surrounding tissue induced by the rigid tools used even in minimally invasive procedures.<sup>1,3,4</sup> An MRI-guided aspiration robot will overcome these limitations reducing the risk associated with the surgical evacuation of ICH. It will allow for real-time targeting of deep-seated hematomas while sparing critical brain structures. This study examines the benefit of using an archbased tube as opposed to straight tubes used in current practice.

Three configurations were tested and were defined as a) a straight line (S1), b) straight line with a single circular arch (SA1), and c) a straight line with two concentric circular arches (SA2) as demonstrated in Figure 1. Nine randomly chosen ICH's in the basal ganglia region were set as targets to test these three configurations using



single arch, SA2: straight line with two concentric arches.



the hematoma (black).

an optimization algorithm that calculates a risk value by summing up the impact on critical structures, i.e., blood vessels and cranial white matter fibers. The spatial distribution of cerebral arteries was defined using Mouches et

Continued on p. 94

al probabilistic atlas and the fiber tracts were set using the diffusion spectrum imaging (DSI) based atlas developed by Yeh et al which is represented in Figure (2).<sup>4,5</sup>

In the 9 tested ICH cases, SA1 and SA2 configurations were associated with a lower risk value than the S1 configuration. Comparing SA1 and SA2, a lower risk value was associated with SA2 in only five of the cases, whereas in the four remaining cases, the risk values of SA1 and SA2 were equal.

The trajectory of an arch-based tube with one or two arches is associated with a better safety profile than a straight tube. In addition, an archbased tube with two arches is safer than a tube with a single arch in only some cases where a more tortuous path is needed. Taken together, an arch-based tube minimizes the risk posed to cranial white matter tracts and blood vessels located along the trajectory to deep ICH. This work lays the foundation for the design of a robot with a dynamic aspiration needle that has the potential to revolutionize the way ICH is treated.

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## A Case of Erythema Elevatum Diutinum Exhibiting a Keloid-like Appearance

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**INTRODUCTION:** Most severe appearing keloids tend to occur around joints due to the increased extensional stimulation of the scar in those areas. On the other hand, erythema elevatum diutinum (EED) appears more commonly on friction sites including extensor surfaces of the extremities and dorsal surfaces of joints. EED-affected areas tend to be more reddish-brown or burgundy in color, and often morphologically appear as plaques or papules.<sup>1</sup>

**CASE PRESENTATION:** A 42-yearold woman presented with firm, browncolored tumorous nodules on her bilateral lower extremities (Figure 1). The patient started noticing the growths after sustaining some insect bites in these areas. The dermatologist she initially visited diagnosed her with keloids and subsequently treated her with triamcinolone injection and steroid tape. However, the patient did not respond to treatment, and the nodules did not soften or reduce in size. When she later visited our keloid specialty outpatient department in Nippon Medical School Hospital, the examination revealed dark-brown colored nodular lesions on bilateral knees, the right tibial region, dorsum of the left foot, the right calcaneal area, and the lateral side of the left foot (Figure 1A). The nodules on her lower extremities manifested in one of





**FIGURE 1:** (A) Preoperative view with the EED nodules on both knees, right tibial region, left dorsum of foot, right calcaneal area, and lateral side of the left foot. (B) Design of the local flap.. {C) Immediately after surgery. (D) Six months post-operative view.

two ways; first type of nodule appeared very similar to keloids, but the other type was partially rounded in shape, unlike a usual keloid. Ultimately, the original diagnosis of keloids was reaffirmed and surgery along with radiation therapy was determined to be the best course of treatment. The nodules were resected under general anesthesia with subsequent administration of 18 gray per 3 fraction continuous radiation therapy. After the initial course of treatment, a biopsy was sent to pathology. The histopathological examination revealed tuberous lesions in the dermis, increased wired collagen fibers, neutrophilic infiltrate with nuclear dust, and edematous endothelial cells in the small vessels (Figure 2). Through these histological findings, the patient was subsequently diagnosed with EED. Post-surgery, the patient reported no recurrence of EED or incidence of abnormal scar formation, including keloids or hypertrophic scars. The patient provided informed consent for the photographs and publication of this case report.

**DISCUSSION:** Whereas clinical findings of EED are similar to that of keloids, the mechanisms of the two conditions differ considerably, leading to varying management strategies. EEDs can be misdiagnosed as Keloids on several grounds; they can both appear morphologically similar, exhibit as stiff lesions, demonstrate chronic inflammation of the reticular dermis, and appear anywhere on the body. The only definitive method of differentiating between the two is through histopathological examination.

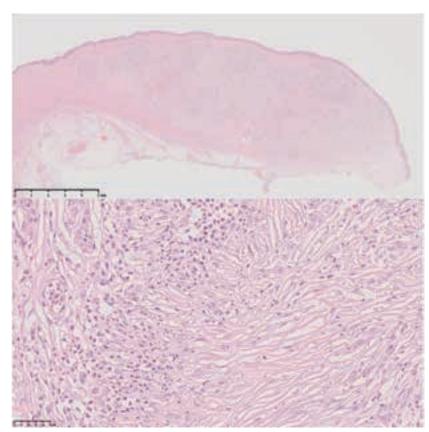
**CONCLUSION:** Diagnosing cutaneous manifestations simply through clinical findings might have its merits as the most cost and time effective method of diagnosis. However, there are instances where further investigation is necessary for accuracy, and this was the case with the patient discussed in this report. Our study suggests that, when treating keloidal lesions on friction sites, EED should be considered as a possible diagnosis, and a biopsy

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should be performed to confirm before administering treatment. On the same token, this report indicates that the medical field could benefit from an inquiry into the mechanism of mass formations of EED nodules that morphologically appear similar to keloids.

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**FIGURE 2:** Nodular lesions in the dermis. In the lesions, increasing characteristic wired collagen fibers, infiltration of neutrophils, and swelling of small endovascular cells are presented.

## Trifecta of Carotid Artery Intervention: Real-World Comparison of Transcarotid Artery Revascularization, Carotid Artery Stenting, and Carotid Endarterectomy

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Acute ischemic stroke is the 5th leading cause of death in the United States and number one cause of disability.1 Carotid artery atherosclerotic stenosis is responsible for up to 30% of ischemic strokes.1 The underlying pathophysiology of the ischemic stroke is plaque rupture and distal embolism.1 Treatment is recommended for the prevention of future stroke in symptomatic patients with >70% stenosis and can be beneficial in those with 50-69% stenosis, depending on patient-specific clinical and anatomical characteristics.1 Carotid endarterectomy (CEA) is an established first-line modality of treatment.1 Transfemoral or transradial carotid artery stenting (CAS) is another treatment modality usually used for patients who cannot undergo open surgery.<sup>1,2</sup> Transcarotid artery revascularization (TCAR) is a relatively new procedure.3,4 This treatment approach carries the advantage of flow reversal during stent deployment and angioplasty to prevent distal embolic complications and thus provide neuroprotection.<sup>5</sup> The purpose of this study was to add to the literature by providing

**TABLE 1:** Univariable and multivariable logistic regression for TIA or stroke within 30 days.

Variable	Odds Ratio	95% Confidence Interval	P-value					
Univariable analysis								
Age	0.99	0.95-1.02	0.631					
Sex (male)	0.40	0.18-0.88	0.024*					
Diabetes mellitus	1.07	0.47-2.43	0.861					
Hypertension	0.88	0.39-1.99	0.768					
Hyperlipidemia	0.82	0.36-1.86	0.644					
Atrial fibrillation	0.81	0.24-2.74	0.738					
Left side	0.90	0.41-1.95	0.797					
Symptomatic	6.83	0.91-50.81	0.060					
Intraprocedural TIA or stroke	2.17	0.27-17.25	0.462					
Multivariable analysis								
Age	0.99	0.95-1.02	0.565					
Sex (male)	0.38	0.17-0.87	0.023*					
Diabetes mellitus	1.1	0.49-2.75	0.718					
Hyperlipidemia	0.76	0.31-1.82	0.760					
Atrial fibrillation	1.04	0.29-3.68	0.951					
Left side	0.77	0.34-1.71	0.526					
Symptomatic	6.49	0.861-49.05	0.070					
Intraprocedural TIA or stroke	2.61	0.30-22.56	0.383					

Abbreviation: TIA, transient ischemic attack \*Statistically significant

real-world data comparing the safety and effectiveness associated with the performance of these carotid revascularization techniques by dual-trained neurosurgeons.

We performed a retrospective review of carotid stenosis databases at two U.S. centers.

Patients treated by CEA, transfemoral CAS, or TCAR for atherosclerotic carotid artery disease were included. Clinical outcomes at 30 days post procedure were compared. A total of 780 patients were included (583 CAS, 165 CEA, and 32 TCAR). Overall, 486 (62.3%) patients were men, and 393 (50.4%) had left-sided carotid disease. Most patients (617; 79.1%) had symptomatic disease. Among the three treatment groups, there were no statistically significant differences with respect to 30-day ischemic events: CAS, 3.8%; CEA, 1.8%; and TCAR, 6.2% (p=0.267); or 30-day mortality rates: CAS, 3.6%;

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CEA, 2.4%, and TCAR, 3.1% (p=0.857). Male sex had significantly lower odds of 30-day transient ischemic attack (TIA) or stroke on both univariable (p=0.024) and multivariable (p=0.023) regression models. Increasing age had significantly higher odds of 30-day mortality on univariable (p=0.006) and multivariable regression (p=0.003). Patients with the occurrence of 30-day TIA or stroke also had significantly higher odds of 30-day mortality on univariable (p<0.001) and multivariable regression (p<0.001).

Our real-world experience suggests that with appropriate selection all three treatment modalities carry comparable safety and effectiveness in revascularization of the carotid artery.

#### ABBREVIATIONS

CAS, carotid artery stenting; CEA, carotid endarterectomy; CI, confidence interval; CMS, Centers for Medicare and Medicaid Services; mRS, modified Rankin Scale; NASCET, North American Symptomatic Carotid Endarterectomy Trial; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; TIA, transient ischemic attack; TCAR, transcarotid artery revascularization

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**TABLE 2:** Univariable and multivariable logistic regression for 30-day mortality.

Variable	Odds Ratio	95% Confidence Interval	P-value				
Univariable analysis							
Age	1.06	1.01-1.11	0.006*				
Sex (male)	0.59	0.27-1.30	0.198				
Diabetes mellitus	1.13	0.49-2.58	0.761				
Hypertension	0.59	0.26-1.31	0.197				
Hyperlipidemia	0.47	0.21-1.03	0.060				
Atrial fibrillation	1.19	0.40-3.55	0.743				
Left side	1.14	0.52-2.51	0.730				
Symptomatic	NA	NA	0.995				
Intraprocedural TIA or stroke	NA	NA	0.999				
30-day TIA or stroke	17.12	6.62-44.24	<0.001*				
Multivariable analysis							
Age	1.08	1.02-1.12	0.003*				
Sex (male)	0.63	0.26-1.55	0.323				
Diabetes mellitus	1.65	0.64-4.20	0.293				
Hypertension	0.53	0.19-1.45	0.221				
Hyperlipidemia	0.57	0.22-	0.256				
Atrial fibrillation	1.29	0.39-	0.672				
Left side	0.95	0.39-2.28	0.911				
Symptomatic	NA	NA	0.995				
Intraprocedural TIA or stroke	NA	NA	0.999				

\*Statistically significant

Abbreviations: NA, not applicable; TIA, transient ischemic attack

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# Bariatric Left Gastric Artery Embolization: An Overview of Mechanism, Technique, and Reported Literature

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Ghrelin, a 28-amino acid hormone, is secreted by the gastrointestinal tract and acts on the central nervous system to stimulate hunger and appetite. Recently, left-gastric artery embolization (LGAE) has been investigated for weight-loss purposes as a minimally invasive procedure.<sup>1,2</sup> Through percutaneous vascular access, the left gastric artery that supplies the ghrelin-producing cells in the gastric fundus is embolized with microspheres. Blood flow restriction in this area reduces ghrelin secretion, achieving hunger suppression and weight-loss.1 In this study, our goal is to describe the mechanism of action,

[Left-gastric artery embolization] is safe and feasible intervention in achieving weight-loss in patients who have failed conservative management and are high risk surgical candidates.

provide a technical illustration, and review the preliminary clinical studies of bariatric LGAE.

First, percutaneous vascular access, such as femoral artery and radial artery, should be established. Next, **TABLE:** Baseline characteristics of studies included in the pooled-study and metaanalysis.

Author/Year	Region	Sample Size	Follow- up	Microsphere (um)	Measured outcomes
Bai 2018	China	5	9 months	500-700	Weight, waist circumference, waist to-height ratio, adipose tissue, ghrelin, leptin, complications
Elens 2018	Belgium	16	12 months	300-500; 500-700	Weight, complications, appetite, satisfactory assessment
Kipshidze 2015	USA	5	24 months	300-500	Weight, ghrelin
Pirlet 2018	Canada	7	12 months	300-500	Weight
Syed 2016	USA	4	6 months	300-500	Weight, ghrelin, leptin, cholecystokinin, complications
Weiss 2019*	USA	20	12 months	300-500	Weight, ghrelin, complications, IWQOL-Lite scores, SF-36 scores, HbA1C, Hunger score, cholesterol, triglyceride, HDL, LDL

\*Certain included data were obtained from previous published preliminary results of the same clinical trial.

catheterization of the celiac artery could be performed with an angiographic catheter. Digital subtraction

> angiography of the celiac artery and superior mesenteric artery would allow the identification of the left gastric artery and other potential accessory gastric arteries. After confirming location with angiography, using a microcath-

eter, microspheres could be injected to embolize the LGA until achieving stasis.

Post-procedural weight loss demonstrated an upward trend in terms of statistical significance at 1-month, 3-month, 6-month, and at the study endpoints (p=0.283, 0.116, 0.064, and 0.045, respectively).1-6 On average, every study suggested weight loss during follow-up periods, and the mean weight loss demonstrated an upward trend overtime. According to the pooled-analysis, by 6-month, the mean weight loss was 9.8 kg, and this value increased to 11.5 kg at or greater than 1 year. Only two studies reported excess weight losses (EWL).<sup>3,5</sup> Both studies suggested an upward trend of EWL over the first 6 months post-bariatric embolization: 8.6, 12.4, and 14.0 kg at 1-month, 3-month, and 6-month respectively.

Three studies measured serum ghrelin levels at baseline and during follow-up.<sup>1,3,4</sup> Although Bai et al and Kipshidze et al observed an initial

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decrease at three months, subsequent ghrelin levels were approaching the baseline. The maximal ghrelin decreased 24 pg/ml from the baseline on average. The mean serum ghrelin at 6-month postprocedural was 365.9 pg/ml, decreased from 453.9 pg/ml at baseline. However, the difference between six months and baseline was not statistically significant (p=0.173).Two studies reported serum leptin levels.<sup>3,4</sup> No apparent trend could be appreciated based on the pooled analysis. No significant difference in leptin levels was found before and after bariatric embolization (p=0.554).

LGAE is safe and feasible intervention in achieving weight-loss in patients who have failed conservative management and are high risk surgical candidates. Serum ghrelin level in clinical setting is not as reliable in predicting weight-loss. This might result from its hourly fluctuation throughout the day. A more reliable test is necessary to characterize its change after LGAE. Future research can focus on maximizing selective reduction of ghrelin-producing cells while avoiding complications such as gastric ulcers. More clinical data and larger sample



**FIGURE:** LGAE mechanism and methodology. Left: X/A-like cells secretes ghrelin that stimulates hunger. Middle: the left gastric artery is catheterized from the radial artery access. Right: Embolization with microspheres leads to local blood flow restrictions, decreasing the amount of ghrelin secretion and suppressing hunger.

size are required before statistically significant conclusions can be drawn.

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# Outcomes and Complications of Breast Augmentation in Transgender Females: A Systematic Review

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Gender dysphoria (GD), a condition of incongruence between an individual's perception of sex and biological identity, has been increasingly recognized in the past decade.1 Based on a nationwide survey in the United States, 0.6% responders identify themselves as transgender.<sup>2</sup> A higher prevalence of co-existing psychiatric illness was observed in this population.3 Genderconfirming surgery (GCS) has been proven effective in improving these individuals' quality of life and alleviating psychological distress.<sup>4</sup> From 2010 to 2015, the number of GCS increased by five times among insured patients in the United States.<sup>5</sup> Among male-tofemale individuals, breast implant is considered the most important compared to other surgical procedures.

Despite extensive literature in oncoplastic breast reconstruction, articles on breast augmentation as GCS were limited to case reports, small case series, and retrospective cohort studies. No society guideline was available regarding the technical aspects of the surgery and postoperative care. While skin necrosis, seroma, hematoma, and capsular contracture were well-described adverse events among breast reconstruction after mastectomy for cancer, their incidence and management among male-to-female patients after GCS were less clear. Thus, the present study aims to evaluate the safety and efficacy of breast augmentation as a GCS for male-to-female patients through meta-analysis of published individual and cohort study data.

PubMed, Embase, and the Cochrane Library were queried for studies published up to March 2021. The following keywords were used: "transgender", "transfeminine", "implant", "augmentation", "breast", and "chest". Primary outcomes of interest were complication (ie hematoma, seroma, infection, capsular contracture, general implant problem, asymmetry/malposition,

hemorrhage, skin or systemic complications), satisfaction, and reoperation rates. Breast implant surgery complications were compared between cis-gender and transgender patients as well.

Quantitative analyses were performed

with STATA 15.1 statistical software (STATA Corp., College Station, TX, USA). Rates were pooled with the -metaprop function and reported in 95% confidence intervals. A chi-square test was performed to analyze the incidence of complications between cisgender vs trans-gender female breast augmentation.

A total of 17 studies, 1958 patients were included in this project. Studies were conducted in various regions including the USA, Netherlands, Belgium, Switzerland, Germany, and France. Complications and outcomes including breast asymmetry/malposition/shape problem, implant rupture,

hematoma, infection, capsular contracture and reoperation rate were collected and analyzed. Among the 17 selected studies, four studies including a total of 723 patients, the incidence of having an asymmetry/malposition/ shape problem is 4%. In three studies, including a total of 689 patients, the incidence of implant rupture is 3.8%. In eight studies, including a total of 1,074 patients, the incidence of hematoma is 0.8%; the incidence of infection is 0.1%. In eight studies, including 1,347 patients, the incidence of reoperation is 11.7%. Further, a chi-square test comparing capsular contracture and implant-related complications between

Gender-confirming surgery (GCS) has been proven effective in improving these individuals' quality of life and alleviating psychological distress.<sup>4</sup>

> cis-gender vs trans-gender breast augmentation surgery was performed. Incidence of capsular contracture was significantly higher in the cis-gender group whereas there is no significant difference in incidence of implant related complications between the two groups.

> Due to lack of standardized report and scant of data, no direct comparison of the outcomes between subglandular vs subpectoral approach of breast augmentation in transgender females can be made. However, the pooled outcomes of complications illustrate



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a variability in the rates of different complications between cis-gender vs trans-gender females. Future standardized comparative studies should be conducted.

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## Application of Virtual Surgical Planning to Reduction Mandibuloplasty for Treatment of Mandibular Hyperplasia Secondary to Acromegaly

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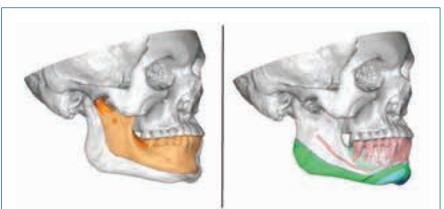


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**INTRODUCTION:** Acromegaly is characterized by slowly progressive somatic abnormal hyperplasia caused by overproduction of growth hormone (GH) and insulin-like growth factor 1 (IGF 1) and is frequently associated with pituitary adenomas. This disorder commonly results in mandibular hyperplasia and orofacial deformities requiring surgical correction.

Here, we describe a novel use of virtual surgical planning in reduction mandibuloplasty for correction of mandibular hyperplasia secondary to acromegaly.

**CASE:** A 25-year-old female presented to our clinic with mandibular hyperplasia secondary to a growthhormone secreting pituitary adenoma, consistent with facial manifestations of acromegaly. This had been treated with a combination of prior surgical resection and lanreotide. Interestingly, she presented with normal occlusion, and reported this to be at her pre-morbid baseline. After clearance by endocrinology, a surgical plan was developed for a reduction genioplasty and mandibuloplasty to reduce her lower facial proportions without altering her current normal occlusion.



**FIGURE 1:** Virtual surgical planning was used to assist in planning ostectomies of the lower mandible for correction of mandibular hyperplasia secondary to acromegalu. (Left) Pre-operative mandible (grey) interposed with a "generic" female mandible (orange). <sup>a</sup>Right) Planned bomne for resection is shown in green, and repositioned bone is shown in blue after T-shaped ostectomy to reduce the chin.

To facilitate intraoperative bone resection, virtual surgical planning (3D systems, Littleton, CO) was used to develop pre-fabricated cutting guides for reduction genioplasty, and ostectomy of the inferior border and gonial angles of the mandible. The planned degree of bone resection was facilitated during a planning session by overlay of the patient's CT scan images with a "generic" female mandible model (Figure 1).

An intraoral approach was used for reduction genioplasty and mandibuloplasty, with a technique similar to that used for feminizing mandibuloplasty.<sup>5</sup> Osseous genioplasty was performed with a T-shaped excision of bone to allow for reduction of chin dimensions in both horizontal and vertical vectors, with reduction amounts of 12.0mm and 7.2mm respectively. Rigid titanium osteosynthesis of the remaining chin segments was performed. Ostectomy of the inferior border of the mandible was continued posteriorly and included the gonial angles to further reduce mandibular proportions. A surgical drain was placed for 24 hours. Routine post-operative oral hygiene and antibiotic prophylaxis was instituted, and the patient recovered uneventfully. A post-operative CT scan demonstrated effective mandibular reduction with contours approximating those of the "generic" female mandible used for surgical planning (Figure 2).

**DISCUSSION:** Acromegaly results in overgrowth of skeletal and soft tissues, with typical enlargement of the mandible being seen. The most prominent facial manifestation of acromegaly is mandibular prognathism due to excessive jaw overgrowth, and the ramus is more often affected than the body of the mandible.<sup>2-3</sup> Patients with acromegaly typically exhibit enlargement of all parts of the neurocranium

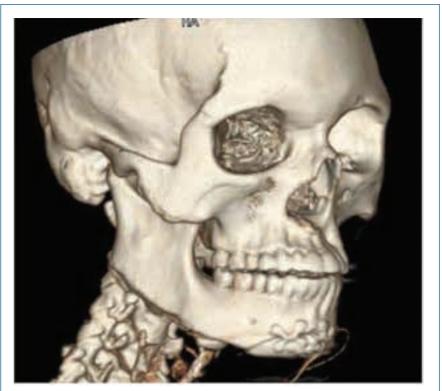
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and orofacial bones, though often sparing the maxilla, and common manifestations include dental malocclusion. This often warrants orthognathic surgery for correction of associated orofacial deformities. "Horseshoe horizontal osteotomy" has also been utilized to reduce the vertical dimension of the body of the mandible.<sup>4</sup>

Interestingly, in our case, the lower facial enlargement was associated with normal occlusion and a plan for lower mandible reduction was implemented. We found the use of VSP in planning the appropriate osteotomies to be a useful tool in determining the degree of bone resection to mirror a "generic" female mandible proportion with a pleasing end result.

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**FIGURE 2:** Post-operative CT scan demonstrates reduced mandible proportions, mirroring those of the "generic" female mandible used for surgincal planning.

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## In Situ Skin Graft to Manage Traumatic Extremity Hematomas in the Elderly: A Novel Technique

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Geriatric patients are at an increased risk of severe injury from relatively minor mechanisms, such as ground level falls. Many are also on anticoagulation due to their morbidity which sometimes present unique injuries requiring special treatments. In this case report, we present a geriatric patient after a fall with a large necrotic hematoma dissecting her skin, most likely due to her anticoagulation. This presents a management challenge for surgeons depending on the wound size and degree of tissue loss.<sup>1</sup> Literature is limited but typical treatment is incision and drainage, debridement, and split thickness skin graft. Here, we treated the patient's large dissecting hematoma with skin avulsion with early evacuation of hematoma followed by in-situ skin grafting (the patient's own traumatic skin flap) and negative pressure wound therapy (NPWT). Others have evaluated similar use of autologous skin grafting in traumatic wounds.5

We describe a case of an 83-year-old female with a past medical history of diabetes, hypertension, hyperlipidemia, congestive heart failure with reduced



ejection fraction, obesity, obstructive sleep apnea, bilateral breast cancer, and vulvar squamous cell carcinoma status post right groin dissection and subsequent lymphedema of the right lower extremity (RLE), presented to the Emergency Department (ED) after sustaining a traumatic injury to her RLE. She reported taking Rivaroxaban daily for atrial fibrillation. The patient avulsed the skin on her RLE and developed a large hematoma measuring 20 x 15cm, distal to the knee. Figure 1 illustrates the skin changes and significant clot burden. The patient underwent resuscitation with two units of packed red blood cells (pRBC) due to persistent hypotension in the ED. Within 24 hours the surgical team brought

the patient to the operating room for wound debridement and washout of subdermal adipose tissue and hematoma. The skin flap was meshed with a #11 blade scalpel to facilitate drainage, then fitted and stapled peripherally along the wound. After securing the skin flap, the surgeon applied a single layer of Adaptec gauze followed by Negative Pressure Wound Therapy (NPWT) using a VAC device (VAC; KCI, San Antonio, Texas). Figures 2-8 demonstrate these stages in succession. The patient received 1 additional unit of pRBC post operatively and remained in the hospital for an overall uncomplicated course. She required pain

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control, physical therapy, and transfer to an acute rehabilitation facility. She presented to the office on post-operative day 5 for wound vac removal. Figure 9 demonstrates the wound's progression, with approximately 60% graft uptake. The surgical team discontinued NPWT and utilized Xeroform with gauze wrap for ongoing outpatient wound care. The wound demonstrated persistence of central necrosis, but ongoing healing elsewhere at the patient's two week follow up visit in figure 10.

Traumatic lower extremity hematomas in the elderly frequently result in surgical consultation, and management techniques widely differ. Despite their frequent presentation to trauma surgeons, traumatic lower extremity hematomas are sparsely represented in literature. No single algorithm exists addressing up-front management, timing of surgical debridement (if necessary), reconstruction style, or subsequent wound care for such injuries. We offer a novel approach using the patient's own avulsed skin as a meshed biologic dressing. We suggest that with ongoing local wound care, this approach has shortened the patient's healing time and bypassed the morbidity of donor site creation in traditional skin grafting. Further studies are needed to confirm this finding.

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## Utilization and Diagnostic Performance of 4Kscore Among White and African American Patients

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The 4Kscore is a relatively new, bloodbased tool used to stratify the degree of prostate cancer disease aggressiveness. Since its advent within the last decade, this cheaper, less invasive test is associated with far fewer complications, and allows for clinical prediction of disease aggressiveness and the subsequent plan of treatment to become more individualized as to avoid overtreatment and unnecessary costs and health burdens to patients and systems alike. Recent studies have indicated that a shift towards a 4Kscore based clinical workup paradigm has the potential to save over 160 million dollars compared to standard of care, defined as prostate biopsy.1

Prostate cancer risk is significantly higher in African American individuals, with reports indicating a nearly two times higher rate compared to White males.<sup>2</sup> Continued integration of 4Kscore into the clinical workup of elevated PSA warrants investigation into the tool's use and performance. The landmark 4Kscore trial to validate the test's performance focused primarily on a cohort of White, Northern European individuals, thereby limiting the tool's external validity across a wider range of demographics.<sup>3</sup> This study aims to assess race-based 4Kscore utilization and efficacy to be able to qualify the performance of the test across patient demographics.

We conducted a single-institution review of patients who underwent prostate biopsy with recorded 4Kscores between 2016-20 and classified patients as White or African American based on self-report (other races excluded). High-risk 4Kscore was defined as values  $\geq$ 7.5%, consis-

tent with conventional interpretation. Clinically significant prostate cancer (csPCa) was defined as a biopsy Gleason score greater than/equal to 3+4. Receiver Operating Characteristic curve analysis was used, along with Area Under the Curve calculation. Contingency tables were constructed in order to determine test performance.

A total of 132 patients were identified (Africcan American n=21, White n=101). 4Kscore was utilized more frequently in White males who underwent biopsy than in African American males (60% vs 29.6%). 4Kscore performed well across both race groups (overall sensitivity=0.96, specificity=0.42, NPV=0.95). There were no appreciable differences between 4Kscore predictions of csPCa between White (sensitivity=0.97, specificity=0.39, NPV=0.96) and African American males (sensitivity=1.0, specificity=0.67, NPV=1.0).

4Kscore is effective in both White and African American patients. There were no differences in performance characteristics between the two groups. However, the results indicate African American males were significantly less likely to have documented 4Kscore than White males, limiting comparison sample size. Our data suggests that

Our data suggests that 4Kscore is a capable tool in assessing risk of harboring csPCa, and further investigation across racial demographics should be continued to promote equitable utilization during clinical workup.

> 4Kscore is a capable tool in assessing risk of harboring csPCa, and further investigation across racial demographics should be continued to promote equitable utilization during clinical workup.

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### Stalled Progress: Medical School Dean Demographics

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Geoffrey Broadbent,

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The COVID-19 pandemic has exacerbated and uncovered the health disparities present in our communities and has increased the push for health equity across the country. With a majority-minority nation on the horizon for 2044, the need for physicians who resemble and represent our population demographics is increasingly important. Historically, minority populations have been restricted from opportunities and promotions in their medical training, memberships, and professional activities, which subsequently excluded them from participating and impacting decisions at the institutional level. Minority physicians are also important in solving the issues revolving around the shortage of primary care physicians. Black and African American physicians do not account for the majority of active physicians in the United States, yet a plurality of Black or African American physicians practiced primary care (41.4% vs 30.6% of White physicians) in 2018.1 Primary care physicians play

**FIGURE 1:** Race/Ethnicity of Medical School Deans. 11% of medical school deans are URMs.

an essential role in the prevention of hospitalizations and the management of chronic conditions, and evidence demonstrates more primary care physicians are associated with better health outcomes. Despite this evidence, it is

estimated that by 2025 there will be a deficit of up to 31,000 adult primary care physicians in the United States.<sup>2</sup>

Medical schools have an important directive: to train the next generation of physicians. Faced with a primary care physician shortage, increasing numbers of under-represented faculty leaving academic medicine,

low representation of women in leadership positions, and an ongoing pandemic, medical schools have a duty to implement solutions to alleviate these issues. Efforts have been made to create more diverse medical school classes, but those efforts are not mirrored in senior faculty demographics. The demographics of medical school deans in comparison with the United States' demographics and the current composition of active physicians was analyzed. We looked at the specialty, race/ethnicity, and gender of medical school deans in 2019. We identified that only 11% of deans were underrepresented minorities, 16% of deans were primary care physicians, and 18% of deans were women.<sup>1</sup> When compared with the makeup of physicians in the

By hiring deans with a variety of race/ethnicities, specialties, and genders, schools set an important precedent that could lead to more pipeline programs, increased underrepresented faculty retention, and more primary care physicians.

> United States and the population as a whole, these numbers are unrepresentative of national demographics.

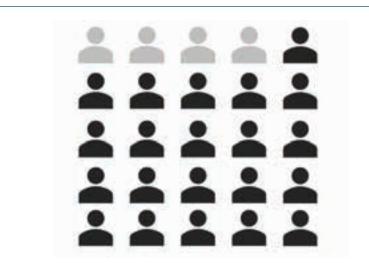
> The diversity of senior leadership matters to students.<sup>3</sup> Medical schools should hire deans and senior leadership that represent a diversity of specialties, genders, races, and ethnicities. Future physicians need to acquire skills to care for increasingly diverse groups by learning about the unique needs of minority populations and

Continued on p. 109

by including social determinants of health, cultural humility, and systemic racism in medical curricula.<sup>4</sup> By hiring deans with a variety of race/ethnicities, specialties, and genders, schools set an important precedent that could lead to more pipeline programs, increased underrepresented faculty retention, and more primary care physicians.

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**FIGURE 2:** Primary Care Practitioners Among Medical School Deans. 16% of medical school deans are primary care practitioners.

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## An Analysis of Quality of National Presentations in Hand Surgery

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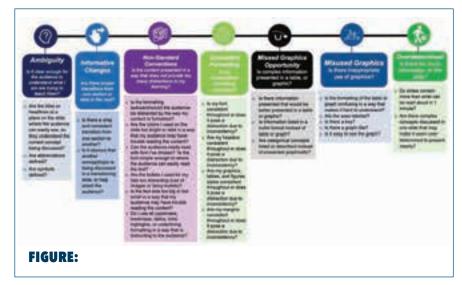
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Effective information transfer relies on the proper use of educational tools. Presentations in surgery are commonly used to share research findings and innovative surgical techniques. Evaluating the quality of presentations

The use of a checklist, with concepts like those presented in this study, to evaluate a presentation may aid in the development of more effective presentations in hand surgery.

will permit us to improve educational materials in hand surgery. Our specific aims were to assess the quality of hand surgery presentations at a national meeting using a checklist of presentation standards from the literature and to identify areas of improvement.

Our sample included presentations from the Clinical Papers Sessions at the 2020 American Society for Surgery of the Hand (ASSH) Annual Meeting. A



modified checklist based on the literature was used to assess the presentations. Two members of the research team extracted data from the included presentations and disagreements were reviewed collaboratively. We calculated the crude mean difference in the percentage of detractions using various presentation characteristics.

> A total of 96 presentations were included in this sample and there was an average of 9.6 detractions per presentation. Misused graphics, ambiguous content (undefined abbreviations, undefined symbols, etc.),

and overdetermined slides for the allotted time were the most common detractions identified in the sample. One-way ANOVA analysis of presenter role found a significant difference in the mean number of detractions (F (2, 93) = 7.36, p = 0.001) among different types of presenters with surgeon presenters exhibiting more detractions than other students and other health care professionals.

The use of a checklist, with concepts like those presented in this study, to evaluate a presentation may aid in the development of more effective presentations in hand surgery. A collaborative peer-review process incorporating feedback from multiple trainees, audience members, and colleagues may facilitate effective information transfer through presentations.

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## The Impact of the COVID-19 Pandemic on Medical School Pathway Programs

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African Americans, Latinos, and Native Americans account for 11.1 percent of U.S. physicians1 while constituting 32.1 percent of the total population.<sup>2</sup> A diverse physician workforce is associated with improved quality of care, increased access to health care services, and reduced health care disparities.<sup>3,4</sup> Medical schools have implemented pathway programs to increase the diversity of the physician workforce. In 2020, the coronavirus (COVID-19) pandemic created a mass disruption for programs across the country with schools adjusting from in-person schooling to a new online environment. The aim of this study is to investigate how pathway programs at medical schools have been impacted by COVID-19.

This cross-sectional mixed-method study was conducted in two phases sequentially. The first qualitative phase consisted of semi-structured interviews with a sample of medical school pathway program administrators and academic leaders. These identified key themes in changes to pathway programs in 2020 compared to previous years. The second quantitative phase consisted of a survey sent to all medical **TABLE 1:** Characteristics of Schools Participating in the Pathway Programs During

 COVID-19 Survey, 2021

Characteristic	Number Invited (% of 198)	Number Participating (% of 112)	Response Rate (%)
School Type			
Allopathic (MD)	155 (78.3)	93 (83.0)	60.0
Osteopathic (DO)	43 (21.7)	19 (17.0)	44.2
Region			-0
Midwest	42 (21.1)	24 (21.4)	57.1
Northeast	43 (21.7)	21 (18.8)	48.8
South	75 (37.9)	40 (35.7)	53.3
West	34 (17.1)	24 (21.4)	70.6
Puerto Rico	4 (2.0)	3 (2.7)	75.0
Institution Type			•
Public	101 (51.0)	59 (52.7)	58.4
Private	97 (49.0)	53 (47.3)	54.6
Institution Classification			•
R1 Doctoral Universities (15)	78 (39.2)	47 (42.0)	61.5
R2 Doctoral Universities (16)	31 (15.6)	14 (12.5)	48.4
R3 Doctoral Universities (17)	12 (6.0)	5 (4.5)	41.7
Medical Schools and Centers (25)	70 (35.2)	44 (39.3)	60.0
All others (18, 19, 21)	7 (2.5)	2 (1.8)	40.0
Total	198 (100)	112 (100)	56.6

schools to further quantify the impact of COVID-19 on programs.

Of the 198 schools invited to participate in the survey phase, 112 responded (56.6%). The response rate for allopathic schools (60%) was greater than that of osteopathic schools (44.2%), and schools geographically located in the western United States (70.6%) responded at a higher rate than those in the northeast (48.8%). One-hundred and six (95%) schools had pathway programs during the pandemic, with community-based schools having less programming. Forty-two (37.5%) respondents reported canceling some

or all of their programs due to the pandemic. Regardless of funding source, most programs reported they were able to retain funding. Of those schools that run elementary grade level pathway programs, above half (52%) closed during the pandemic. This contrasts with the percentage of high school (10%), undergraduate (8%) and post-graduate (7%) pathway programs that were closed during the pandemic. Table 2 lists the specific programmatic activities included across pathway programs. The number of

Continued on p. 112

schools providing distanced learning support doubled during the pandemic and growth was equivalent in all groups. The most common program type offered was mentoring, which was least affected by the pandemic, along with distanced learning support. There were significant relationships between Carnegie classification and academic support (Fischer exact p=0.052;  $\chi 2$ p=0.002) as well as Carnegie classification and psychosocial support (Fischer exact  $p=0.045 \chi^2 p=0.03$ ). Additionally, public universities represented 13 of the 16 research opportunities that were halted due to the pandemic (p=0.041). In assessing opinions of school leadership, most support increased funding for psychosocial support (87%) and distance learning (88%) post-pandemic. Narrative responses described challenges in keeping students engaged in the virtual environment and equity issues regarding broadband internet access, while at the same time allowing for broader reach. Budget effects seemed to be generally mixed depending on funding source.

Provided Before Continued Providing During **Program Type** Pandemic (Percent of Total Pandemic (Percent of Respondents, n=112) Program-Type Providers) Academic Support 95 (84%) 91 (95%) 58 (94%) Test Prep 62 (55%) 21 (19%) **Distanced Learning Support** 21 (100%) Mentoring 103 (92%) 100 (97%) **Psychosocial Support** 73 (65%) 67 (91%) Research 64 (80%) 80 (71%) Shadowing/Internship 88 (79%) 37 (42%) **Financial Support** 70 (63%) 64 (91%)

Although the long-term impacts of the COVID-19 pandemic on the diversity of the physician workforce will take decades to elucidate, this study provides insight into the early and potential impacts of the pandemic on these important pathway programs.

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### Medical School During a Pandemic: A Retrospective Study on **United States Medical School Reopening Policies**



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BACKGROUND: The COVID-19 pandemic has resulted in innumerable unprecedented challenges in the medical education system. Among other factors, personal protective equipment (PPE) restrictions, contact limitations, and social distancing measures have all significantly altered the structure of undergraduate medical education and have required rapid adaptation to an ever-changing environment. As the pandemic surpasses one year in duration and the undergraduate medical education system concludes its first full pandemic year, we reflect on how medical schools have responded thus

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far to this crisis, where the current data stands in relation to safety of school reopening, and how the structure of undergraduate medical education has been changed forever.

For the majority of institutions, in-person courses and rotations were halted abruptly in mid-March as schools were forced

to transition to a completely virtual learning environment for the remainder of the 2019-2020 academic year1.1 Anatomy, skills labs, and in-person

problem-based learning sessions ceased.<sup>2</sup> Instead of traditional clinical work, students on rotations completed their clinical training using virtual cases.<sup>3</sup> A subset of second-year preclinical students (including the author, Klein) became trapped in a cycle of exam cancellations and clerkship delays. Away acting internships, international electives, conference attendance, and interviews were prohibited immediately due to travel restrictions.3,4 Lab closures effectively quelled many significant summer research projects.4,5 In effect, undergraduate medical education came to a screeching halt, and school administrators had to act swiftly to ensure that student training proceeded as safely as possible. The

The COVID-19 pandemic has resulted in a radical upheaval of undergraduate medical education at both the preclinical and clinical levels.

> 2019-20 academic year ended with most pre-clinical and clinical students (pre-clinical and clinical) learning from home, wondering whether they would be returning to campus in the fall.

> Heading into the 2020-21 academic year with the knowledge that the COVID-19 pandemic would affect the fall semester at the very least, many

> > Continued on p. 114



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MHS, MSIII

medical schools developed plans to reopen in some capacity.

**METHODS:** The publicly available reopening plans of U.S. MD programs were evaluated at the start of fall semester and at the end of fall semester.

**RESULTS:** All schools adopted a version of hybrid medical education, and mask use, social distancing of more than 6 feet at all times, and enhanced disinfection of common areas were universally implemented. Twenty-three of 25 medical schools continued to require that students attend activities like anatomy lab and clinical skills simulations in-person. Every school prohibited clinical students from taking care of patients with a confirmed or suspected diagnosis of COVID-19. Strategic testing of asymptomatic medical students for COVID-19 was not widely implemented at the time of this study.

#### **CONCLUSION:** The COVID-19

pandemic has resulted in a radical upheaval of undergraduate medical education at both the preclinical and clinical levels. In the span of one year, preclinical education transitioned from traditional, classroom-based learning to a predominantly hybrid model. The elimination of in-person large lectures and focus on small group discussion has generated a much more interactive learning environment, despite, in some cases, students being dispersed across the country. Additionally, clinical students learnedare learning in a completely different environment from their predecessors and will be more prepared than previous generations to handle similar crises in their own careers.

For further reading, please visit https:// hphr.org/31-article-klein/ for the full article.

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### Do Orthopedic Surgery Residency Program Websites Address Diversity and Inclusion?

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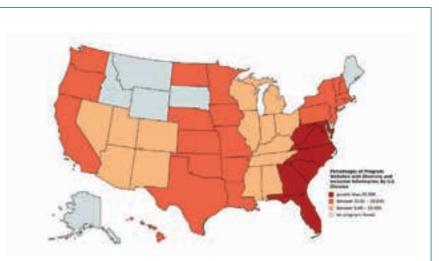


Orthopedic surgery is one of the least diverse medical specialties.<sup>1,2</sup> Other medical specialties have employed diversity-related initiatives to increase the number of students underrepresented in medicine (URM).<sup>3</sup> Furthermore, with the suspension of visiting student rotations during the COVID-19 pandemic, medical students used residency program websites as a main source of program-specific information.<sup>4</sup>

The purpose of this study was to measure the extent to which orthopedic surgery residency program websites describe diversity and inclusion initiatives.

The Electronic Residency Application Service was used to identify U.S. orthopedic surgery residency programs. The programs' websites were reviewed, and data on commitments to diversity and inclusion were collected. Descriptive statistics of these data were generated.

There were 192 residency programs identified; three were excluded from the analysis due to lack of websites. Of the remaining 189 residency program websites, only 55 (29.10%) contained information on diversity and inclusion. Information on a commitment to improving diversity and inclusion was the most prevalent data point found among program websites, although it was found on only 15% of program sites.



**FIGURE:** The map shows percentages of U.S. orthopaedic surgery residency program websites with diversity and inclusion information by geographical divisions according to the U.S. Census.

**TABLE:** Percentages of orthopaedic surgery residency program websites (n = 189) providing information on diversity and inclusion.

Type of information	Paresetage of program. Welk steak committing information
Department specific Wyb site for disersity and industry.	\$79
Commitment to diversity and inclusion	15.09
Diversity-related apportunities for early separate to arthrands surgery	6.74
Links to a sometigneensets specific Web atta for dwaratty and industors	0.47
Une essertant hise	104
Auditains restations for eludents units represented in multipline	466
Datable are faculty inversity	1.65
Any diversity and industry-related efformation	25.13

Orthopedic surgery residency programs rarely address topics related to diversity and inclusion on their program websites. An emphasis on opportunities for URM students and initiatives related to diversity and inclusion on program Websites may improve URM outreach and serve as one method for increasing URM matriculation into orthopedic surgery.

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## A Pilot Randomized Controlled Trial of Text Messaging to Increase Tobacco Treatment Reach in the Emergency Department

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**INTRODUCTION:** Automated text messaging programs have been studied as a treatment tool, but have not been studied as an outreach tool to increase the reach of smoking cessation treatment.

**AIMS AND METHODS:** Two distinct text messaging programs were developed. One was aimed at connecting smokers to quitline phone counseling via text message (Text4Coach [T4C]) and the other was aimed at connecting smokers to a smoking cessation text messaging program (Text&Quit [T&Q]). Adult daily smokers with Medicaid insurance (N = 80) were recruited from the Emergency Department at an urban hospital and randomized to T4C or T&Q. The primary outcome was program reach.

**RESULTS:** Outreach text messages were found to have moderately high uptake, with the majority of participants (63.8%) opting into their assigned tobacco treatment program and younger and female participants

	Total ( <i>N</i> = 80)	T&Q ( <i>n</i> = 40)	T4C(n = 40)
Age, mean (SD)	42.2 (11.6)	42.4 (12.4)	42.1 (10.8)
Gender, <i>n</i> (%)			
Male	31 (38.8)	17 (42.5)	14 (35.0)
Female	49 (61.2)	23 (57.5)	26 (65.0)
Education, n (%)			
Less than high school	20 (25.0)	11 (27.5)	9 (22.5)
High school or more	60 (75.0)	29 (72.5)	31 (77.5)
Race, <i>n</i> (%)			
African American	72 (90.0)	36 (90.0)	36 (90.0)
Other	8 (10.0)	4 (10.0)	4 (10.0)
Employment, <i>n</i> (%)			
Employed (full or part time)	36 (45.0)	20 (50.0)	16 (40.0)
Unemployed or don't work	44 (55.0)	20 (50.0)	24 (60.0)
Annual income, <i>n</i> (%)			
Up to \$15,000	44 (55.7)	19 (48.7)	25 (62.5)
Greater than \$15,000	35 (44.3)	20 (51.3)	15 (37.5)
Cigarettes per day, mean (SD)	8.5 (5.1)	8.3 (5.0)	8.6 (5.2)
Quit attempt in the past year, n (%)	58 (72.5)	29 (72.5)	29 (72.5)
FTCD <sup>a</sup> score, mean (SD)	3.1 (1.4)	3.1 (1.6)	3.0 (1.3)
Admitted to ED	12 (15.0)	7 (17.5)	5 (12.5)
Top reasons for ED visit			
Orthopedic <sup>b</sup>	23 (30.1)	8 (22.2)	14 (37.8)
Internal organ <sup>c</sup>	12 (16.4)	5 (13.9)	7 (18.9)
Nonspecific <sup>d</sup>	16 (21.9)	9 (25.0)	7 (18.9)
Other	23 (31.5)	14 (38.9)	9 (24.3)

ED = emergency department; T&Q = Text&Quit; T4C = Text4Coach.

<sup>a</sup>Fagerstrom Test for Cigarette Dependence.

<sup>b</sup>Includes any joint, limb, muscle, or skeletal pain.

<sup>c</sup>Includes pain in any internal organs, including abdominal pain.

<sup>d</sup>Includes general symptoms such as fever, cough, nausea, and dizziness.

more likely to opt in (p < .01). Receipt of the treatment portion of the program differed among the programs with 67.5% of T&Q receiving the treatment program and 27.5% of T4C receiving the program (p < .001). Most participants across both groups replied to at least one message (71.3%) and very few unsubscribed from the service over the 3-week trial. The majority of participants reported overall satisfaction with their program (63.8%), found it helpful for quitting smoking (60.0%) and would recommend the program to a friend

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(62.5%). Overall, 11 (13.8%) participants reported being abstinent from smoking for the past 7 days at follow-up, with no differences between groups.

Conclusions: Outreach text messages were found to have moderately high reach among Medicaid smokers. Larger trials are needed to evaluate the impact of such programs on helping low-income smokers quit.

**IMPLICATIONS:** Automated text messaging programs have been tested as a treatment tool, but have not been tested as an outreach tool to increase the reach of smoking cessation treatment. This study tests a new way of conducting outreach to smokers in a health system through text messages. It tests the effect of outreach on (1) rates of opting in and (2) successful treatment delivery. Results may inform new models of providing outreach for tobacco treatment in health systems. **TABLE 2:** Program Engagement and Smoking-Related Outcomes

	Total (N = 80)	T&Q (n = 40)	T4C (n = 40)
Reach and acceptability			
Program uptake, n (% joined)	51 (63.8)	27 (67.5)	24 (60.0)
Received program, n (% received program)a	38 (47.5)	27 (67.5)	11 (27.5)
Replied to at least one message, n (%)b	57 (71.3)	29 (72.5)	28 (70.0)
Replied to the program to set quit date, n (%)	N/A	22 (55.0)	N/A
Unsubscribed, n (% opted-out)	2 (2.5)	0 (0.0)	2 (5.0)
Program satisfaction, n (% agreeing)c			
Overall satisfaction	51 (63.8)	26 (65.0)	24 (60.0)
Helpfulness for quitting	48 (60.0)	24 (60.0)	24 (60.0)
Recommend to friend	50 (62.5)	24 (60.0)	26 (65.0)
Experienced technical problems, n (%)c	5 (6.3)	2 (5.0)	3 (7.5)
	Total ( $n = 69$ )	T&Q (n = 34)	T4C (n = 35)
Self-reported smoking outcomes			
Seven-day point prevalence abstinence, n (%)	11 (15.9)	8 (23.5)	3 (8.3)
Seven-day point prevalence abstinence,	11 (13.8)	8 (20.0)	3 (7.5)
with imputation for missing, n (%)d			
Set quit date, n (%)	25 (37.3)	16 (48.5)	9 (26.5)
Quit attempt, n (%)	44 (62.9)	23 (67.7)	21 (58.3)
Change in cigarettes per day, mean (SD)	-2.7 (6.6)	-1.9 (8.2)	-3.5 (4.6)
Longest continuous period without smoking, mean (SD)	3.2 (4.4)	3.4 (5.1)	2.9 (3.6)
Use of any additional smoking cessation services in the past 3 weeks, n (%)	50 (71.4)	24 (70.6)	26 (72.2)
Type of smoking cessation service used, n (%)	·		
Telephone helpline or quitline	10 (14.3)	3 (8.8)	7 (19.4)
Counseling from a doctor or nurse	5 (7.1)	3 (8.8)	2 (5.6)
Self-help materials	6 (8.6)	2 (5.9)	4 (11.1)
E-cigarettes	4 (5.7)	2 (5.9)	2 (5.6)
Website	3 (4.3)	1 (2.9)	2 (5.6)
Other	23 (32.9)	13 (38.2)	10 (27.8)
Medication	22 (31.4)	9 (26.5)	13 (36.1)
Nicotine patch	15 (21.4)	8 (23.5)	7 (19.4)
Nicotine gum	7 (10.0)	1 (2.9)	6 (16.7)
Nicotine lozenges	1 (1.4)	1 (2.9)	0 (0.0)
Varenicline or Chantix	2 (2.9)	2 (5.9)	0 (0.0)

QL = quitline; T&Q = Text&Quit; T4C = Text4Coach. Bold indicates significant differences.

a Program is assigned treatment program of T&Q or QL counseling.

bExcludes texting STOP to opt out.

cSelf-report: n = 35.

dN = 80.

## Characteristics of Patients Experiencing Homelessness at an Urban Academic Hospital

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**INTRODUCTION:** Any given night, an estimated 553,000 individuals experience homelessness in the United States. Many turn to hospitals for health care, food, and shelter. These factors and lack of follow-up care upon discharge contribute to high rates of early readmission and frequent ED visits. Due to frequently missed homelessness status by health care providers, it is difficult to assess patient demographics and readmission rates among this population.

The Homeless Management Information System (HMIS) collects information on individuals that have stayed at shelters or transitional housing in Washington, D.C. We utilized the HMIS to identify patients experiencing homelessness at an urban academic hospital.

**METHODS:** Full names and birthdates from adults in HMIS were searched in the Electronic Medical Record (EMR) to locate patient matches. Inclusion criteria were having had at least 1 ED visit (without admission) or hospital admission from 9/1/2019-2/29/2020. Descriptive statistics were performed for demographics (gender, race, age, family status) and encounter information from the EMR. We used Fischer's exact test or unpaired t-test to compare the demographics of patient matches to those of HMIS-listed individuals who did not have hospital records.

**RESULTS:** Out of 5,025 HMIS entries searched, 2,523 (50.2%) had hospital records, with 702 patients

(14%) having had at least 1 ED visit or admission in our 6-month timeframe. From 702 patients, we reviewed 586 ED visits without admission and 188 admissions (up to 1 ED visit and 1 admission per

patient). 2507 unmatched persons in HMIS were used as non-patient comparisons. Most patients were single adults without families (93.5%). Most patients had Medicaid (39.59% of ED visits, 54.26% of admissions) or municipally-funded insurance for low-income residents (29.18% of ED visits, 30.85% of admissions). 23.04% of patients who visited the ED without admission and 7.54% of admitted patients had no insurance. The most common primary diagnosis was acute ingestion or drug abuse/overdose (15.8%) in ED visits, and psychiatric disease (19.5%) in admissions. Primary teams caring for admitted patients were Internal Medicine (37.0%), Psychiatry (20.0%), OB/GYN (15.4%), and

Cardiology (14.5%), Surgery (11.8%), and Intensive Care (3.18%). The 30-day ED revisit rate including only ED visits without admission was 27.99%. 10.11% of admitted patients were readmitted within 30 days. Patients were, on average, older [45.23 years old (SD=14.7) versus 43.26 (SD=15.92);p=0.0034], more commonly African American (87.32% versus 77.22%; p<0.0001) and less commonly Hispanic (4.42% versus 9.45%; p<0.0001) when compared to non-patients. Fewer homeless patients than non-patients were male (59.26% versus 71.44%; p<0001).

Any given night, an estimated 553,000 individuals experience homelessness in the United States. Many turn to hospitals for health care, food, and shelter.

> **CONCLUSION:** Homeless patients in this urban academic hospital were mostly middle-aged African American men. Compared to non-patients, there was a higher percentage of women and African Americans among patients, and a lower percent of Hispanics. More admitted patients had Medicaid and more ED visits without admission were among uninsured patients. More than half of admitted patients were cared for by Internal Medicine and Psychiatry teams. Readmission rates were low, however nearly one-third of ED visits had a subsequent ED visit within 30 days. This information may help guide the distribution of resources for interventions within hospitals.

## Use of a Shelter Database to Determine Missed Identification of Homelessness at an Urban Academic Hospital

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Approximately 40% of firsttime adult shelter users have an Emergency Department (ED) visit or hospitalization within one year of shelter entry. Physicians must know patients' housing statuses to develop appropriate care plans after discharge. Standardized tools for universal screening exist, however, the rate of correct identification of homelessness appears to be low and is not widely studied. One barrier to study is the lack of "true" comparison information without surveying patients in real-time.

We investigated the rate of correctly identified homelessness documented during ED visits and hospital admissions. We used the Homeless Management Information System (HMIS) to identify individuals who stayed at shelters or transitional housing in Washington, D.C., during a 6-month period and compared this to Electronic Medical Records (EMRs) during the same time period.

HMIS data on adults using homeless services between 9/1/2019-2/29/2020 was shared with researchers through a data use agreement. Using names and dates of birth, 5,025 individuals from the HMIS were searched in the EMR. Inclusion criteria were age >17, matching to a record in the EMR, and having at least one ED visit or inpatient admission within the same 6-month period. Charts were reviewed for documentation of housing status for up to 2 ED visits and 2 inpatient admissions per matched

patient, including where in the chart it was documented. Simple percentages were calculated and Fisher's exact test was used to compare rates in the ED versus admissions. This study was approved

by the George Washington University IRB.

Out of 5,025 HMIS entries searched, 2,523 (50.2%) had EMR charts, with 702 patients (14%) having had at least 1 ED visit or admission in the 6-month study period. Out of 813 ED visits without admission (586 patients; 227 with second visits), housing insecurity was identified in 37% (303/813). Out of 220 admissions (188 patients; 32 second admissions), housing insecurity was identified in 64% (140/220). The difference in identification of housing insecurity during ED visits versus admissions was significant (p<.0001). Among ED patients whose housing insecurity was correctly documented,

documentation was in the physician note (89%), social work note (22%) or nursing note (15%). Among admitted patients whose housing insecurity was correctly documented, documentation was in the physician note (72%), social work note (56%), discharge summary (54%), discharge note (46%), initial ED physician note (37%) or ICD-10 coded using Z59.0 (19%).

Our data show that homelessness was not documented in at least onethird of hospital admissions and two-thirds of ED visits for patients who used shelters or transitional housing. More data points may have

Our data show that homelessness was not documented in at least one-third of hospital admissions and two-thirds of ED visits for patients who used shelters or transitional housing.

> been missed, as other patients may have had housing insecurity without utilizing shelters or transitional housing. Homelessness may be more often correctly documented during admissions due to the more thorough nature of the encounter, additional time available, better documentation, and need to create more detailed discharge plans that incorporate housing barriers. Some EMRs incorporate screening alerts to improve identification of housing insecurity, however George Washington University's EMR lacks these. Further study should include the impact of using these tools on correctly identifying housing insecurity.



### Racial Disparities in the Cost of Unplanned Hospitalizations After Breast Reconstruction and Abdominoplasty Procedures

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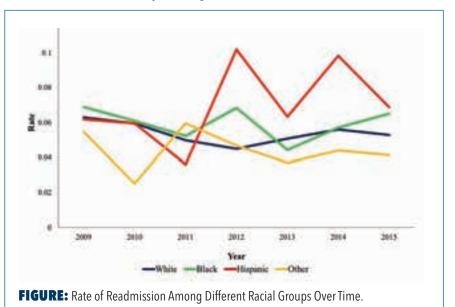


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Race has been identified as a social determinant of health associated with numerous surgical outcomes. Given the national attention to disparities in health care, understanding the variation in the health care provided to minorities becomes increasingly important. Plastic surgery researchers have investigated the effect of sexual orientation, sex, and race on care.1-4 Nonetheless, the current literature on race focuses on access of plastic surgery care and traditional outcomes.2,5 Efforts to reduce health disparities continue to increase and becomes more important as the United States (US) health care system transitions to a value-based system. In this study, we examined the effect of race on the rate and cost of unplanned hospitalizations after abdominoplasty and breast reconstruction procedures.

We performed a population-based analysis of patients in the Healthcare Cost and Utilization Project (HCUP) from 2006 to 2015. Adult patients undergoing implant-based and autologous breast reconstruction and



abdominoplasty were included in our study. We calculated the rate of unplanned emergency department and hospital visits and associated expenditures among patients of different races. Multivariable analyses were performed to determine the association among race and readmissions and health care expenditures.

A total of 17,745 patients were included in the final cohort. The rate of an unplanned visit after discharge was five percent. In a univariate analysis, Black patients (6%) and Hispanic patients (7%) had a significantly higher rate of readmissions compared to White patients (5%). However, after controlling for patient-level characteristics, race was not an independent predictor of an unplanned hospital visit. In this study, we did not find any significant difference in readmission rates or cost of readmissions for different racial groups over time. Figure 1 illustrates rate of readmission among different racial groups and Figure 2 depicts the average cost of readmission among different racial groups from 2009 to 2015. The cost of readmission for non-White patients was significantly higher than for White patients: Black patients (\$12,491), Hispanic patients (\$12,216), or patients included in the other category (\$18,838) had greater average cost for their readmission compared to White patients (\$10,537). Additionally, in our expenditure model, Black patients (adjusted cost ratio, 1.28 [95% CI, 1.05 to 1.56]) and Hispanic patients (adjusted cost ratio, 1.27 [95% CI, 1.03 to 1.58]) were at increased odds of incurring a greater cost for their readmission compared to White patients.

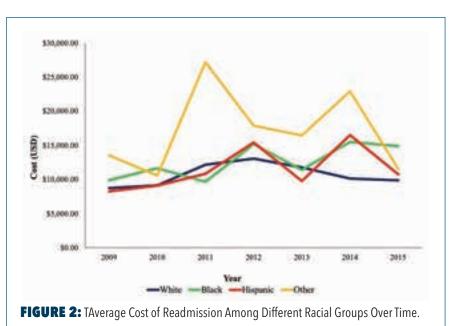
It is imperative to identify the numerous racial disparities that exist in medicine. Developing solutions on the consequences of racial disparities is integral to create equitable care for individuals among different racial groups, sexual orientations, gender identities, and socioeconomic statuses. Although

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race is not an independent predictor of an unplanned hospital visit after surgery, racial minorities bear a higher cost burden after controlling for insurance status, further stimulating health care disparities. Adjusted payment models may be a strategy to reduce disparities in surgical care, fostering more equitable care. Additionally, both direct and indirect measures of disparities should be used when examining health care disparities to identify consequences of inequities more robustly.

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## Patient Characteristics Associated with Missed Identification of Homelessness at an Urban Academic Hospital

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**INTRODUCTION:** A recent study found that 10% of emergency department (ED) patients experiencing homelessness had their housing status documented by the health care team. Identification of homelessness may inform care decisions and direct patients toward community resources, both of which may improve health outcomes. Standardized screening tools for homelessness exist but are not commonly used. We investigated patient characteristics associated with missed identification of homelessness to inform the development and implementation of effective screening strategies.

**METHODS:** We used the Homeless Management Information System (HMIS), a database of information on individuals who have stayed at shelters or transitional housing in Washington, D.C. to identify homeless individuals. Full names and dates of birth from adults in HMIS between 9/1/2019-2/29/2020 were searched in our Electronic Medical Record (EMR) for matches. Inclusion criteria were having had at least 1 ED visit or inpatient admission during the 6-month period. Charts were reviewed for documentation of homelessness for up to 2 ED visits and 2 inpatient admissions per patient within the 6-month period. Instances of missed identification of homelessness were recorded. We used multivariable logistic regression to identify patient characteristics independently correlated with missed identification of homelessness, including

age, gender, race, primary diagnosis, type of insurance, and prior or current use of shelters or transitional housing. We report adjusted Odds Ratios (aOR). This study was

approved by the George Washington University IRB.

**RESULTS:** Out of 5,025 adults in HMIS, 2,523 (50.2%) had hospital records, and 14% (702 patients) met inclusion criteria. Housing insecurity was correctly identified in 37% of ED visits (303/813 visits) and 64% of admissions (140/220 admissions). In the final multivariable model with visits nested within patients, significant independent predictors of missed homelessness during ED visits included prior or current use of transitional housing (aOR 1.92 [95% CI 1.07-3.44], p=.03), Black or African American race (aOR 2.13 [1.33-3.40] p=.0016) and having DC Alliance insurance (aOR 1.65 [1.14-2.40], p=.009). Homeless patients aged 60 or older were more likely to be correctly identified (aOR 0.40 [0.26-0.61],

p<.0001), as were those with primary psychiatric diagnoses (aOR 0.24 [0.13-0.42], p<.0001). During hospital admissions, missed homelessness was significantly associated with having DC Alliance insurance (aOR 2.76 [1.29 – 5.93], p=.009); correct identification was associated with a primary psychiatric diagnosis (aOR 0.14 [0.04-0.49], p=.002).

**CONCLUSIONS:** In this study, homelessness was not documented in a large percentage of patients during ED visits and hospital admissions. Characteristics associated with missed

In this study, homelessness was not documented in a large percentage of patients during ED visits and hospital admissions.

> documentation were different for ED visits and admissions, but it is unclear why having DC Alliance insurance was associated with this for both. DC Alliance covers District residents <200%FPL who are not eligible for Medicaid or Medicare. Use of transitional housing was associated with missed identification in the ED, which may reflect that health care teams are better at picking up housing insecurity when present in its most severe forms, highlighting the need to use standardized screening tools. Having a primary psychiatric diagnosis was associated with correct identification in both settings, which may indicate that components of the psychiatric interview include housing screening questions.

## Missed Identification of Homelessness in Subsequent Encounters Despite Prior Documentation in the Electronic Medical Record

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**INTRODUCTION:** Homelessness is often underrecognized in the healthcare setting, preventing quality discharge planning, care coordination, and connection to community resources. Once found, effective documentation of homelessness in the electronic medical record (EMR) can inform future providers. We investigated how prior homeless documentation in the EMR influenced the identification of patient homelessness in subsequent encounters.

**METHODS:** The Homeless Management Information System (HMIS) is a database of individuals that have stayed at shelters or transitional housing in Washington, D.C. Full names and dates of birth for adults in HMIS from Sept. 1, 2019 to Feb. 29, 2020 were searched in our EMR to locate matching patient records. Inclusion criteria were having had at least one ED visit without admission or inpatient admission at our hospital during the 6-month period. Charts were reviewed for documentation of homelessness for up to the first two ED visits and first two inpatient admissions per patient during the 6-month period. We then examined the persistence of correct homeless identification among two consecutive encounters: ED visit to ED visit, ED visit to admission, admission to admission, or admission to ED visit. Univariable logistic regression was used to analyze the association between correct identification of homelessness at the

first encounter with correct identification at the second. For second encounters, we examined the difference in identification rate between ED visits and admissions using Fischer's exact test.

**RESULTS:** Using the HMIS, we identified 702 patients experiencing home-

lessness; from their hospital records we reviewed 813 ED visits and 220 admissions. Among patients for whom homelessness was correctly identified during a sentinel ED visit, it was again identified in 63.86% of 83 ED visit second encounters compared to 90.91% of 22 admission second encounters (p=0.0177). There was a significant association between correct identification of homelessness in the sentinel ED visit and the ED visit second encounter  $(\beta = 9.717, p < 0.0001)$  or admission second encounter ( $\beta$ =7.778, p=0.0208). Among patients for whom homelessness was correctly identified during a sentinel admission, it was again identified in 81.25% of 16 admission second encounters compared to 54.05% of 37 ED visit second encounters (p=0.0728). There was a significant association between the identification of homelessness in the sentinel admission and the admission second encounter ( $\beta$ =13, p=0.0318) or ED visit second encounter ( $\beta$ =12.94, p=0.0403).

**CONCLUSION:** These data suggest that homelessness is more often correctly documented during hospital admissions than ED visits. Correct identification in the EMR during a sentinel ED visit or admission was associ-

Among patients for whom homelessness was correctly identified during a sentinel ED visit, it was again identified in 63.86% of 83 ED visit second encounters compared to 90.91% of 22 admission second encounters (p=0.0177).

> ated with correct identification during a subsequent encounter, however this was less often true when the subsequent encounter was in the ED. Whether homelessness was documented during a sentinel admission or sentinel ED visit, both resulted in successful identification in only about 60% of second ED visits. This suggests that ED providers are less likely to locate existing homeless status information in the EMR. This may reflect that our health system's EMR has separate applications for ED and admission documentation, with inpatient providers more commonly accessing both applications. These findings highlight the need for effective screening and documentation of housing status in an EMR location easily accessed by all providers.

## Designing an Educational Brochure for Malawian Families of Children with Sickle Cell Disease

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Annually, there are approximately 400,000 children born with sickle cell disease (SCD); 90% of these children live in sub-Saharan Africa.<sup>1</sup> Affected children are at risk for a range of health effects, most importantly silent or overt strokes that can cause cognitive and neurological impairments.<sup>2</sup> Despite the high prevalence and incidence of SCD in sub-Saharan Africa, medical monitoring for disease status is frequently

less than in high-income countries.<sup>2</sup> Even if patients are found to be at high risk of adverse consequences of SCD, medical interventions are infrequently available.<sup>2</sup> This is the case in Malawi, a country where 1 to 3% of all children are affected.<sup>1,3</sup>

Transcranial Doppler (TCD), which has recently become available in Malawi, is reliably used to assess the risk of strokes in children with SCD. Because this technology is new to this region, there are concerns that families do not understand why TCD is being performed. In response, we created and validated an educational brochure for families of children with SCD who were enrolled in a TCD monitoring clinic at Queen Elizabeth Central Hospital in Blantyre, Malawi. We reviewed educational brochures about SCD and other disease processes in use in other African countries.

Following these models, we developed questions and answers related to SCD and TCD using simple language. The narrative was translated into Chichewa, a regional, native language. We obtained feedback on the pilot version after review by Malawian nurses and parents for content validity and ease of understanding. We then revised the brochure accordingly. The final product was illustrated and printed, creating a deliverable, educational brochure focused on Malawian families of children with SCD. Future directions for this work may include interventional clinical trials to ascertain whether family education using this brochure improves compliance with medications, clinic attendance, and SCD outcomes.

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### A Decade of Increased Utilization and Declining Reimbursement of CTA and CT Perfusion of the Head in Medicare Beneficiaries

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To evaluate recent trends in national procedural volume of computed tomography angiography (CTA) and computed tomography perfusion (CTP) of the head with specific evaluation of emergency department (ED) utilization.

Physician Summary Procedure Files (PSPS) from the Centers for Medicare and Medicaid Services (CMS) were obtained for the years 2010 – 2019. Total fee-for-service Medicare beneficiaries were obtained from CMS Program Statistic Reports. CT Angiography and CT Perfusion procedures were identified using current procedural technology (CPT) codes. Annual procedural volume was analyzed. Subsequent analysis by procedure location including office, inpatient hospital, outpatient hospital, and emergency rooms was then performed.1,2

From 2010 to 2019, the total number of Medicare fee-for-service beneficiaries ranged from 36.0 million to 38.7 million persons. Total number of CTA studies increased from 138,189 to 550,903 per annum, a gain of 299%. Total number of CT Perfusion studies increased from 10,096 to 60,297 per annum, a gain of 497% (Fig. 1C). After adjustment for Medicare enrollment,





**FIGURE 1: A.** CTA Head and CT Perfusion procedures performed per 100,000 feefor-service Medicare beneficiaries, 2010-2019. **B.** Percentage of Reimbursement of CTA Head and CT Perfusion by Medicare, 2010-2019. **C.** CTA head and CT perfusion procedural volume, charges, and reimbursement 2010–19, in Medicare Fee-For-Service Beneficiaries.

these values represent an increase in CTA utilization from 383.9 to 1,428.1 (+272%) per 100,000 persons per year, and an increase in CTP utilization from

28.0 to 156.3 (+457%) per 100,000 persons per year (Fig. 1A).

Over the study period, a statistically significant increase in the proportional procedural volume of both CTA Head and CT perfusion were performed in the emergency department (Fig. 2). The proportion of CTA Head procedures performed in

the emergency department rose from 13.9% in 2010 to 43.4% in 2019 (p < 0.001), with the largest single-year increase occurring between 2015 and 2016 (26.8% to 34.3%, +7.5%, p < 0.001) and the second largest increase occurring between 2018 and 2019 (39.9% to 43.3%, +3.5%, p < 0.001). Utilization of CT Perfusion in the emergency

department also rose from 30.8% to 49.4% (p < 0.001) between 2010 and 2019. The largest single-year increase occurred between 2018 and 2019 (43.6%

Our analysis captured over 36 million Medicare beneficiaries and revealed that on a per capita basis, use of both head CTA and cerebral CTP studies increased several-fold over the last decade.

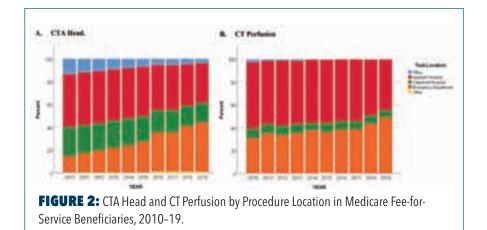
to 49.4%, +5.8%, p < 0.001) with the second highest single-year increase occurring between 2017 and 2018 (38.2% to 43.6%, +5.4%, p < 0.001).

Percent reimbursement of CTA of the head and CT perfusion were evaluated by comparing yearly charges

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to Medicare compared to reimbursement for each procedure (Fig. 1B). Predictably, there was a decrease in CT perfusion payments, which declined approximately 100% in reimbursement rate between 2011 and 2013. There was also a decrease in reimbursement for CTA head from Medicare between 2010 and 2019, which fell from 21.7% to 17.6% (-20%).

Our analysis captured over 36 million Medicare beneficiaries and revealed that on a per capita basis, use of both head CTA and cerebral CTP studies increased several-fold over the last decade. Likewise, during this study period, we found a statistically significant increase in the procedural volume of both CTA Head and CT perfusion performed in the emergency department. With the advent



of Medicare's episode-based bundled payments beginning in 2013, there was near complete decline in CT perfusion reimbursement with the greatest drop occurring between 2011 and 2013 with an approximately 20% drop in payment for the bundled procedure of CTA head.

#### **REFERENCES:**

- Total Medicare enrollment: Total, original Medicare, and Medicare Advantage and other health plan enrollment, calendar years 2010-2015. CMS Program Statistics 2016.
- Total Medicare enrollment: Total, original Medicare, and Medicare Advantage and other health plan enrollment, calendar years 2013-2018. CMS Program Statistics 2019.

## The Future of Telehealth: What We Need to Know to Harness Its Potential

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Health care made the abrupt and rapid transition to providing services remotely via telehealth during the SARS-CoV-2 pandemic.

Formerly a tool to increase access to care in primarily rural areas, telehealth was scaled up to become the dependedupon mode of health care delivery despite a lack of evidence-based preparation and tested infrastructure. To ensure the improved quality and efficacy of telehealth services in future, it is incumbent upon policymakers, researchers, and the public health community to conduct data collection and evaluation while the pandemic continues.

This article acknowledges known limitations of current telehealth technologies, questions the potential impact of widespread implementation on patient care, outlines current gaps in evaluation, and points to further avenues for study.

# Fusion

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