BU CTSI

11th Annual Translational Science Symposium

In Memory of David Seldin, MD, PhD

Advancing Health Equity through Translational Science: Addressing Outcomes Impacted by Social Determinants of Health

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Poster Presentations

1. RIGHT-SIDED VS LEFT-SIDED LEFT BUNDLE AREA LEAD IMPLANTS – A SUCCESS

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Introduction:

Background: His bundle pacing has been challenging for right-sided (RS) access. Success rate for RS left bundle area pacing (LBAP) lead implants is unknown.

Objective: In this study we (1) explore the feasibility and safety of RS implants compared to left-sided (LS) implants and any differences in techniques, and (2) compare pacing parameters acutely and chronically.

Methods: Procedural and pacing characteristics and electrophysiology parameters in consecutive 245 patients who underwent LBAP between October 2019 and December 2021, were extracted from the medical records. Data on RS and LS implants was compared. Anatomical failure was defined as inability to advance the lead into the septum. Electrophysiologic failure was defined as QRS duration >130 msec and/or ventricular activation time (VAT) >90 msec. No special procedural or tool modifications were applied during the RS procedures.

Results: RS devices were implanted in 31 patients; 214 patients received LS implants. C315™ sheaths (Medtronic, Inc, Minneapolis, MN) were used in all implants. Procedural and pacing characteristics between the RS and the LS implants were comparable (Table). There was no difference in chronic pacing characteristics between the RS and LS groups.

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Table: Procedural and pacing characteristics in patients with RS vs. LS direct conduction system pacemaker implantation.

	Right-sided (N = 31)	Left-sided (N = 214)
Anatomic failure	**0%**	**2%**
Electrophysiological failure	**13%**	**11%**
Capture threshold, *Volts*	0.5 [0.3]	0.5 [0.3]
QRS width, *msec*	119 [15]	114 [12]
VAT, *msec*	75 [18]	78 [11]
Procedure time, *min*	70 [29]	80 [37]
Fluoroscopy time, *min*	8.7 [5.6]	8.0 [5.9]
Revision surgery	**3%**	**6%**

Continuous variables are given as median [interquartile range]. Binary variables described as percentage.

Conclusion: RS LBAP is highly successful and comparable to the LS access. Sheath modification is not required for RS approach. Acute and chronic pacing characteristics between both anatomical approaches are similar.

2. WNT/BETA-CATENIN SIGNALING DRIVES AGE-DEPENDENT ORAL SQUAMOUS CELL CARCINOMA EVOLUTION

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Introduction: Oral Squamous Cell Carcinoma (OSCC), a major subtype of Head & Neck Cancer, is associated with high morbidity and few therapeutic options. This malignancy is driven, in part, by epigenetic reprogramming, associated cell plasticity, and cellular senescence directed by β-catenin in complex with CREB-binding protein (CBP) and mixed lineage leukemia methyltransferase 1 (MLL1). Increasing evidence suggests cell plasticity and cellular senescence are associated with aggressive cancer traits. Given the median age of OSCC diagnosis is 66 years, I hypothesized that aging promotes OSCC evolution to advanced disease.

Methods: To examine the effects of aging on OSCC cell plasticity and senescence, we adapted a syngeneic mouse model of tobacco-associated oral carcinogenesis. This model utilizes a mouse cell line, 4MOSC1, derived from 4-nitroquinoline-1 oxide-induced tongue tumors which, when implanted into mouse tongues, generates tumors that recapitulate human OSCC mutanome. The growth of 4MOSC1 orthotopic tumors was studied in 6- and 80-week-old mice. Tumors were allowed to develop for 18 days, and were harvested and processed for histopathology, immunofluorescence and immunoblot analyses.

Results: showed that tumors grew at a faster rate and to a greater overall size in old mice compared to their young cohorts. OSCC harvested from the old mice displayed statistically significant reduction in

membranous E-cadherin concomitant with increased Cbp and H3K4me3 abundance, suggesting an age-associated upregulation of β-catenin/Cbp/Mll1 epigenetic activity. Increased expression of Bmi1 and Keratin 14 supported increased cell plasticity in aged mice OSCC. Further, tumors from aged mice exhibited augmented cellular senescence, as judged by the disruption of Lamin B1 nuclear membrane integrity along with increased H3K9me3 repressive epigenetic marks.

Conclusion: These data suggest that aging is associated with increased □-catenin/Cbp/Mll1 epigenetic signaling, cell plasticity and cellular senescence, which collectively contribute to the evolution of OSCC.

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3. COMORBIDITY BURDEN AMONG INDIVIDUALS WITH A SCHIZOPHRENIA SPECTRUM DISORDER: AN EXPLORATION OF SOCIODEMOGRAPHIC CHARACTERISTICS

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Introduction: Chronic physical illness among patients with schizophrenia spectrum disorders (SSDs) reduces 13-15 years of life expectancy. Individuals with lower socioeconomic (SES) status face greater structural barriers to sustained engagement in healthcare. Here, we examined sociodemographic characteristics of individuals with and without severe comorbidity. We hypothesize that a higher proportion of individuals from neighborhoods with low SES and individuals from racial/ethnic minority groups will have a severe comorbidity burden compared to other groups.

Methods: We conducted a cross-sectional electronic medical record (EMR) study at an urban safety-net hospital with at least one visit between 2015 and 2022 with a billing diagnosis of an SSD. Adults aged > 50 years with Charlson Comorbidity Index (CCI) data were included. Individual-level EMR demographic data was connected to American Community Survey data to calculate neighborhood-level deprivation. Differences in sociodemographic characteristics were compared between individuals with and without severe comorbidity burden (defined as CCI > 4) using chi-square tests.

Results: Of 2,545 patients, 54.7% were male, 53% were non-Hispanic Black, 82.6% were English-speaking. The median age was 64 (IQR 14) and median neighborhood socioeconomic vulnerability was 0.76 (IQR 0). A total of 19.9% of patients had severe comorbidity burden and median CCI was 2 (IQR 3). A higher proportion of non-Hispanic Black and Hispanic individuals had severe comorbidity compared to non-Hispanic white individuals (22.6% vs. 21.9% vs. 15.1% respectively, $p<0.001$).

Conclusions: Our findings further support that physical comorbidity burden is high among older adults living with a SSD. Several hundred patients met criteria for severe comorbidity burden, which is associated with less than 25% estimated 10-year survival in the general population. Our next step is to run age-adjusted multi-level regression analyses to further explore the interplay between comorbidity burden and sociodemographic factors in SSDs.

4. DEMOGRAPHIC FACTORS ASSOCIATED WITH DIFFERENTIAL ACCESS TO TREATMENT IN KERATOCONUS PATIENTS AT A U.S. URBAN SAFETY NET HOSPITAL

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Introduction: The purpose of this study is to examine the effects of demographic factors on patients' odds of corneal crosslinking (CXL) and medical contact lenses (CL), as well as the association of these factors with the level of keratoconus severity at presentation. Certain demographic factors (area deprivation index (ADI), race/ethnicity, language, and insurance) will affect rates of access to CXL and CL treatment and severity at presentation.

Methods: CXL and CL treatment odds based on demographic features were calculated using univariate logistic regression. Significance was assessed using chi-squared likelihood ratios. Multivariate logistic regression models were used to calculate odds ratios adjusted for age and the aforementioned factors. Tukey's method was used to compare subgroups at a 5% family-wise error rate. Amsler-Krumeich (AK) classification as well as keratoplasty rates were used to classify severity at presentation, and univariate logistic regression was used to calculate the odds of a high AK score by demographic factors.

Results: There was no significant association between ADI and CXL treatment (p=0.514) or CL access (p=0.744). Multivariate analyses showed that patients whose primary language was not English were less likely to have CK access (OR_{adj}=0.65, 95% CI 0.42-0.96, p=0.031). Insurance status (p=0.028) and race/ethnicity (p=0.028) also had significant associations with CXL treatment. When adjusted for all other factors, White patients were more likely to receive CXL relative to Black patients (OR_{adj}=7.44, 95% CI 2.20-27.02). White also presented with less severe keratoconus, with lower odds of high AK scores relative to Black patients (OR=0.38, 95% CI 0.17-0.82). Additionally, there was no significant association between demographic factors and keratoplasty rates.

Conclusions: Disparities exist in access to treatment for keratoconus, as well as severity on presentation, for commonly disadvantaged groups. Further studies are warranted to investigate these disparities further to more equitably reduce disease burden for these communities.

5. MOTIVATIONAL INTERVIEWING FOR LOVED ONES: RANDOMIZED CONTROLLED TRIAL OF BRIEF TRAINING FOR FIRST EPISODE PSYCHOSIS CAREGIVERS

EMILY KLINE

Introduction: Research shows that family involvement in psychosis treatment leads to better patient outcomes. Interventions that involve and counsel family members may improve patient outcomes by addressing barriers to treatment adherence and lowering family expressed emotion, thereby creating a less

stressful and more supportive home environment. Learning to use motivational interviewing communication skills may help caregivers to decrease conflict and expressed emotion and improve treatment adherence.

Methods: The current study is a pilot randomized controlled trial testing the impact of "Motivational Interviewing for Loved Ones" (MILO), a brief five-hour psychoeducational intervention for caregivers, in a sample of family members of individuals with early course psychosis (N = 40). Using a randomized crossover design, caregivers were randomized to either immediate MILO or a six-week waitlist control condition; all participants eventually received the intervention.

Results: Caregiver participants experienced large (d = 1.08–1.43) and significant improvements in caregiver wellbeing, caregiver self-efficacy, family conflict, and expressed emotion. There was no change over time in caregiver-reported patient treatment adherence. Relative to waitlist, MILO had significant effects on family conflict and expressed emotion, a trending effect on perceived stress, and no effect on parenting self-efficacy or treatment adherence.

Conclusions: MILO showed benefits for caregivers of FEP patients in this small, controlled trial. Further testing in a larger randomized controlled trial is warranted to better characterize MILO's effects for caregivers and patients across a range of diagnoses.

6. THE TRANSACTIONAL NATURE OF AUTISTIC YOUNG ADULTS' SOCIAL AND SENSORY EXPERIENCES

SHARADA KRISHNAN, GAEL ORSMOND

Introduction: Many autistic individuals experience sensory processing differences, but most research has focused on autistic children (Hantman et al., 2022). It is important to understand sensory experiences during young adulthood, when autistic young adults (AYA) must navigate sensory experiences in new situations and social demands. The purpose of this study was to understand how AYA perceive and manage sensory experiences in everyday contexts of young adulthood.

Methods: This qualitative study included 14 AYAs aged 20-26 years. Participants had a professional autism diagnosis and did not have intellectual disability. Individual semi-structured interviews were conducted via Zoom. Interview questions focused on sensory experiences in daily contexts (e.g., home, work, social). Data were analyzed with principles of grounded theory. Initially, open coding identified sensory experiences and the daily contexts described by AYA. Initial coding showed that the social context was prominent in AYA's sensory experiences. Thus, focused coding sought to further understand the relationship between sensory and social experiences of AYA.

Results: Analyses yielded two overarching findings: (1) AYA's sensory and social experiences are transactional, whereby AYA's sensory experiences are shaped by and shape their social experiences, and (2) navigating sensory experiences requires negotiations with the social context. Negotiations included establishing sensory boundaries with other people, evaluating trade-offs between sensory experiences and social participation, developing sensory self-understanding through social influences, and (un)masking sensory experiences and weighing societal experiences.

Conclusion: The findings highlight aspects of sensory experiences unique to young adulthood, reflecting the heightened social influences of this developmental period. AYA's sensory and social experiences are inextricably linked, and AYA's negotiations of sensory and social experiences mirror the developmental tasks of young adulthood: developing autonomy, relationships, and self-identity (Cicchetti & Rogosch, 2002;

Arnett et al., 2014). These findings underscore the need for services to acknowledge the contextual, social aspects of sensory experiences in AYA.

References:

Arnett, J. J., Žukauskienė, R., & Sugimura, K. (2014). The new life stage of emerging adulthood at ages 18–29 years: Implications for mental health. *The Lancet Psychiatry*, *1*(7), 569–576. https://doi.org/10.1016/S2215-0366(14)00080-7

Cicchetti, D., & Rogosch, F. A. (2002). A developmental psychopathology perspective on adolescence. *Journal of Consulting and Clinical Psychology*, *70*, 6–20. https://doi.org/10.1037/0022-006X.70.1.6

Hantman, R. M., Johnston, E. B., & Tager-Flusberg, H. (2022). Parental perspectives: How sensory sensitivities impact the transition to adulthood in adolescents and young adults with autism spectrum disorder. *Journal of Autism and Developmental Disorders*, 1-19. https://doi.org/10.1007/s10803-022-05815-5

7. STORYTELLING THRU DANCE: INTEGRATING CULTURAL PERSPECTIVES INTO MED. EDUCATION

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Introduction: Postpartum depression (PPD) is a mood disorder involving the occurrence of a depressive episode in a birth-giver within 12 months of childbirth. PPD is challenging due to its associated stigma and poor screening tools. Provider understanding of the symptoms and experience of PPD is essential for improving health outcomes. One potential avenue for destigmatizing PPD while increasing providers' understanding of PPD is through narrative-based learning, which is effective in fostering empathy and improving understanding of the patient experience. Given the social and cultural stigma associated with PPD, particularly in South Asian communities, we have created a dance film which teaches the audience about PPD through Indian classical dance with the purposes of 1) increasing clinical knowledge about PPD (signs, symptoms, and interventions), 2) increasing understanding of the patient experience, and 3) conveying the cultural context of stigma towards PPD in the South Asian community. We hypothesized that viewing of our dance film would foster participant empathy and enhance participants' knowledge of PPD symptoms and resources within the context of cultural stigma and challenges faced in the South Asian community.

Methods: To assess the effectiveness of this film as a medical education tool, it was presented to medical students at Boston University Chobanian and Avedisian School of Medicine. Afterwards, participants engaged in focus group discussions (FGDs) and their comments were recorded, transcribed, and coded for emerging themes through NVivo qualitative analysis software.

Results: The qualitative analysis demonstrates that the FGDs elicited themes including the humanization of stigmatized illnesses through narrative learning, facilitation of health care providers' cultural humility and knowledge, and dissemination of resources and knowledge related to PPD.

Conclusion: Our work with participants in medical training demonstrates that using creative learning modalities enhances student understanding of medical topics and can supplement the academic dissemination of information in the medical curriculum.

8. DEVELOPING A NEW HIGHLY SENSITIVE MESO SCALE DISCOVERY (MSD) BIOMARKER IMMUNOASSAY FOR CHRONIC KIDNEY AND EYE DISEASE.

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Introduction: Both kidney failure and blindness are common complications of poorly controlled diabetes mellitus, which afflicts over 150 million people around the world. The kidney and eye share several structural similarities and developmental pathways that may account for their shared susceptibility as end-organ complications of diabetes. SLIT is a ligand for ROBO receptors. SLIT/ROBO pathway plays essential roles in kidney and eye development. Published ELISA results showed upregulation of SLIT protein expression in both chronic kidney and eye diseases. However, the low sensitivity and dynamic range of the ELISA assay has made the SLIT biomarker results unreproducible.

Methods: We developed a highly sensitive Meso Scale Discovery (MSD) immunoassay using an electrochemiluminescence detection technique with a greater dynamic range that may replace previously developed ELISAs for biomarker SLIT detection. In a process similar to a sandwich ELISA assay, we detected and quantified standard SLIT recombinant protein and unknown SLIT concentration in patient samples using the MESO QuickPlex SQ120 instrument.

Results: Our data showed a greater dynamic range and more precise and accurate readings on a lower concentration of SLIT biomarker using the MSD assay (LLOD=5 pg/ml, ULOD=20,000 pg/ml) compared to regular ELISA (1,000 pg/ml, ULOD=50,000 pg/ml). We also found the optimal concentrations of the capture and detection antibodies that best suit the SLIT measurements. Besides the newly developed SLIT MSD assay being able to detect low protein levels, we also discovered 7-fold higher SLIT levels in eye vitreous humor compared to blood samples in diabetic patients.

Conclusions: We have developed a highly sensitive MSD assay across 4 orders of magnitude for novel biomarker SLIT in diabetic patients, which may be used in probing mechanisms of eye and kidney complications of diabetes and lead to a new diagnostic tool for both chronic kidney and eye diseases.

9. DEEPSOZ: A ROBUST DEEP MODEL FOR JOINT TEMPORAL AND SPATIAL SEIZURE ONSET LOCALIZATION FROM MULTICHANNEL EEG DATA

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Introduction: Epilepsy is a neurological disorder characterized by spontaneous and recurring seizures. Roughly 30% of epilepsy patients are drug resistant. In such cases, the best alternative treatment is to surgically resect the seizure onset zone (SOZ) in the brain. Scalp electroencephalography (EEG) is the foremost modality used to monitor epileptic activity. However, it requires expert visual inspection of the signals, which is time-consuming and prone to the subjective biases of the clinicians. Computer-aided tools for EEG largely focus on the task of (temporal) seizure detection. Hence, we propose a robust deep learning framework, called DeepSOZ, to simultaneously detect and localize seizure activity from multichannel scalp EEG.

Methods: DeepSOZ consists of a transformer encoder to generate multiscale encodings. The global branch is combined with an LSTM for seizure detection. In parallel, we employ attention-weighted multi-instance pooling of channel-wise encodings to predict the SOZ. We train DeepSOZ with supervision to generate predictions on the order of each second (temporal) and EEG channel (spatial). We validate DeepSOZ via bootstrapped nested cross-validation on a dataset of 120 patients curated from the Temple University Hospital corpus.

Results: As compared to baseline approaches, DeepSOZ provides robust performance in our multi-task learning setup. In seizure detection, DeepSOZ achieved an AUC-ROC score of 0.901±0.027 at the window-level and a sensitiv- ity of 0.808±0.106 at the seizure-level with a low false positive rate. In spatial localization, DeepSOZ achieves an accuracy of 73.1±6.1% with uncertainty ¡0.1 across multiple occurrences of the seizure.

Conclusions: DeepSOZ leverages a novel neural network architecture and training strategy for robust and informative seizure detection and SOZ local- ization from scalp EEG. Beyond predictive performance, we also quantify the intra-seizure and intra-patient uncertainty of DeepSOZ as a first step to establishing its trustworthiness for integration into the clinical workflow for epilepsy.

10. INCREASING ACCESS TO MINDFULNESS FOR PERSONS WITH CHRONIC LOW BACK PAIN IN A TELEHEALTH-DELIVERED PRAGMATIC TRIAL

NGUYEN, TRA MORONE, NATALIA

Introduction: Access to mindfulness, a first-line non-pharmacologic treatment for chronic low back pain (cLBP), has been limited. Integrating mindfulness into a group telemedicine platform presents a promising path to overcome access to care barriers and scale the dissemination of this treatment. The OPTIMUM trial (Optimizing Pain Treatment in Medical Settings Using Mindfulness) tests a telehealth-delivered group

mindfulness program for persons with cLBP in the primary care setting. We describe our strategies on implementing an accessible & welcoming virtual platform for persons with cLBP.

Methods: The trial incorporates an 8-week medical group mindfulness clinical pain program modeled on Mindfulness-Based Stress Reduction (MBSR) and delivered through a telehealth and videoconferencing format at three different healthcare sites. The intervention is led by an experienced MBSR instructor and co-led by a primary care provider with assistance of research staff for technical support. Prior to the start of the intervention, research staff offer one-on-one technical assistance and study materials to help participants become familiar with the videoconferencing platform. Demographic data conducted at baseline, and post-intervention interviews were collected to evaluate the acceptability and usability of the intervention beyond the trial.

Results: 451 participants were recruited, and participants' mean age was 52.1 years (SD 14.6). 315 (69.8%) were female, 194 (43%) were Black, and 217 (48.1%) were White. 127 (30.9%) had an income < $25,000, 152 (33.8%) held a high school degree, and over 70.5 % (318) of the study population had cLBP for more than five years. Only 53.4% (235) reported very much comfortable with videoconferencing at baseline. Qualitative interviews highlighted participants' interest in continuing the program as the program creates a sense of community.

Conclusion: By integrating an evidence-based group mindfulness pain program into the primary care setting via a telehealth-delivered model, we identify opportunities to expand the availability of non-pharmacologic treatments to an underserved population.

11. SPATIAL AND SOCIAL CONNECTEDNESS OF PEOPLE WHO SMOKE DRUGS WITH TUBERCULOSIS IN RURAL SOUTH AFRICA

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Introduction: People who smoke illicit drugs (PWSD) are at increased risk of tuberculosis (TB) disease, but transmission has not yet been studied in this population. Understanding the spatial mobility and social connectedness of PWSD with TB allows for the identification of high-risk locations and may assist with designing targeted interventions to reduce TB transmission.

Methods: We report on 73 participants recruited via respondent-driven sampling or the clinic from 2021-2023 in Worcester, South Africa. All participants were ≥15 years old, had microbiologic TB confirmation, and screened urine positive for methamphetamine or methaqualone. Social contact questionnaires were administered to record locations and geospatial coordinates frequented in the 1-2 years prior to TB diagnosis. We estimated centrality measures of weighted, non-directed activity space networks to identify frequented locations and the interactions between them and explored the spatial architecture of social networks for PWSD with TB disease. We identified two geospatial archetypes for individual participants; residentials report using drugs in private settings, whereas *travelers* represent those who use drugs in geographically diverse areas outside of the home.

Results: The activity space network displayed varying degrees of connectivity among nodes (2 to 82 connections per node; mean = 10.8). Closeness centrality values varied in proximity to others (0.0014 to 0.0034; mean=0.003), while betweenness centrality identified nodes playing critical roles in connecting different parts of the network (0.0 to 3097.37; mean=119.13). 58 (79%) participants were classified as residentials. A significantly higher proportion of residentials were living with HIV compared to travelers (38% vs. 7%, p=0.020, Table 1).

Conclusion: Network-based analyses offer insights into candidate locations for spatially targeted screening to curb the spread of TB among PWSD. Given that a majority of participants were identified as using drugs in private settings, interventions that extend beyond public venues may be needed to effectively reach PWSD and interrupt TB transmission.

Table 1: Characteristics of PWSD with TB disease by smoked drug use archetype

	Residentials (N=58)	Travelers (N=15)	Total (N=73)	p value
Age, years	36 (31, 38)	42 (33, 44)	36 (32, 41)	0.053
Born Male	43 (74.1%)	14 (93.3%)	57 (78.1%)	0.109
Ethnicity				0.157
Mixed Ancestry	51 (87.9%)	15 (100.0%)	66 (90.4%)	
Black African	7 (12.1%)	0 (0.0%)	7 (9.6%)	
Current living situation				0.492
Formal	36 (62.1%)	10 (66.7%)	46 (63.0%)	
Informal	21 (36.2%)	4 (26.7%)	25 (34.2%)	
No fixed residence	1 (1.7%)	1 (6.7%)	2 (2.7%)	
Unemployed	52 (89.7%)	12 (80.0%)	64 (87.7%)	0.311
Marital status				0.822
Married	5 (8.6%)	1 (6.7%)	6 (8.2%)	
Living together with partner	15 (25.9%)	2 (13.3%)	17 (23.3%)	
Widow/widower	2 (3.4%)	1 (6.7%)	3 (4.1%)	
Divorced or separated	5 (8.6%)	2 (13.3%)	7 (9.6%)	
Never married	31 (53.4%)	9 (60.0%)	40 (54.8%)	
Gang membership				0.385
Currently in a gang	10 (17.2%)	4 (26.7%)	14 (19.2%)	
Previously in a gang	12 (20.7%)	1 (6.7%)	13 (17.8%)	
Never in a gang	36 (62.1%)	10 (66.7%)	46 (63.0%)	
Imprisoned, ever	50 (86.2%)	12 (80.0%)	62 (84.9%)	0.549

	Residentials (N=58)	Travelers (N=15)	Total (N=73)	p value
Network Size (N=67)	25 (10, 60)	30 (16, 34)	30 (10, 50)	0.975
Alcohol, ever use	49 (84.5%)	12 (80.0%)	61 (83.6%)	0.676
Current alcohol use (N=61)				0.795
Never	15 (30.6%)	5 (41.7%)	20 (32.8%)	
Once or Twice	12 (24.5%)	3 (25.0%)	15 (24.6%)	
Monthly	10 (20.4%)	3 (25.0%)	13 (21.3%)	
Weekly	11 (22.4%)	1 (8.3%)	12 (19.7%)	
Daily or Almost Daily	1 (2.0%)	0 (0.0%)	1 (1.6%)	
Only uses tik	4 (6.9%)	0 (0.0%)	4 (5.5%)	0.295
Only uses mandrax	5 (8.6%)	3 (20.0%)	8 (11.0%)	0.209
BMI (N=72)				0.797
Severely Underweight	4 (7.0%)	1 (6.7%)	5 (6.9%)	
Underweight	21 (36.8%)	5 (33.3%)	26 (36.1%)	
Normal Weight	29 (50.9%)	9 (60.0%)	38 (52.8%)	
Overweight and Obese	3 (5.3%)	0 (0.0%)	3 (4.2%)	
Living with HIV	22 (37.9%)	1 (6.7%)	23 (31.5%)	0.020
Previous TB	26 (44.8%)	4 (26.7%)	30 (41.1%)	0.203

12. DEMOGRAPHIC AND REGIONAL TRENDS OF ACUTE MYOCARDIAL INFARCTION-RELATED MORTALITY IN YOUNG ADULTS IN THE US, 1999-2020

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Introduction: There has been a considerable reduction in deaths from acute myocardial infarction (AMI) in the middle-aged and elderly population but there is limited data on AMI mortality trends in younger populations.

Methods: We used data from the US Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiologic Research (CDC WONDER) database from January 1999 to December 2020. Young adults aged 15 to 44 years with AMI listed as an underlying or contributing cause of death were included. AMI-related age-adjusted mortality rates (AAMRs) per 100,000 population and annual percentage change (APC) in mortality rates were calculated both overall and stratified by sex, race/ethnicity, and geographical region.

Results: Between 1999 and 2020, there were 81,272 AMI-related deaths among young adults. Of these, 23,474 (28.9%) were among women and 57,798 (71.1%) were among men. Additionally, 54,379 (66.9%) were White, 17,022 (20.9%) were Black, and 6,859 (8.4%) were Hispanic. The overall AAMR decreased from 3.87 (95% CI: 3.76-3.98) in 1999 to 2.53 (95% CI: 2.44-2.62) in 2019 but increased to 2.99 (95% CI: 2.89-3.09) in 2020. Young men had higher average AAMR (4.49; 95% CI: 4.45-4.52) than women (1.84; 95% CI: 1.81-1.86). Non-Hispanic Black or African population had the highest average AAMR (5.07; 95% CI: 4.99-5.15) and showed an increase from 2015 to 2020 with a corresponding APC of 4.4% (95% CI:1.8% to 7.1%). Geographically, the South had the highest AMI-related AAMR of 4.26 (95% CI: 4.22-4.30) with the lowest in the Western states with an AAMR of 1.84 (95% CI: 1.80-1.87).

Conclusions: There was a general decrease in AMI-related mortality rates for young adults from 1999 to 2019 with noticeable differences in demographic features such as gender, racial/ethnic group and geographical region. These disparities in AMI-related mortality appeared to be further accentuated during the first year of the COVID-19 pandemic.

13. ADAPTATION AND DISSEMINATION OF A RACE-BASED STRESS, TRAUMA, AND EMPOWERMENT (RBSTE) CLASS FOR COMMUNITY CHURCHES

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Introduction: Racism is a public health problem that drives a range of health disparities among racially marginalized people. Black people in the US endure a higher stress burden and lower access to quality care caused by structural racism. That is, Black people in the US endure the additive burden of racism-based stress (RBS)—defined as psychological stress or emotional injury reactions that are experienced in response to structural and individual racism**.** This study aims to adapt the Race-based Stress, Trauma, and Empowerment (RBSTE) curriculum for Boston Community Churches and Boston Medical Center patients. The contextual information gathered from stakeholders (i.e., RBSTE developers, clinicians, patients, and church members) will improve our understanding of the local population's needs and how to tailor RBSTE's curriculum and implementation plan.

Methods: We use Chambers and colleagues' Adaptome Model to systematically adapt the intervention for setting, audience, and delivery. We will translate observations and feedback from our four stakeholder groups to implement an adapted version of RBSTE that will improve health equity for Black patients. Integration of feedback from the four stakeholder groups will occur over three phases: (1) pre-trial (intervention was selected and revised), (2) trial in which consultation meeting notes with clinicians and church leaders characterize reactive modifications to RBSTE and its implementation; and (3) post-trial in which the manual and program implementation design was further revised based on feedback from the four stakeholder groups.

Results: We present findings and process details from our systematic and iterative approach to adaptation in phase 1. Themes from field notes of meetings with stakeholders yielded the need to adapt

RBSTE for spiritual bypassing, preparing for resistance to practices such as mindfulness through making them culturally appropriate, and adapting the material to fit in the context of immigrants.

14. SUBSTANCE USE AND FUNCTIONALITY AMONG COURT-INVOLVED PATIENTS WITH MENTAL ILLNESS

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Introduction: Assisted Outpatient Treatment (AOT) is a civil procedure,[1] where court-ordered, community-based,[2] mental health treatment is provided to individuals whose difficulty with voluntary outpatient treatment led to interactions with mental health and criminal justice systems.[2] In 2020, a modified, voluntary, criminal case-based, AOT program was implemented in Massachusetts. The Boston Outpatient Assisted Treatment Program (BOAT), provides patients with serious mental illness (SMI) with social, mental health, and substance use disorder treatment to achieve recovery and avoid incarceration. We assessed the impact of substance use on functioning among a cohort of BOAT patients.

Methods: A total of (N=180) patients enrolled in the BOAT program between 2021 and 2023; 85 patients completed the Short Form Health Survey (SF12) at program enrollment.[3] The international classification of diseases was used to define disorders: alcohol use (F10.10-F10.99), opioid use (F.11.10-F11.99), cannabis use (F12.1-F12.99), sedative use (F13.1-F13.99), cocaine use (F14.1-F14.99), and stimulant use (F15.10-F15.99).[4] Patients with these diagnoses were categorized as having substance use disorder or alcohol use disorder (SUD or AUD). We performed bivariate analyses to compare patients with vs. without SUD or AUD

Results: Among BOAT patients with completed SF12, 52.5% were diagnosed with SUD or AUD. Patients with SUD or AUD had a significantly lower mean physical health score than those without SUD or AUD (45 ±10.7 vs 50.3 ± 8.4; p-value = 0.0193). Patients with SUD or AUD had a lower mean mental health score compared to patients without SUD or AUD (41.7 ±11.5 vs 45.2; p-value = 0.078). The mean mental health scores for both groups are lower than the United States population mean score of 50 points. [5]

Conclusion: Elevated rates of SUD or AUD among BOAT patients had negative impacts on functionality. Our findings underscore the necessity of expanding substance use services for individuals in AOT programs.

15. LUNG ADENOCARCINOMA EXPRESSION OF THE ARYL HYDROCARBON RECEPTOR PROMOTES IMMUNOSUPPRESSION IN THE TUMOR MICROENVIRONMENT

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Introduction: Immunotherapy has shown dramatic results in treating cancer, but only a minority of patients benefit. Therefore, there is an unmet medical need to understand the regulation of immune suppression in tumors. We have shown that the aryl hydrocarbon receptor (AhR) is a central player in regulating immune checkpoints in lung adenocarcinoma (LUAD). Within the malignant cell, we determined using qPCR and western blotting that AhR regulates expression of several genes important to suppressive immune signaling, including IDO-1 and PD-L1. Notably, the presence of IFNγ boosts the expression of these AhR-regulated suppressive genes.

Methods: Using an *in vivo* murine model of LUAD, we determined that transplantation of AhR-knockout (KO) LUAD cells leads to partial and up to complete rejection of tumor formation in some mice. AhR-KO-injected mice that do form tumors have increased T cell infiltration, activation, and signaling in the tumor, whereas wild-type (WT) LUAD challenge leads to faster and larger tumor formation with less immune infiltration and greater expression of AhR agonist, kynurenine. Prior exposure to AhR-KO malignant cells is also able to confer protection from challenge with WT LUAD cells in some mice. To identify specific T cell subsets involved in AhR-related tumor immunity, we performed single cell RNA sequencing of $CD3^+$ tumor infiltrating lymphocytes.

Results: This sequencing revealed a cytotoxic T cell population with granzyme and perforin-generating ability unique to AhR-KO tumors. WT tumors were found to have multiple unique $CD4^+$ and $CD8^+$ populations with transcriptomes consistent with naïve, exhausted, and suppressive functions.

Conclusion: This evidence supports a role for the AhR as a driver in remodeling of the tumor microenvironment. Identifying T cell phenotypes key to this anti-tumor immune response begins to elucidate how AhR in the malignant cell promotes immunosuppression and thus paves the way for future AhR-related therapies and biomarkers relevant to improving patient treatments.

16. INSIGHTS INTO THE DESIGN OF KEAP1 INHIBITORS FROM MACHINE LEARNING AND MOLECULAR DYNAMICS

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Introduction: Kelch-like ECH-associated protein 1 (Keap1) is an important drug target for inflammation, multiple sclerosis, and Azheimer's Disease. Keap1 binds the transcription factor nuclear factor erythroid 2-related factor 2 (Nrf2) *via* a high affinity DxETGE motif (K_D ~ 20 nM) and at a low affinity DLG motif. Under basal conditions, Keap1 mediates the ubiquitination and degradation of Nrf2, thus keeping Nrf2 levels low. Under conditions of oxidative stress, Keap1 is inactivated by reaction with Reactive Oxygen Species, causing Nrf2 to accumulate and migrate to the nucleus where it upregulates antioxidant response element (ARE) genes.

Methods: Our lab is interested in targeting the DxETGE binding site on Keap1 using macrocyclic peptides. Here, we describe how machine learning (ML) and molecular dynamics (MD) are being used to elucidate how conformational effects in Keap1 and in the cyclic peptide ligands relate to ligand binding affinity. Specifically, we use the ML method of Partial Least Squares Regression to show that subtle local changes in Keap1 structure upon ligand binding distinguish between high affinity and low affinity ligands.

Results: The results suggest aiming for ligands that optimally complement the "high affinity conformation state" of Keap1 could be a useful principle for designing next-generation cyclic peptide ligands. We are also using MD simulations of a set of existing cyclic peptide ligands with different binding affinities to understand how structural changes to the linker region of these macrocyclic ligands affects the conformational preferences of the Keap1-binding regions.

Conclusions: The results show that our lead inhibitor accesses several distinct conformations, a degree of flexibility that likely diminishes its affinity for Keap1. Different linker structures impose different conformational constraints on the Keap1-binding regions of the ligand. This analysis potentially provides a route to designing linkers that would constrain the Keap1-interacting region in the optimal conformation for binding to this target.

17. SPATIAL FREQUENCY DOMAIN IMAGING AS A NOVEL METHOD TO QUANTIFY SKIN CHANGES IN SCLERODERMA

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Introduction: Systemic sclerosis (SSc) is an autoimmune disease characterized by excessive collagen deposition in the skin and other organs. While the modified Rodnan skin score (mRSS) is the gold standard for skin fibrosis assessment in SSc, it has notable limitations. Spatial Frequency Domain Imaging (SFDI) is a non-invasive optical technique using near-infrared light for objective and quantitative skin fibrosis evaluation. We aim to correlate SFDI with mRSS and histology scores and assess its use in detecting longitudinal skin changes in SSc patients.

Methods: SFDI parameters (μs' and Rd) were obtained from two patient cohorts. In the first cohort, SFDI data were collected at six measurement sites (bilateral forearms, hands, and fingers) from 8 healthy controls (HC) and 10 SSc patients. A physician assessed mRSS, and forearm skin biopsies were obtained to assess for fibrosis. In the second cohort, which included 6 SSc patients from the first cohort and 2 new HCs, we analyzed the correlation between longitudinal changes in SFDI parameters (μs') and mRSS.

Results:

1. Significant difference in μs´ between healthy controls, SSc patient at sites with no skin fibrosis (mRSS = 0), and sites with skin fibrosis (mRSS > 0).
2. Strong correlation between Rd and histology scores for fibrosis (ASMA and Trichrome)
3. Strong correlation between longitudinal changes in μs' with changes in mRSS scores

Conclusions: Our studies suggest SFDI as a promising quantitative and objective method for scleroderma skin assessment. It has the capability to differentiate early skin changes in SSc patients with an MRSS of 0 from those observed in healthy controls. Moreover, SFDI measurements exhibit a significant correlation with both mRSS and histology scores, highlighting its potential as an objective assessment tool. Additionally, SFDI can detect longitudinal skin changes in SSc patients, making it an asset for monitoring disease progression and treatment efficacy.