**Perinatal bipolar disorder and major depression: outcomes from a mother-baby partial hospital program**

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**Purpose:** Perinatal mood disorders including major depression and bipolar disorder significantly impact maternal and child outcomes and can require intensive treatment beyond traditional outpatient services. Mother-bay day hospitals (MBDH) are specialized partial hospital programs (PHP) that offer a critical bridge between inpatient and outpatient treatment yet evidence regarding effectiveness across mood disorders remains limited. This study compared clinical correlates and treatment outcomes of MBDH treatment for perinatal mothers with major depression (MD) and bipolar disorder type 1 (BP1) and 2 (BP2). **Methods:** Pregnant/postpartum (≤12 months) women completing ≥4 MBDH days were assessed pre/post-treatment using the Edinburgh Postnatal Depression Scale (EPDS), Generalized Anxiety Disorder-7 scale (GAD-7), and Barkin Index of Maternal Functioning (BIMF). **Results:** Among participants (n=362), 83% had mood disorders including 67% (n=202) with MD, 13% (n=39) with BP1, and 20% (n=60) with BP2, with comparable demographics across groups. Initial EPDS scores were significantly lower in BP1 (M=17.05, SD=6.77) versus BP2 (M=19.12, SD=4.47) and MD groups (M=19.82, SD=5.22), while baseline GAD-7 and BIMF measurements showed no between-group differences. All diagnostic groups demonstrated significant improvements ($p<0.001$) in depression, anxiety, maternal functioning, and suicidality. Despite prevalent (>39%) social determinants (food/housing insecurity, inadequate social support), these factors were not associated with differential treatment response. **Conclusion**: Perinatal patients with bipolar disorder and major depression and moderate to severe symptoms had significant and similar improvements in clinical outcomes following MBDH treatment.

# Evaluating Differences in Major Depressive Disorder and Bipolar Disorders: Clinical Evaluation of the Mother Baby Day Hospital

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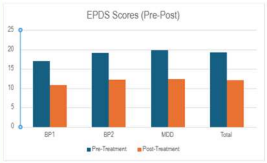
## INTRODUCTION

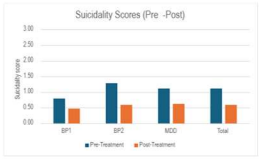
- The Redleaf Center Mother Baby Day Hospital is a partial hospitalization program for women with perinatal mental health concerns that provides group psychotherapy, psychiatry, and complementary medicine approaches to perinatal mental health. The program aims to facilitate bonding through the integration of the child in the therapeutic process.
- Studies that examine this model of therapy are limited especially for perinatal patients with mood disorders.
- Given this limited outcomes research and the high prevalence and impact of perinatal mood disorders, we aimed to extend analysis of our MBDH to determine the clinical correlates of perinatal patients with major depression and bipolar spectrum disorders and evaluate treatment outcomes across diagnostic groups.

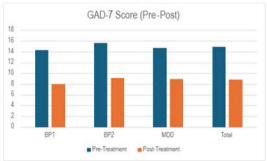
## METHODS

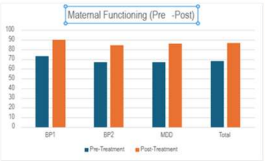
- Participants included patients of the Mother Baby Day Hospital (MBDH) at the Redleaf Center with a diagnosis of bipolar disorder or MDD that completed at least four days of treatment and who answered all questionnaires (n= 301) between April 2013 and September 2019.
- We collected validated pre-post self-report measures of depression (Edinburgh Postnatal Depression Scale [EPDS]), anxiety (Generalized Anxiety Disorder Scale [GAD7]), and maternal functioning (Barkin Index for Maternal Functioning [BIMF])Demographic information and diagnosis information was collected from medical records.
- Data was analyzed in SPSS using ANOVAs and chi-square tests for analysis beyond descriptive analysis.

## RESULTS

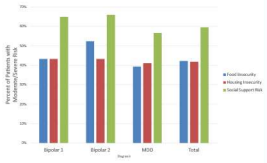



- Among the 301 patients with mood disorders, 67.1% (n=202) had MDD and 32.9% (n=99) had Bipolar spectrum disorder, with 13.0% (n=39) Bipolar type 1 and 19.9% (n=60) Bipolar type 2 (two of these patients had cyclothymia)
- There were no statistically significant differences in the demographic variables across diagnostic groups. The sample was about 75% White, non-Hispanic women with 17% Black or African American, and small numbers of Hispanic/Latina, Asian, American Indian/Alaska Native, Native Hawaiian/Pacific Islander, and other ethnicity women (see Table 1). Education levels showed approximately 23% with high school and 26% with some college and the rest with college or greater degrees. Most were married (59%) or partnered (11%) but about 29% were single. 56% were privately insured with publicly insured 43% (and 1% self-pay). The majority were postpartum (86%) and 54% were first-time mothers. Women were aged 18-45 years (M = 30.16 years) and stayed in treatment 4-29 days (M = 14.01 days).
- Participants with BP1 came into treatment with lower EPDS scores than other groups.
- Participants with MDD were more likely to have a co-morbid anxiety disorder than other groups.
- Participants across all diagnostic groups showed significant improvements ($p<0.001$) in depression, anxiety, and maternal functioning as measured by EPDS, EDPS-Q10 (suicidality question), GAD-7, and BIMF, respectively. There were minimal differences between groups on their treatment response: those with BP2 had a slightly greater reduction in suicidality scores than those with BP1.




**Psychosocial Risk Factors**

## DISCUSSION

- Perinatal patients with moderate to severe symptoms of bipolar type 1 and 2 and major depression had similar improvements in depression, anxiety and maternal functioning in a partial hospitalization setting.
- Our study also revealed significant struggles with basic needs, but they were not associated with differential treatment response in our sample. This suggests that women experiencing financial and social adversity can still benefit from partial hospital programming, even when these underlying social challenges persist.
- Next steps are integrating data from 2019 to present to create a more complete understanding of factors, allow for comparison between different bipolar types and other maternal mental conditions, and see if pre- and post-COVID changed factors or outcomes.

## FUNDING AND DISCLOSURES

Funding for this work was donated to the Redleaf Center for Family Healing from the Lynne and Andrew Redleaf Family Foundation and other funders.
Special thanks to Emerythi Baby for helping make this poster.

**Title:** Referrals to perinatal mental health services and equity: A descriptive analysis

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**Funding:** Funding for this work was provided to the Redleaf Center for Family Healing from the Lynne and Andrew Redleaf Family Foundation and other funders.

Abstract

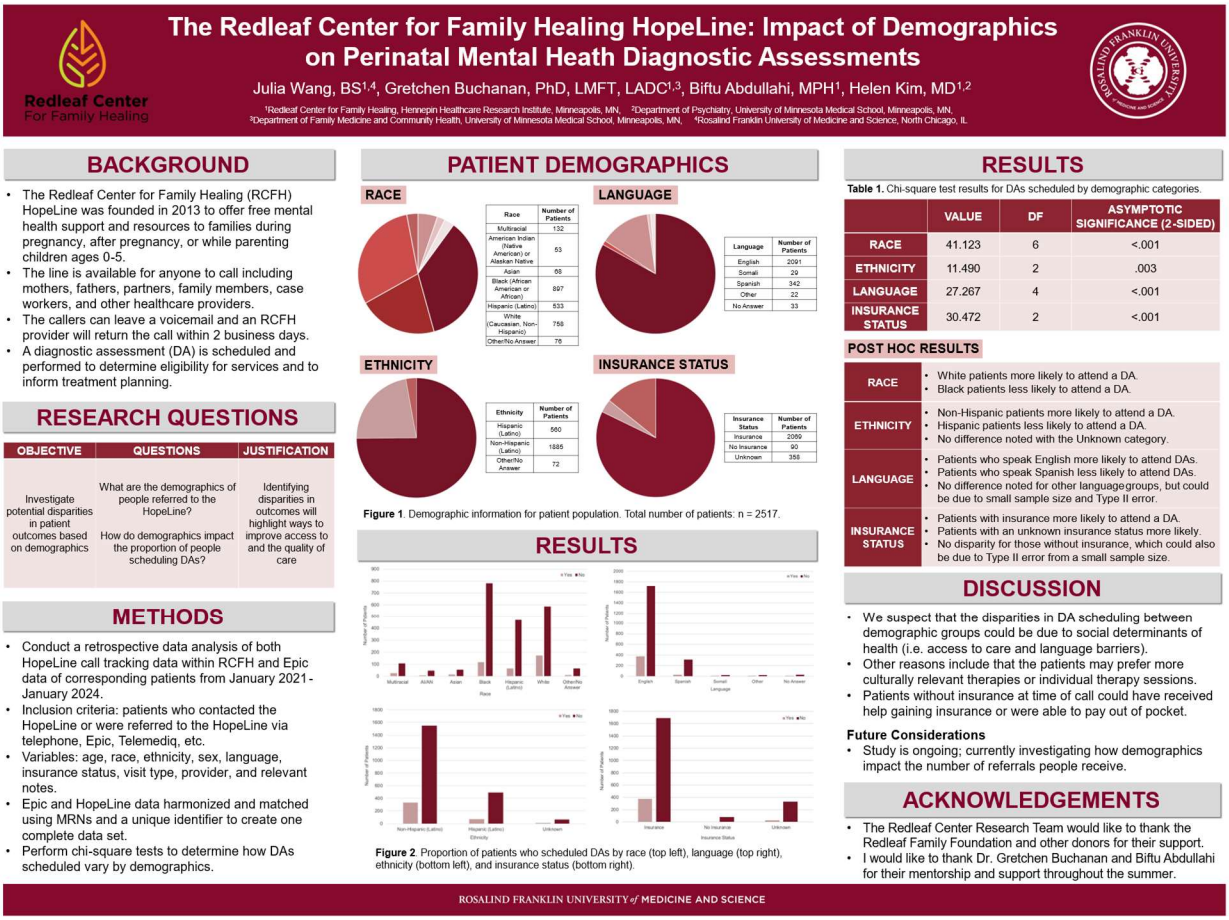
**Objective:** The Redleaf Center for Family Healing (RCFH) is a specialty perinatal mental health and psychiatry program with partial hospitalization and intensive outpatient services located in an urban safety-net hospital. This evaluation aimed to evaluate who is referred, referral sources and outcomes, and to determine potential disparities and reasons.

**Methods:** We conducted a retrospective data analysis of call tracking and Epic data from January 2021-January 2024 ($N$ = 2518 unique individuals). Data harmonization between Epic and Excel data used MRNs, encounter IDs, and dates. Variables included age, race, ethnicity, sex, language, insurance status, visit type, provider, and relevant notes. Analyses include descriptive, chi-square, and regression analysis.

**Results:** Of the 2518 individuals referred, 34.2% were non-Hispanic White, 33.7% were Black, 19.5% were Hispanic, 4.6% multiracial, 2.9% Asian, 2.1% American Indian/Alaska Native, and 2.9% other/declined. Referees averaged 30 years old (range 16-71, SD = 7.64) and most (82%; 14% unknown) had insurance. Total referrals in the 3-year period averaged 1.41 (range 0-10, SD = 1.03), with an average 5.2 pre-programming contacts (range 0-44, SD = 4.42; includes referrals and diagnostic assessments), and 761 diagnostic assessments completed. Chi square analyses indicated disparities across race, ethnicity,

language, and insurance status. Post-hoc analyses showed patients were more likely to have a completed DA who were White, non-Hispanic, spoke English, and who had insurance.

**Conclusion:** The diversity of the sample provides unique insights into the perinatal mental health needs of a metropolitan U.S. population and how various characteristics are related to engaging in services and barriers even within a safety-net context.



# The Redleaf Center for Family Healing HopeLine: Impact of Demographics on Perinatal Mental Heath Diagnostic Assessments


Julia Wang, BS[1,4], Gretchen Buchanan, PhD, LMFT, LADC[1,3], Biftu Abdullahi, MPH[1], Helen Kim, MD[1,2]

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## BACKGROUND

- The Redleaf Center for Family Healing (RCFH) HopeLine was founded in 2013 to offer free mental health support and resources to families during pregnancy, after pregnancy, or while parenting children ages 0-5.
- The line is available for anyone to call including mothers, fathers, partners, family members, case workers, and other healthcare providers.
- The callers can leave a voicemail and an RCFH provider will return the call within 2 business days.
- A diagnostic assessment (DA) is scheduled and performed to determine eligibility for services and to inform treatment planning.

## RESEARCH QUESTIONS

| OBJECTIVE | QUESTIONS | JUSTIFICATION |
|---|---|---|
| Investigate potential disparities in patient outcomes based on demographics | What are the demographics of people referred to the HopeLine?<br>How do demographics impact the proportion of people scheduling DAs? | Identifying disparities in outcomes will highlight ways to improve access to and the quality of care |

## METHODS

- Conduct a retrospective data analysis of both HopeLine call tracking data within RCFH and Epic data of corresponding patients from January 2021 - January 2024.
- Inclusion criteria: patients who contacted the HopeLine or were referred to the HopeLine via telephone, Epic, Telemediq, etc.
- Variables: age, race, ethnicity, sex, language, insurance status, visit type, provider, and relevant notes.
- Epic and HopeLine data harmonized and matched using MRNs and a unique identifier to create one complete data set.
- Perform chi-square tests to determine how DAs scheduled vary by demographics.

## PATIENT DEMOGRAPHICS

**RACE**

| Race | Number of Patients |
|---|---|
| Multiracial | 132 |
| American Indian (Native American) or Alaskan Native | 53 |
| Asian | 68 |
| Black (African American or African) | 897 |
| Hispanic (Latino) | 533 |
| White (Caucasian, Non-Hispanic) | 758 |
| Other/No Answer | 76 |

**LANGUAGE**

| Language | Number of Patients |
|---|---|
| English | 2091 |
| Somali | 29 |
| Spanish | 342 |
| Other | 22 |
| No Answer | 33 |

**ETHNICITY**

| Ethnicity | Number of Patients |
|---|---|
| Hispanic (Latino) | 560 |
| Non-Hispanic (Latino) | 1885 |
| Other/No Answer | 72 |

**INSURANCE STATUS**

| Insurance Status | Number of Patients |
|---|---|
| Insurance | 2099 |
| No Insurance | 90 |
| Unknown | 358 |

**Figure 1**. Demographic information for patient population. Total number of patients: n = 2517.

## RESULTS



**Figure 2**. Proportion of patients who scheduled DAs by race (top left), language (top right), ethnicity (bottom left), and insurance status (bottom right).

## RESULTS

**Table 1.** Chi-square test results for DAs scheduled by demographic categories.

| | VALUE | DF | ASYMPTOTIC SIGNIFICANCE (2-SIDED) |
|---|---|---|---|
| RACE | 41.123 | 6 | <.001 |
| ETHNICITY | 11.490 | 2 | .003 |
| LANGUAGE | 27.267 | 4 | <.001 |
| INSURANCE STATUS | 30.472 | 2 | <.001 |

**POST HOC RESULTS**

| | |
|---|---|
| RACE | • White patients more likely to attend a DA.<br>• Black patients less likely to attend a DA. |
| ETHNICITY | • Non-Hispanic patients more likely to attend a DA.<br>• Hispanic patients less likely to attend a DA.<br>• No difference noted with the Unknown category. |
| LANGUAGE | • Patients who speak English more likely to attend DAs.<br>• Patients who speak Spanish less likely to attend DAs.<br>• No difference noted for other language groups, but could be due to small sample size and Type II error. |
| INSURANCE STATUS | • Patients with insurance more likely to attend a DA.<br>• Patients with an unknown insurance status more likely.<br>• No disparity for those without insurance, which could also be due to Type II error from a small sample size. |

## DISCUSSION

- We suspect that the disparities in DA scheduling between demographic groups could be due to social determinants of health (i.e. access to care and language barriers).
- Other reasons include that the patients may prefer more culturally relevant therapies or individual therapy sessions.
- Patients without insurance at time of call could have received help gaining insurance or were able to pay out of pocket.

**Future Considerations**

- Study is ongoing; currently investigating how demographics impact the number of referrals people receive.

## ACKNOWLEDGEMENTS


- The Redleaf Center Research Team would like to thank the Redleaf Family Foundation and other donors for their support.
- I would like to thank Dr. Gretchen Buchanan and Biftu Abdullahi for their mentorship and support throughout the summer.


ROSALIND FRANKLIN UNIVERSITY of MEDICINE AND SCIENCE

Title: Impact of Climate Change on Pediatric Frostbite and Cold-Weather Injuries: Insights from Local and National Databases for Targeted Interventions

Lexy M Kindt, MD; Charly Vang, MPH; Emily Colonna, MS; Rediat Tilahun, MS; Kyle Schmitz, MD; Derek C Lumbard, MD; Rachel M Nygaard, PhD;

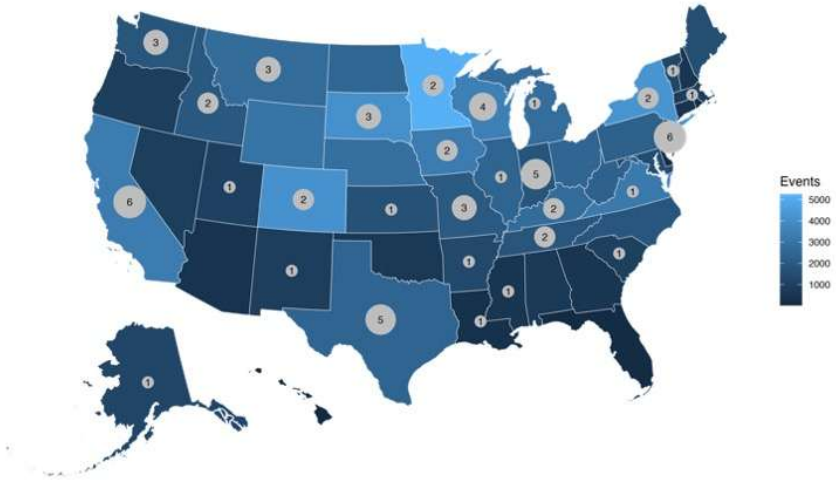
Background: Extreme weather events are increasing in regions unaccustomed to freezing temperatures, placing more children at risk for frostbite and cold-related injuries, which can lead to significant morbidity and mortality. Many medical centers lack established frostbite management protocols, where early identification and treatment are essential. This study reviews pediatric cold-weather injuries across multiple databases to delineate the extent and management of these injuries and identify geographic areas where targeted intervention programs could be most impactful. We hypothesize that the utilization of multiple databases will allow us to identify specific geographic areas where targeted cold-weather intervention programs could be most impactful.

Methods: A retrospective study of data from the National Oceanic and Atmospheric Administration Storm Event Database (NOAA) (2016-23), the National Readmission Database (NRD) (2016-20), and a hospital burn registry (2017-22). Pediatric patients (age <18) diagnosed with frostbite or cold-related injuries were included. We analyzed the frequency of events, demographics, treatment, outcomes, and readmission rates.

Results: We identified 11 pediatric frostbite admissions at our institution between the ages of 3 to 17 (64% >11 years). Treatment modalities included rapid rewarming, thrombolytics, and perfusion imaging, with no resulting amputations. We used the NRD to evaluate pediatric injuries nationally since standard management for severe frostbite injury includes an approximately one month delayed-planned readmission to promote preservation of digit length in cases amputation is required. We identified 73 pediatric frostbite admissions with 15 classified as severe frostbite and 8 were treated with thrombolytic therapy. There were 10 readmissions, 4 amputations, and 5 were treated for cellulitis. Not all cold-related injuries, especially fatalities, result in hospital treatment, so we used the NOAA database to identify cold-weather event associated fatalities. We found 65 pediatric fatalities out of a total of 1122 total cold-related fatal events (Fig 1). Pediatric mortality did not coincide with highest or lowest cold-weather events.

Conclusions: This is the first study to integrate multiple national databases to track pediatric cold-weather injuries and fatalities. This comprehensive understanding of regional risks identifies states where potential educational interventions could prevent pediatric cold-weather injury and fatality. Limitations to current public health data tracking underscores the necessity of integrating multiple data sources to comprehensively understand the impact of cold-weather injuries in the U.S.

Practice: Tailored intervention programs coupled with cold-weather management protocols implemented at emergency medical centers across the United States can safeguard children against the adverse effects of cold weather.




# Impact of Climate Change on Pediatric Frostbite and Cold-Weather Injuries:

## Insights from Local and National Databases for Targeted Interventions

Emily Colonna, MS; Charly Vang, MPH; Lexy M Kindt, MD; Rediat Tilahun, MS; Kyle Schmitz, MD; Derek C Lumbard, MD; Rachel M Nygaard, PhD

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Hennepin Healthcare

Our findings highlight expanded risk for cold-related trauma in the U.S. Educational interventions could help prevent pediatric cold-related morbidity and mortality. Limitations of public health data emphasize the need for integrating diverse data sources to better understand the full impact of cold-weather injuries in the U.S.

**Significance:** Extreme weather events are becoming more common in regions that typically don't experience freezing temperatures, putting children at greater risk for frostbite and cold-related injuries, which can cause significant harm. This study examines pediatric cold-weather injuries across several databases to assess their frequency, management strategies, and identify areas where targeted intervention programs could have the greatest impact.

**Methods:** We focused on pediatric patients (<18 years) diagnosed with frostbite or cold-related injuries. Our analysis includes the frequency of events, patient demographics, treatment approaches, outcomes, and readmission rates.

Data Sources:

- National Oceanic and Atmospheric Administration (NOAA) Storm Event Database (2016-2023) – Cold-weather fatalities
- National Readmission Database (NRD) (2016-2020) – National frostbite cases and readmissions
- Hospital Burn Registry (2017-2022) – Localized patient outcomes

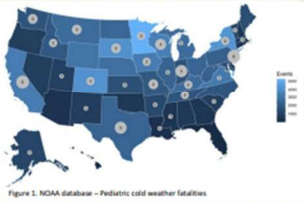

Figure 1. NOAA database – Pediatric cold weather fatalities

**Results:** Not all cold-related injuries, especially fatalities, result in hospital treatment, so we used the NOAA database to identify cold-weather event associated fatalities. We found 65 pediatric fatalities out of a total of 1,122 cold-related fatal events **(Figure 1).**

**National Readmission Database: (Figure 2 and 3).**

- 73 pediatric frostbite cases identified, with 15 severe cases.
- Treatments Included:
  - 8 received thrombolytics
  - 10 readmissions
  - 4 amputations
  - 5 treated for cellulitis
- Outcomes:
  - Time to amputation: 4 – 7 days
  - Hospital length of stay: 15.8 days

**Institutional Data:**

- 11 cases (ages 3-17)
- 64% >11 years
- Treatments included:
  - rapid rewarming
  - thrombolytics
  - perfusion imaging
- Outcomes:
  - No amputations

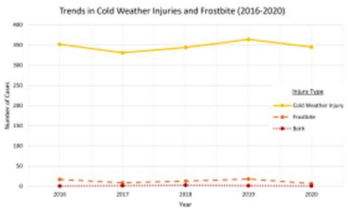


Figure 2. NRD cold weather injuries by year

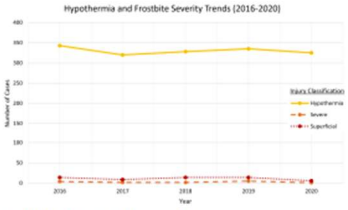


Figure 3. NRD frostbite severity and hypothermia by year

**Take Aways:**

- First study integrating multiple databases for pediatric frostbite tracking.
- Highlights gaps in public health data tracking for cold-weather injuries.
- Hospitals should implement frostbite treatment protocols.
- Education on cold exposure risks must be expanded, especially in unexpected regions.

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**Abstract:**

This study examines geospatial and socioeconomic shifts in assault-related firearm injuries in Minneapolis before and after the COVID-19 pandemic and the murder of George Floyd. Using Level 1 trauma registry data (2018-2023), we analyzed 1,121 cases to assess changes demographic and injury patterns. Spatial autocorrelation and Kernel Density Estimation revealed increased clustering of injuries in socioeconomically deprived neighborhoods, measured by the Index of Concentration at the Extremes (ICE). While demographic patterns remained similar, shifts in injury severity and hospitalization were observed. These findings provide insight into how major societal events reshape violence patterns in already vulnerable communities and underscore the critical role of hospital-based violence intervention programs (HVIPs) in disrupting cycles of violence by helping address systemic inequities exacerbated by these events.

**4-6 Indexing Keywords:**

- Community violence
- Health disparities
- Firearm violence
- Spatial epidemiology
- Violence prevention
- Hospital-based violence intervention

# Identify the Areas and Populations Most Impacted by the Increase in Firearm Injuries in Minneapolis Following the COVID-19 Pandemic and the Murder of George Floyd

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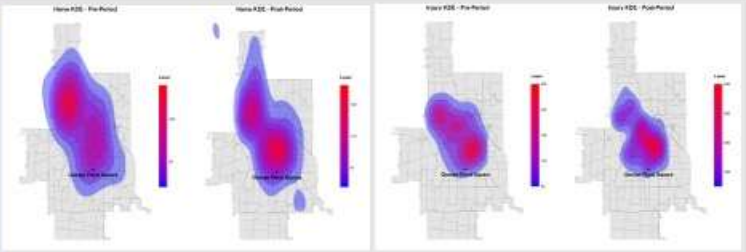
**Purpose:** Firearm injuries surged by 34% nationwide in the year following the COVID-19 pandemic and the murder of George Floyd, with Minneapolis being one of many cities experiencing a significant increase in violence. This study examines the geospatial and socioeconomic patterns of firearm injuries in Minneapolis during the pre-period (January 2018–March 2020) and post-period (May 2020–December 2023), identifying the most impacted areas and populations to inform targeted public health interventions and violence prevention strategies.

**Methods:** A total of 1,121 assault-related firearm injury cases from January 2018 to December 2023 were identified in a Level 1 trauma center's trauma registry. Cases with confirmed assault intent and valid geolocation data for both home and injury sites were included (606 cases). Descriptive statistics summarized patient characteristics, while spatial analyses utilized Moran's I and Kernel Density Estimation (KDE) to identify and visualize changes in the spatial clustering of injury and home locations between the Pre-Event and Post-Event periods. These methods provided insights into temporal and geospatial shifts in firearm violence patterns.



**Results:** Injury locations demonstrated increased clustering within socioeconomically deprived census tracts during the post-period, with a 32% increase in clustering (Moran's I: 0.5674 pre-period to 0.7473 post-period).

**Conclusions:** This study identifies neighborhoods at greater risk of firearm injuries, with geospatial shifts toward more socioeconomically deprived areas. These findings highlight the potential of place-based programs, such as hospital-based violence intervention programs (HVIPs), to address secondary violence prevention and mitigate the broader impact on disadvantaged neighborhoods following significant events.

**Acknowledgements:** This research was supported by the Agency for Healthcare Research and Quality (AHRQ) and Patient-Centered Outcomes Research Institute (PCORI) grant P30HS029744. Additional support for the Minnesota Learning Health System Mentored Career Development Program (MN-LHS) is offered by the University of Minnesota Center for Learning Health System Sciences, Office of Academic Clinical Affairs, and Clinical Translational Science Institute (grant UL1TR002494). The content is solely the responsibility of the authors and does not necessarily represent the official views of AHRQ, PCORI, or MN-LHS

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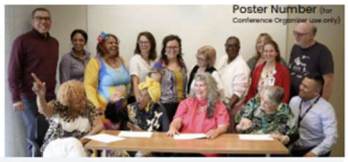
**Title:** Heart health, wellness, and homelessness: Early open trial results of CV-HOMES

**Authors:** KD Vickery, AR Hyson, AM Busch, and the Quorum for Community-Driven Wellness Research

**Abstract:** People who have experienced homelessness (PEH) die decades sooner than their housed peers. Heart disease is the leading cause of chronic disease death among this population. PEH in MN have 3x higher death due to heart disease than the general MN population. We conducted design and feasibility research to create the Cardiovascular risk homeless support (CV-HOMES) program. CV-HOMES offers behavioral activation based wellness coaching to improve multiple health behaviors for PEH. We report on results from an early phase open trial with N=7 participants. We found CV-HOMES to be highly acceptable but found site-specific recruitment challenges which limited feasibility. The Lifes Essential 8 cardiovascular health score (0-100) was feasible but had notable challenges including the length of time it took to collect and the interpretability of the nutrition instrument in our population. We plan for a larger pilot randomized trial with a revised recruitment strategy to continue to develop CV-HOMES.

# Heart health, wellness, and homelessness: Early open trial results of CV-HOMES

KD Vickery, AR Hyson, AM Busch
and the Quorum for Community-Driven Wellness Research



Poster Number (for Conference Organizer use only)

## Setting

This project is a partnership between Hennepin Healthcare Research Institute, the Quorum team, and a local housing provider, Catholic Charities of St. Paul and Minneapolis.

## Background, Unmet Need

People who have experienced homelessness (PEH) die decades sooner than their housed peers. Heart disease is the leading cause of chronic disease death among this population. PEH in MN have 3x higher death due to heart disease than the general MN population.

## Aims of the Project

**Aim 1.** Adapt our team's previous behavioral activation based heath coaching models (D-HOMES, NCT05258630 and BA-HD, NCT04158219) to address CV risk reduction among people who have experienced homelessness (CV-HOMES).

**Aim 2.** Assess the feasibility & acceptability of CV-HOMES for people who have experienced homelessness in a single arm treatment development trial (n=8). *Focus of this poster.*

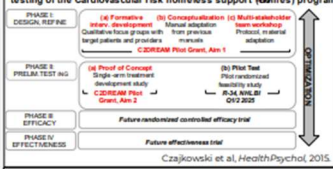
## Study Population

Inclusion criteria:

- Adults (age 18+) with past homelessness, now in supportive housing at single Minneapolis facility
- Qualifying need + interest to work on health behavior change
- Prior diagnosis of:
  - Hypertension, and/or
  - High cholesterol, and/or
  - Prediabetes, type 2 diabetes, and/or
  - Any form of heart disease

## Tx. Development Framework

**Fig. ORBIT -Model representation of the intervention development and testing of the Cardiovascular risk homeless support (CVHmes) program**




Czajkowski et al, *HealthPsychol*, 2015.

## Community Engagement

This work is led by the Quorum community-engaged research team. Members include researchers, housing staff, and people impacted by chronic disease and housing instability. The team has met monthly since 2015 to guide research. They focuses on the "pile up" of chronic conditions especially the overlap of physical and behavioral health, and the "run around" systems often put onto people. This project deepens our partnership with local housing provider Catholic Charities.

Quorum FOR COMMUNITY-DRIVEN WELLNESS RESEARCH

## Study Design

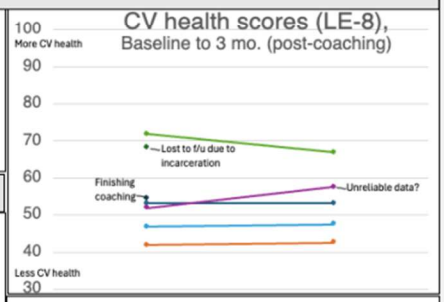
| Coach visits | Visit 1 | Visit 2 | Visit 3-10 |
|---|---|---|---|
| | Baseline | | 3 mo. |

CVHOMES Cardiovascular Health Homeless Support

- 1:1 coaching
- In-person or phone
- Behavioral activation:
  - Self-monitoring
  - Values-assessment
  - SMART goals re: wellness, health behavior (1 or 2)

## Results

- High Acceptability: 31 of 32 (CSQ-8 by 4 of 5 participants); positive feedback in post-coaching interviews
- Eventual primary trial outcome of **Life's Essential 8 Cardiovascular health score** (Lloyd-Jones et al., *Circ*, 2022) was feasible. Challenges:
  - Length of time needed
  - Participant interpretation of nutrition and other instruments
  - Alignment of incremental behavior change with scoring algorithms




## Conclusions

- Low feasibility with recruitment at a single site:
  - Safety concerns: Location change
  - Competing priorities, E.g.) domestic violence, Incarceration, custody
- High acceptability and desire for wellness coaching.
- Next steps: Funding for pilot randomized control trial with broader recruitment strategy

Funding Support: NIH/NIMHD P50MD017342

Contact: Katherine.Vickery@hcmed.org, www.hhcjlab.org

Common and unique patterns of gene expression and chromatin accessibility in the rat medial prefrontal cortex across different phases of opioid use disorder.

Shirelle X. Liu[1,2], Peter Muelken[4], Zia L. Maxim[1], Aarthi Ramakrishnan[5], Molly S. Estill[5], Mark G. LeSage[1,3,4], John R. Smethells[3,4], Li Shen[5], Phu V. Tran[2], Andrew C. Harris[1,3,4], and Jonathan C. Gewirtz[1,6]

[1]Department of Psychology, [2]Pediatrics, and [3]Medicine, University of Minnesota; [4]Hennepin Healthcare Research Institute; [5]Icahn School of Medicine at Mount Sinai; [6]Arizona State University

(241/250 words) Opioid use disorder (OUD) is associated with altered patterns of gene expression and their regulation. Little is known, however, about how these changes occur along the trajectory from initial drug exposure to OUD. We investigated genome-wide transcription (RNA-seq) and chromatin accessibility (ATAC-seq) in the medial prefrontal cortex of male and female rats in three paradigms modeling the initial response to passive, repeated morphine exposure (Withdrawal-Induced Anhedonia (WIA)), persistent use (Demand), and relapse (Reinstatement). Weighted Gene Co-Expression Network Analysis revealed decreased connectivity in a myelination/oligodendrocyte gene network module in morphine-exposed WIA rats and in an inflammation module in morphine-self-administering Demand rats. Follow-up Ingenuity Pathway Analysis indicated sex-specific alterations in activity in canonical pathways and upstream regulators consistent with these functions. We next conducted a Variance Partitioning Analysis to identify transcriptional signatures associated with OUD resilience or vulnerability across all three paradigms. We found that variation in gene expression attributable to OUD vulnerability was associated with epigenetic regulation across the three paradigms. HOMER motif analysis of ATAC-seq data revealed changes in accessibility to a small set of transcription factor (TF) binding sites, some that were shared by the 3 paradigms and others that were unique to each. In conclusion, we have identified changes in gene networks, upstream regulators, biological pathways, and TF binding motifs that are either phase-specific or span all three phases along the OUD trajectory. We have also identified a set of changes that covary with individual differences in OUD vulnerability.

This work was supported by NIH/NIDA grant U01 DA051993 (Gewirtz and Harris, MPI), University of Minnesota Doctoral Dissertation Fellowship (Liu), and the Hennepin Healthcare Research Institute Career Development Award (Harris, LeSage, and Smethells, PI).

# Common and unique patterns of gene expression and chromatin accessibility in the rat medial prefrontal cortex across different phases of opioid use disorder

Shirelle X. Liu[1,2], Peter Muelken[4], Zia L. Maxim[1], Aarthi Ramakrishnan[5], Molly S. Estill[5], Mark G. LeSage[1,3,4], John R. Smethells[3,4], Li Shen[5], Phu V. Tran[2], Andrew C. Harris[1,3,4], and Jonathan C. Gewirtz[1,6]

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## Background

We aim to identify transcriptional and epigenetic mechanisms underlying individual differences in vulnerability across several stages of opioid use disorder (OUD). OUD vulnerability was modeled in three paradigms modeling the initial response to passive, repeated morphine exposure (Withdrawal-Induced Anhedonia (WIA) measured using intracranial self-stimulation (ICSS)), persistent use (Demand in an i.v. morphine self-administration (MSA) model), and relapse (Reinstatement of extinguished MSA).

We are currently determining differences in the medial prefrontal cortex (mPFC) transcriptomes (via RNA-seq) and epigenomes (via ATAC-seq) in "Resilient (Res)" and "Vulnerable (Vul)" rats in each of our three behavioral models.

## Methods

**WIA:** Indexed as the increase in ICSS thresholds (% baseline) measured 24 hrs after each of repeated daily injections of 5.6 mg/kg morphine HCl (i.e., during spontaneous withdrawal, Fig 1A).

**Demand:** Rats first acquired i.v. MSA (0 or 0.4 mg/kg/inf) under a FR 3 schedule until acquisition criteria were met (≥ 5 infusions / session, ≤ 20% variability, and > 2:1 active: inactive lever ratio across 3 sessions). The response requirement per infusion was then incrementally increased each day (FR 1-FR 96; Fig 1B). Demand was indexed using α, which measures the degree to which MSA was maintained as a function of changes in unit price (FR / unit dose). Lower α values indicate greater reinforcement efficacy (Fig 1C).

**Reinstatement:** After acquisition of MSA (0 or 0.4 mg/kg/inf) under an FR 1 schedule, saline extinction in the absence of the drug-associated cue light was tested for at least 21 sessions and until extinction criteria (≥75% reduction in active lever pressing and no trend for 3 consecutive sessions) were met. Reinstatement was indexed as the increase in active lever responses upon re-exposure to a priming injection morphine (1.0 mg/kg) and the cue light (Fig 1D).

**RNA/ATAC-seq:** Performed using Illumina NovaSeq at a depth of ~100 million reads per sample.

**Data analysis:**

- Ingenuity Pathway Analysis (IPA) of RNA-seq data (Figs 2, 4, and 6): Morphine-treated rats were first assigned to "Resilient (Res)" (High WIA, High α, or Low reinstatement) or "Vulnerable (Vul)" (Low WIA, Low α, or High reinstatement) groups based on a median split of the behavioral scores. RNA-seq data were analyzed using standard pipelines and quality control analyses. Res and Vul groups were compared to saline-treated animals to generate lists of differentially expressed genes (DEGs) using DESeq2 R.
- Weighted Gene Co-expression Network Analysis (WGCNA, Figs 3 and 5) of RNA-seq data: Gene co-expression network and modules were constructed with all morphine animals. Changes in module connectivity were calculated between all morphine vs. saline animals. Gene Ontology (GO) Enrichment Analysis was employed to define biological process and cellular component associated with each module.
- ATAC-seq data (Table 1): diffReps was utilized to find differential sites between comparison groups. HOMER was utilized to identify motifs of transcription factors (TFs) among differential sites.

## Conclusions

- "Resilient" (High WIA, High elasticity, or Low reinstatement) rats exhibit greater changes in canonical pathways in comparison to "Vulnerable" rats (Fig 2).
- WGCNA analysis implicates inhibition of a gene network mediating oligodendrogenesis and myelination in WIA (Fig 3), and a gene network mediating immune response in Demand (Fig 5).
- While male and female rats show the same overall regulatory differences between Res/Sal and Vul/Sal comparisons, detailed processes show sex-specific effects (e.g., Fig 6).
- HOMER analysis of ATAC-seq data reveals that AP1 family are specifically associated with the pharmacological effects of morphine (i.e., morphine versus saline), while MEF2 and bHLH families are also associated with vulnerability (i.e., Res vs. Vul). Nuclear Receptor (NR) family binding motifs are enriched only in Reinstatement (Table 1).

**This work is supported by NIH/NIDA grant U01 DA051993 (Gewirtz/Harris, co-PIs), and University of Minnesota Doctoral Dissertation Fellowship (Liu).**

## Results

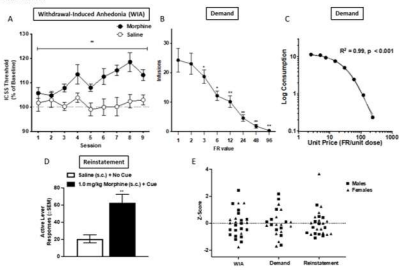


Fig 1: (A) ICSS thresholds (% Baseline, Mean ± SEM) during spontaneous morphine withdrawal). ** Different from Saline (main effect), p < 0.01. (B) Infusions at each FR (Mean ± SEM) during Demand testing. *,** Different from FR 1, p < 0.05 or 0.01. (C) Exponential demand function for morphine during Demand testing. (D) Active lever presses (Mean ± SEM) during Sal + No Cue or Mor + Cue conditions following extinction of MSA. ** Different from Sal + No Cue, p < 0.01. Data are collapsed across sex in Figs 1A – 1D because there were no significant effects of sex in any behavioral model. n = 10-16/sex/morphine group; n = 5-8/sex/saline group. (E) Z-score distribution for individual morphine rats shown in panels (A)-(D).

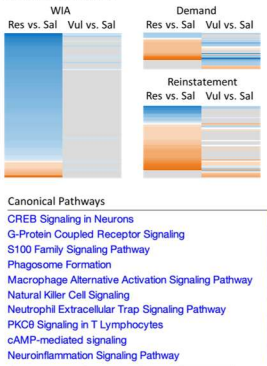


Fig 2: IPA canonical pathway analysis of DEGs in males. Top panel, heatmaps of all analyzable pathways, with detectable pattern in at least one comparison. Bottom panel, top 10 canonical pathways ranked by z-score. Orange, positive z-score; Blue, negative z-score; White, z-score = 0; Grey, pattern not detected; Square with a dot, absolute z-score < 1.

A

| Module | # of Genes | MeDC | p-value |
|---|---|---|---|
| "darkturquoise" | 160 | -7.41 | <2.20E-16 |
| "plum1" | 86 | -1.40 | <2.20E-16 |
| "purple" | 531 | 0.43 | <2.20E-16 |
| "saddlebrown" | 125 | -0.38 | 0.02 |
| "steelblue" | 124 | -2.85 | 0.02 |

B

| Gene Ontology Term | # of Genes | Fold Enrichment | q-value |
|---|---|---|---|
| **Biological process** | | | |
| CNS myelination | 7 | 39.47 | 5.98E-06 |
| Oligodendrocyte development | 9 | 24.53 | 2.84E-06 |
| Oligodendrocyte differentiation | 11 | 15.64 | 4.89E-06 |
| Axon ensheathment | 11 | 14.16 | 3.26E-06 |
| Gliogenesis | 12 | 5.96 | 1.90E-03 |
| **Cellular component** | | | |
| Myelin sheath | 11 | 26.45 | 3.40E-09 |

Fig 3: Analysis of connectivity changes in WGCNA module between Mor and Sal group in WIA. (A) Among 41 total modules built with morphine animals, 5 exhibited significant changes in connectivity relative to saline controls (p < 0.05). (B) Genes in module "saddlebrown" were mapped to myelination/oligodendrocytes.

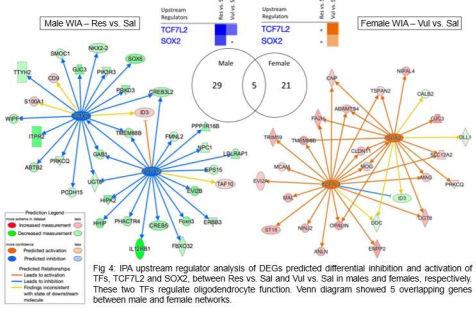


Fig 4: IPA upstream regulator analysis of DEGs predicted differential inhibition and activation of TFs, TCF7L2 and SOX2, between Res vs. Sal and Vul vs. Sal in males and females, respectively. These two TFs regulate oligodendrocyte function. Venn diagram showed 5 overlapping genes between male and female networks.

A

| Module | # of Genes | MeDC | p-value |
|---|---|---|---|
| "blue" | 4218 | -0.04 | 0.02 |
| "lightcyan" | 349 | -0.41 | <2.20E-16 |
| "magenta" | 987 | -0.14 | 0.04 |
| "darkorange" | 162 | -0.59 | <2.20E-16 |
| "skyblue" | 154 | -4.56 | <2.20E-16 |
| "white" | 158 | -3.81 | <2.20E-16 |

B

| Gene Ontology Term | # of Genes | Fold Enrichment | q-value |
|---|---|---|---|
| **Biological process** | | | |
| Immunoglobulin mediated immune response | 9 | 9.86 | 7.98E-03 |
| B cell mediated immunity | 9 | 9.48 | 5.45E-03 |
| Lymphocyte mediated immunity | 9 | 7.11 | 2.63E-02 |
| Leukocyte mediated immunity | 10 | 6.38 | 2.67E-02 |

Fig 5: Analysis of connectivity changes in WGCNA module between Mor and Sal group in Demand. (A) Among 37 total modules built with morphine animals, 6 exhibited significant changes in connectivity relative to saline controls (p < 0.05). (B) Genes in module "white" were mapped to immune response/neuroinflammation.

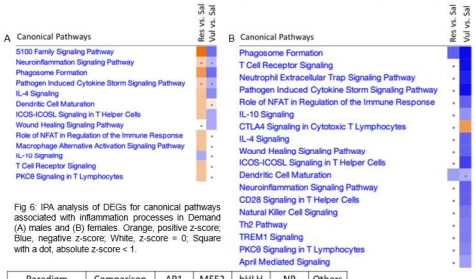


Fig 6: IPA analysis of DEGs for canonical pathways associated with inflammation processes in Demand (A) males and (B) females. Orange, positive z-score; Blue, negative z-score; White, z-score = 0; Square with a dot, absolute z-score < 1.

| Paradigm | Comparison | AP1 | MEF2 | bHLH | NR | Others |
|---|---|---|---|---|---|---|
| WIA | Res vs. Vul | 0 | 0 | 0 | 0 | 0 |
| | Res vs. Sal | 8 | 2 | 0 | 0 | 0 |
| | Vul vs. Sal | 10 | 0 | 0 | 0 | 0 |
| Demand | Res vs. Vul | 0 | 3 | 7 | 0 | 0 |
| | Res vs. Sal | 7 | 2 | 1 | 0 | 0 |
| | Vul vs. Sal | 7 | 2 | 1 | 0 | 0 |
| Reinstatement | Res vs. Vul | 0 | 4 | 1 | 0 | 5 |
| | Res vs. Sal | 7 | 0 | 0 | 3 | 0 |
| | Vul vs. Sal | 0 | 0 | 0 | 4 | 4 |

Table 1: HOMER motif analysis for male Res vs. Vul, Res vs. Sal, and Vul vs. Sal ATAC-seq data. Families of the top 10 significantly enriched motifs and numbers of motifs in each family were shown.

**Title: Centering Community Voices: A Delphi Study on Defining Success in Hospital-Based Violence Intervention Programs**


**Abstract:**

Hospital-based violence intervention programs (HVIPs) have become essential strategies for disrupting cycles of violence and promoting recovery. However, success is often defined by institutional metrics rather than by the communities these programs aim to serve. This study used a modified Delphi method to elevate the voices of a multidisciplinary Community Advisory Board (CAB) composed of survivors, clinicians, community advocates, and frontline practitioners. Over three iterative phases—an open-ended survey (n=12), focus group (n=10), and final ranking activity (n=8)—CAB members identified and prioritized success indicators for HVIP participants. Thematic analysis revealed nine key domains, including mental health and well-being, violence prevention, safety and stability, and engagement. Mental health and violence prevention were consistently ranked as foundational to healing and transformation. Findings underscore the need for trauma-informed, culturally responsive care, peer mentorship, and long-term support systems. This community-informed framework challenges traditional evaluation models and provides actionable guidance for more equitable, context-driven HVIP practice and policy.


## Centering Community Voices: A Delphi Study on Defining Success in Hospital-Based Violence Intervention Programs


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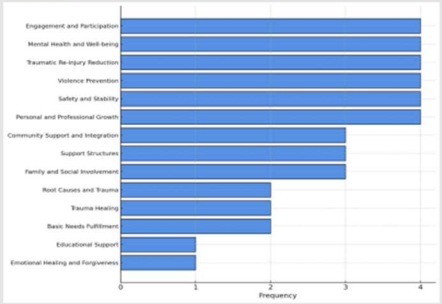
Department of Surgery, Hennepin Healthcare, Minneapolis, MN

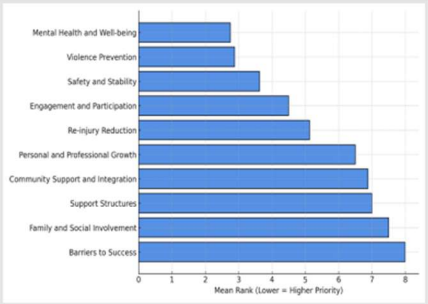

Hennepin Healthcare

**Background:**

- Hospital-based violence intervention programs (HVIPs) aim to reduce re-injury, retaliatory violence and promote recovery.
- However, success metrics are inconsistently defined and often driven by institutional goals, not community input.
- This study uses a modified Delphi approach to co-define meaningful HVIP success measures from the perspective of survivors, frontline providers, and community experts.

**Objective:** To establish a community-developed framework for evaluating HVIP success using consensus from a Community Advisory Board (CAB).




**Key Quotes**

"You can't do any of this without mental health. That's where it starts—and that's where it breaks down if you ignore it."

"The hospital is where we can break the cycle. They're hurt. They're scared. That's when we need to be there."

**Methods:**

**Design:** 3-phase modified Delphi

**Participants:** 12 CAB members with lived or professional violence-related experience

**Phases:**

- Phase 1: REDCap survey with open-ended success indicators (n=12)
- Phase 2: Focus group discussion and theme refinement (n=10)
- Phase 3: Ranking of success themes (n=8)

**Analysis:** Manual thematic analysis with CAB feedback at each stage

**Conclusions:**

. Centers survivor and frontline voices in defining programmatic success.

. Calls for culturally responsive, trauma-informed, and relational evaluation models.

. Offers a field-informed alternative to justice- and cost-centered metrics.

. Can inform national HVIP funding priorities and program design.

A community-led Delphi process revealed that success in HVIPs extends beyond re-injury to include healing, safety, engagement, and equity. This approach underscores the need for survivor-defined, trauma-informed metrics in public health and hospital-based interventions.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Department of Surgery Hennepin Healthcare @HennepinTrauma

**Effects of prenatal electronic nicotine delivery system (ENDS) aerosol exposure on impulsive behavior in rats**

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Minneapolis, MN

Use of electronic nicotine delivery systems (ENDS) in pregnant women is increasing. Cigarette smoking during pregnancy has well-established long-term developmental consequences in offspring, including increased risk of tobacco use disorder and impulsivity-related disorders such as attention deficit hyperactivity disorder (ADHD). These adverse effects are generally attributed to nicotine, but other toxicants in tobacco smoke may also play a role. Although ENDS contain lower levels of many of those toxicants, they can deliver as much or more nicotine as combustible cigarettes and contain chemicals that are relatively low or absent in cigarette smoke (e.g., propylene glycol). ENDS use during pregnancy may therefore pose many of the same risks as smoking, or could present unique risks. Although some animal studies of prenatal ENDS exposure have demonstrated adverse behavioral effects in offspring, none have studied impulsive behavior, a key facet of ADHD. The purpose of the present study was to establish a clinically relevant model of prenatal ENDS exposure and examine its effects on impulsivity in early adult offspring. Pregnant female rats were exposed to room air (N=4) or ENDS aerosol (N=4) from gestational day 1 to birth. Daily ENDS exposures were 100 3-sec (75 ml) puffs from an ENDS containing commercial e-liquid (18 mg/ml nicotine) delivered over 5 hr. Beginning on postnatal day 55, premature responding (impulsive action) was examined in offspring (2/sex/litter) under a differential-reinforcement-of-low-rate (DRL) schedule of food delivery over a range of DRL intervals (5-20 sec). Effects of s.c. nicotine (0 - 0.4 mg/kg) were then evaluated under DRL 20 sec. ENDS exposure produced clinically-relevant maternal serum nicotine levels (23±3.3 ng/ml) throughout pregnancy. Premature responding at stability did not differ between groups at any interval. However, female ENDS-exposed rats showed higher premature responding during initial transition to DRL 10 ($p<0.05$) but not 20 sec. Nicotine increased premature responding at a lower dose (0.1 mg/kg) in ENDS-exposed rats compared to controls ($p<0.05$). This study establishes a clinically-relevant model of maternal ENDS use during pregnancy and suggests that prenatal ENDS exposure can increase sensitivity to nicotine's impulsivity-related effects. These findings extend the current breadth of adverse effects of prenatal ENDS exposure in animal models and the potential risks of ENDS use during pregnancy in humans.

*Funding:* Funding for this study was provided by NIH/NIDA grants R01 DA048899 (LeSage, MPI) and a Hennepin Healthcare Research Institute Career Development Award (LeSage). These funding institutions had no role in the study design, data collection, data analysis, interpretation

of the data, manuscript preparation, or decision to submit the presentation. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or Food and Drug Administration.

# Effects of prenatal electronic nicotine delivery system (ENDS) aerosol exposure on impulsive behavior in rats

Mark G. LeSage[1,2], Sarah Wilde[1], and Andrew C. Harris[1,2]
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[2] Department of Medicine, University of Minnesota, Minneapolis, MN

## Background

An increasing number of women are using electronic nicotine delivery systems (ENDS) during pregnancy, with prevalence as high at 15% reported in some studies. (1, 2) Around 30% of pregnant women who use ENDs have never smoked cigarettes, suggesting significant ENDS use during pregnancy for reasons other than harm reduction. (3)

Cigarette smoking during pregnancy has well-established long-term developmental consequences in offspring, including increased risk of impulsivity-related disorders such as attention deficit hyperactivity disorder (ADHD). These adverse effects are generally attributable to nicotine, but other toxicants in tobacco smoke may also play a role. (4, 5)

Although ENDS contain lower levels of many of those toxicants, they can deliver as much or more nicotine as combustible cigarettes and contain chemicals that are relatively low or absent in cigarette smoke (e.g., propylene glycol). ENDS use during pregnancy may therefore pose many of the same risks as smoking, or could present unique risks.

Although some studies of prenatal ENDS exposure in animal models have demonstrated several adverse behavioral effects in offspring (e.g. short-term memory impairment (6)), none have studied impulsive behavior, a key facet of ADHD.

The purpose of the present pilot study was to establish a clinically relevant model of prenatal ENDS exposure and to examine its effects on locomotor activity and impulsivity in early adult offspring.

## Methods

**Apparatus:** A Buxco "E-cigarette, Vape, and Tobacco" (EVT) generator (Data Sciences International, St. Paul, MN) was used to generate and deliver ENDS aerosol. The system consisted of a computer-controlled aerosol generator (Figure 1) that puffs from a mod-type ENDS (Protank 3, MT32 coil, KangerTech) containing a commercial ENDS liquid (Fruity-Striped Gum, 18 mg/ml nicotine, Gothic Vapor). Aerosol was delivered to a clear acrylic mass-dosing chamber (Figure 2). The chamber consists of four compartments with perforated walls and multiple inlet ports that allow even distribution of aerosol to four rats simultaneously. A mass flow unit pumped ambient room air through an intake valve and tubing at a flow rate of 5 L per minute to provide an air stream into which the aerosol is mixed and delivered to the chamber. This flow rate was chosen so that aerosol clears from the chamber within 5 min after a bout, allowing rats to breathe relatively clean air between bouts as humans do. The chamber was in a fume hood, with aerosol evacuated into the hood via exhaust ports in the chamber compartments

**Puffing protocol:** Ten 75 ml puffs (3-sec each) with a 30-sec inter-puff interval every 30 min for a total of 10 inhalation bouts (100 puffs total) over 5 hrs. This puff volume is consistent with recommended puffing parameters for ENDS research (7).

**Procedure:** Female rats were mated in-house. After mating, they were placed in the dosing chamber and exposed daily to room air (N=4) or ENDS aerosol (N=4) according to the puffing protocol above from gestational day 1 to birth. An i.v. blood sample was taken 10 min after the exposure session each week to measure serum nicotine concentrations.

Beginning on postnatal day (PD) 50, offspring (N=4 per litter, 2 per sex) were placed in a locomotor activity chamber for 30-min per day for 5 consecutive days to measure locomotor activity. On postnatal day 55, rats were trained to lever press for food pellets under a fixed-ratio 1 schedule. Once trained, premature responding (impulsive action) was examined under a differential-reinforcement-of-low-rate (DRL) schedule of food delivery. Under this schedule, pressing the active lever produced a food pellet only after a specified delay had elapsed since the previous active lever press. Premature presses made on the active lever during the delay reset the delay timer and are considered a measure of impulsive action. The DRL interval was 5 sec until responding was stable, then 10 sec for 5 sessions and 20 sec until responding stabilized. Then, the effects of s.c. nicotine (0 - 0.4 mg/kg) injections 10 min prior to sessions were evaluated under the DRL 20 sec schedule.

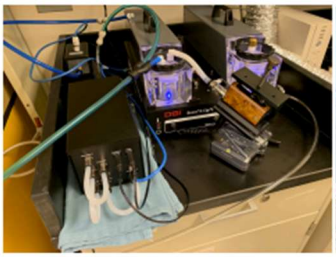

**Figure 1.** ENDS aerosol generator.

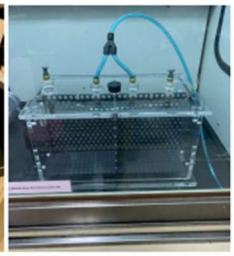

**Figure 2.** ENDS aerosol exposure chamber.

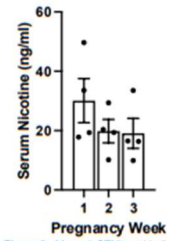


**Figure 3.** Mean (±SEM) and individual serum nicotine levels in during each week of pregnancy.

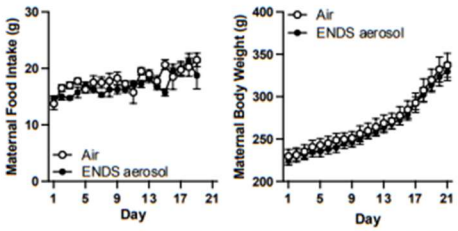


**Figure 4.** Mean (±SEM) food intake (left panel) and weight gain (right panel) in ENDS aerosol (solid circles) and air (open circles) exposed dams during pregnancy.

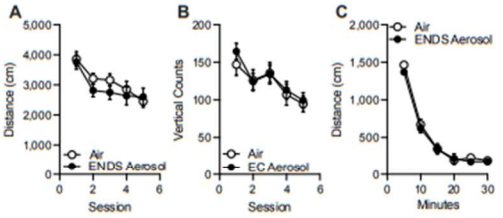


**Figure 5.** Mean (±SEM) total horizontal distance (A) and vertical counts (B) during each locomotor activity session in offspring prenatally exposed to air or ENDS aerosol. Mean (±SEM) total horizontal distance during consecutive 5 min intervals, averaged across all 5 sessions (C) in each prenatal exposure group.

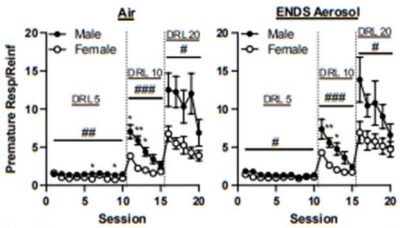


**Figure 6.** Mean (±SEM) premature responding as a proportion of the number of reinforcers earned during the first 10 sessions at DRL 5 sec and first 5 sessions at DRL 10 and 20 sec in male and female offspring prenatally exposed to air (left panel) or ENDS aerosol (right panel). Main effect of sex, #p < 0.05, ##p < 0.01, ###p < 0.001. Simple effect of sex, *p < 0.05, **p < 0.01.

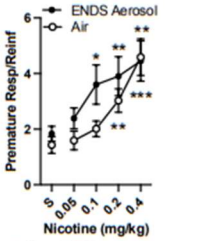


**Figure 7.** Mean (±SEM) premature responding after s.c. injection of saline (S) or nicotine in each prenatal exposure group. Different from saline (S), *p < 0.05, **p < 0.01, ***p < 0.01

## Results and Conclusions

ENDS exposure produced clinically-relevant maternal serum nicotine levels (10-50 ng/ml) throughout pregnancy (Figure 3). There were no significant changes in nicotine levels over time. There were no effects of prenatal ENDS aerosol exposure on maternal food intake or weight gain (Figure 4), and no effect on litter size or weight (data not shown).

There was no effect of prenatal ENDS aerosol exposure on overall or within-session measures of locomotor activity in offspring (Figure 5).

There were significant sex differences in premature responding (impulsivity) in both exposure groups (Figure 6). Males in both exposure groups showed higher premature responding compared to females during the initial sessions at each DRL interval (Figure 6). However, premature responding under the DRL 20 sec schedule did not differ between sexes at stability.

Offspring prenatally exposed to ENDS aerosol did not exhibit higher baseline (i.e., trait) impulsivity. Although the main nicotine effect ($p=0.15$) and interaction ($p=0.07$) only approached significance, nicotine increased premature responding under the DRL schedule at a lower dose (0.1 mg/kg) compared to saline in ENDS-exposed rats compared to controls (Figure 7). As such, prenatal ENDS exposure may increase offspring responsiveness to impulsivity-inducing variables (e.g. impulsive states), such as nicotine exposure.

This study establishes a clinically-relevant model of maternal ENDS use during pregnancy and suggests that prenatal ENDS exposure may increase sensitivity to nicotine-induced impulsivity. These findings extend the current breadth of adverse effects of prenatal ENDS exposure in animal models and the potential risks of ENDS use during pregnancy in humans. However, larger studies are need to confirm these findings.

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## Acknowledgements

Supported by Career Development Awards from Hennepin Healthcare Research Institute (LeSage, Harris). The authors thank Irina Stepanov and Aleksandra Alcheva for measurement of serum nicotine concentrations.

Society for Behavioral Medicine - Abstract for D-HOMES Spanish

**Title: Expanding the Diabetes Homelessness Medication Support program (D-HOMES) to Spanish-speaking Hispanic adults**

Oscar Oranday Perez[1], Katherine Diaz Vickery[1], Rose A. Hyson[1], Silvio Kavistan[1], Andrew M. Busch[1]

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**Abstract:**

**Significance:** Hispanic adults have significantly higher rates of diabetes with earlier, more severe complications and death than non-Hispanic whites. They also have higher rates of homelessness which exacerbates complications of diabetes. Furthermore, those who primarily speak Spanish have significantly lower medication adherence than English-speaking Hispanics.

**Objective:** Adapt the Diabetes Homeless Medication Support (D-HOMES) behavioral treatment manual using culturally appropriate guidance to enhance medication adherence of Spanish-speaking Hispanic adults living with type 2 diabetes.

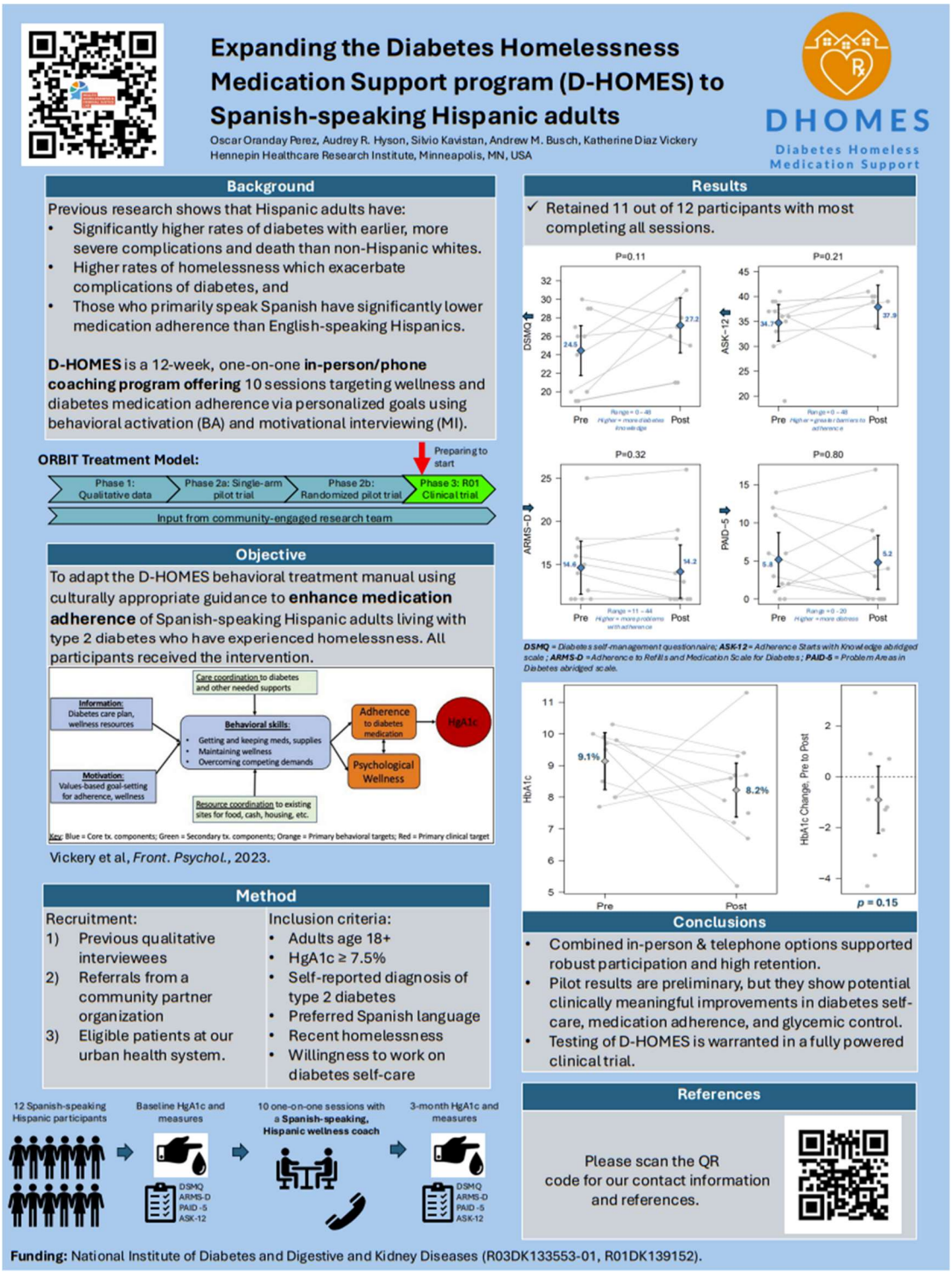
**Method:** Our open trial pilot study enrolled 12 Spanish-speaking participants from 1) interested participants from previous qualitative interviews, 2) referrals from a community partner organization, and 3) eligible patients at our urban health system. Inclusion criteria were self-reported diagnosis of type 2 diabetes, preferred Spanish language, recent homelessness, and willingness to work on diabetes self-care. They were offered 10 one-on-one sessions over 3 months (approximately weekly) delivered in-person or by phone from a Spanish-speaking, Hispanic diabetes wellness coach. The coach used motivational interviewing and behavioral activation to improve medication adherence, provide diabetes education, and support resource/care coordination. Assessments were done at baseline and 3 months by Spanish-speaking, Hispanic staff. Participants self-reported measures of mood, quality of life, problem areas in diabetes, medication adherence, homelessness plus physical measurements like HbA1c.

**Results:** We engaged and retained 11 participants, with most completing all sessions. Diabetes self-management and medication adherence improved from baseline to 3 months (DSMQ increased 2.7 points from 24.5 to 27.2, $p = 0.11$; ASK-12 improved 3.2 points from 34.7 to 37.9, $p = 0.21$; ARMS-D decreased -0.4 points from 14.6 to 14.2, $p = 0.32$; PAID-5 decreased -0.4 points from 5.2 to 4.8, $p = 0.80$). Glycemic control (Hb A1c) also improved changing -0.9%, from 9.1% at baseline to 8.2% at 3-months ($p = 0.15$).

**Conclusions:** Combined in-person & telehealth options supported robust participation and high retention. Early results indicate potentially important improvements in diabetes self-care, medication adherence, and glycemic control. The results combine with other treatment development work in English and Spanish to develop a feasible behavioral trial for fully powered testing in a larger clinical trial.

**Keywords:** Homelessness, Diabetes, Hispanics, Spanish-speaking Hispanics, medication adherence, behavioral activation, Health of Marginalized Populations.

**Funding:** National Institute of Diabetes and Digestive and Kidney Diseases (R03DK133553-01).



Characteristics of Frostbite Injury and Barriers to Thrombolytics Treatment at HCMC

Rediat Tilahun, MS; Charly Vang, MPH; Emily Colona, MS; Derek C Lumbard, MD FACS; Rachel M Nygaard, PhD.

Department of Surgery, Hennepin County Medical Center, Minneapolis, MN

**Purpose**: Timely administration of thrombolytics is important for reducing the risk of amputation following severe frostbite injury. The majority of frostbite patients (95%) will see improvements in limb salvage following treatment with thrombolytics. Understanding the contraindications of thrombolytics is essential for making informed treatment decisions and minimizing adverse effects. The use of thrombolytics is contraindicated in patients with conditions that increase the risk of bleeding, such as recent trauma, cerebrovascular accident (CVA), gastrointestinal bleeding, severe hypertension, or bleeding diathesis. This study examines patients admitted to HCMC between October 2024 and May 2025, focusing on contraindications noted at the time of admission.

**Methods**: A total of 218 patients were admitted due to cold-related injury, hypothermia, and frostbite. Data were collected on demographics, degree of frostbite, history of injury, freeze-thaw cycles, significant trauma, use of anticoagulants, recent surgery, bleeding, and blood pressure at the time of arrival to the emergency department. Additionally, patients with frostbite severity of grades 2, 3, and 4 were categorized and included for further analysis. Among those with severe frostbite and an arrival time under 12 hours, additional data were collected on the time of incident and time since rewarming.

**Results**: N = 207 patients did not meet the criteria to receive tPA at the time of admission to the ED due to “absolute or relative” contraindications. N = 11 patients received tPA. N = 4 patients left against medical advice (AMA) or refused care. N = 16 patients were further analyzed to identify additional tPA contraindications that were not captured by the “absolute or relative” criteria. Among these, N = 4 had good perfusion on SPY imaging despite presenting with severe frostbite at the time of admission. N = 7 patients were unable to provide a history, or their injuries occurred under unknown circumstances. N = 1 patient was on ECMO, which contraindicates tPA use.

**Conclusion**: Most patients did not receive thrombolytics due to “relative contraindications”, not associated with risk of adverse events following thrombolytics, such as arrival time > 12 hours or unclear freeze-thaw cycles. Understanding the demographics of patients with severe frostbite who do not receive thrombolytics and addressing the barriers to timely treatment can help improve outcomes following frostbite injury.

Additional education is needed to support providers in weighing the low risk of thrombolytic-related complications (<5%) against the substantial benefits of limb salvage. Notably, the treatment window at HCMC is significantly shorter than at other high-volume frostbite centers, yet even patients treated beyond 12 hours post-injury have achieved 100% limb salvage in some cases.

# Characteristics of Frostbite Injury and Barriers to Thrombolytics Treatment at HCMC

Rediat Tilahun, MS; Charly Vang, MPH; Emily Colona, MS; Derek C Lumbard, MD FACS; Rachel M Nygaard, PhD.
Department of Surgery, Hennepin County Medical Center, Minneapolis, MN

**Purpose:** Timely administration of thrombolytics is important for reducing the risk of amputation following severe frostbite injury.[1,2] The majority of frostbite patients (95%) will see improvements in limb salvage following treatment with thrombolytics.[3]

Understanding the contraindications of thrombolytics is essential for making informed treatment decisions and minimizing adverse effects. The use of thrombolytics is contraindicated in patients with conditions that increase the risk of bleeding, such as recent trauma, cerebrovascular accident (CVA), gastrointestinal bleeding, severe hypertension, or bleeding diathesis.

**Methods:** A total of 218 patients were admitted due to cold-related injury, hypothermia, and frostbite between October 2024 and March 2025. Data were collected on demographics, degree of frostbite, history of injury, freeze-thaw cycles, significant trauma, use of anticoagulants, recent surgery, bleeding, and blood pressure at the time of arrival to the emergency department. Additionally, patients with frostbite severity of grades 2, 3, and 4 were categorized and included for further analysis. Among those with severe frostbite and an arrival time under 12 hours, additional data were collected on the time of incident and time since rewarming.

**N = 207** patients did not receive thrombolytics at the time of admission
**N = 11** patients received thrombolytics
**N = 4** patients left AMA or refused care
**N = 4** patients had good perfusion on imaging assessments after rapid rewarming

**Table 1. Injury Characteristics**

| | |
|---|---|
| Frostbite Degree, N (%) | |
| 0 | 81 (39.9%) |
| 1 | 34 (16.7%) |
| 2 | 39 (19.2%) |
| 3 | 30 (14.8%) |
| 4 | 2 (1.0%) |
| Undetermined/AMA | 17 (8.4%) |

| **Table 2. Thrombolytics contraindications,** N (%) | |
|---|---|
| Fracture | 7 (3.4%) |
| Existing Intracranial Abnormality | 7 (3.5%) |
| Current GI Bleed | 3 (1.5%) |
| Stroke history | 4 (2%) |
| Recent Surgery | 9 (4.5%) |
| High Blood Pressure (unresponsive) | 47 (23.2%) |
| Current Anticoagulation/Antiplatelet therapy | 20 (9.9%) |
| Late Arrival 12+ hours | 79 (38.9%) |
| Freeze/Thaw Cycle | 13 (6.4%) |
| Undetermined/Not documented | 80 (39.4%) |

**Conclusions:** Most patients did not receive thrombolytics due to "relative contraindications", not associated with risk of adverse events following thrombolytics, such as arrival time > 12 hours or unclear freeze-thaw cycles. Understanding the demographics of patients with severe frostbite who do not receive thrombolytics and addressing the barriers to timely treatment can help improve outcomes following frostbite injury.

**Future Directions:** Additional education is needed to support providers in weighing the low risk of thrombolytic-related complications (<5%) against the substantial benefits of limb salvage.[3,4] Notably, the treatment window at HCMC is significantly shorter than at other high-volume frostbite centers, yet even patients treated beyond 12 hours post-injury have achieved 100% limb salvage in some cases.[3]

This work part of the FROST Multicenter study funded by the Military Burn Research Program Department of Defense.
The views presented are those of the speaker and do not necessarily represent the views of the Department of Defense or its components.

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**Associations of Chronic Kidney Disease with Brain-derived Tau Levels: A pilot study**

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4. Department of Psychiatry, University of Pittsburg

**Background.** Blood-based biomarkers of Alzheimer's Disease (AD) have been developed to identify AD pathology. Brain-derived tau (bdtau) is a novel AD blood-based biomarker that is specific for AD-type neurodegeneration. Kidney function affects levels of many AD blood-based biomarkers. The extent to which kidney function affects serum levels of bdTau is unknown.

**Methods.** We measured levels of bdTau in 443 stored serum samples from the baseline BRINK (BRain IN Kidney Disease) study visit.

**Results.** Participants (mean age 69.2 years, 50.3% female, 15.9% African American) with reduced estimated glomerular filtration rate (eGFR) had higher bdTau levels than those with preserved eGFR (bdTau 54.6 pg/mL [SD 24.5] for eGFR <15 mL/min/1.73m$^2$, 34.2 [20.5] for eGFR 15-30, 22.9 [23.4] for eGFR 30-45, 16.8 [19.9] for eGFR 45-60, and 9.2 [9.1] for eGFR >60). The trend was consistent for all levels of cognitive impairment (no cognitive impairment to severe cognitive impairment) and persisted following adjustment for demographics and comorbidities.

**Conclusions.** Lower eGFR is associated with increased serum levels of bdTau. Associations of eGFR with bdTau are not explained by degree of cognitive impairment. Kidney function needs to be considered when interpreting bdTau levels.

# Associations of Chronic Kidney Disease with Brain-derived Tau Levels: A pilot study

Kerry M. Sheets, MD, MS[1,2]; Joseph M. Curran, MS[3]; Michelle M. Mielke, PhD[3]; Thomas K. Karikari, PhD[4]; Anne M. Murray, MD, MS[1,2]
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## INTRODUCTION

- The ATN Frameworks suggests that Alzheimer's Disease (AD) is the result of accumulation of amyloid beta ("A"), then accumulation of tau ("T"), and finally neurodegeneration ("N").
- Blood-based biomarkers of AD have been developed to identify AD pathology. Previously, cerebrospinal fluid samples or advanced imaging (e.g., Amyloid PET-CT) were needed to identify AD pathology in older adults.
- Brain-derived tau (bdtau) is a novel blood-based biomarker of AD that is specific for AD-type neurodegeneration.
- Kidney function affects levels of many AD blood-based biomarkers.
- **Research question: To what extent does kidney function impact levels of serum bdTau?**

## METHODS

- We measured levels of bdTau in stored serum samples from the BRINK (BRain IN Kidney Disease Study) cohort.
- BRINK participants had a blood draw and comprehensive neuropsychologic testing at the baseline study visit.

BRINK
BRain IN Kidney Disease Study

## RESULTS

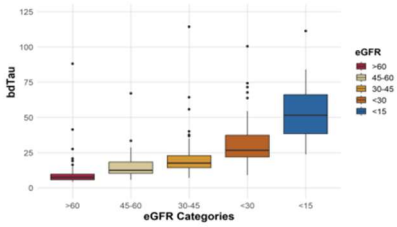


**Figure 1.** Serum bdTau levels by eGFR.

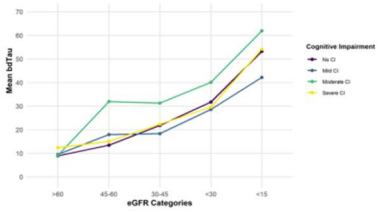


**Figure 2.** Serum bdTau levels by eGFR and cognitive status.

## PARTICIPANTS

| | eGFR >60 (n=147) | eGFR 45-60 (n=98) | eGFR 30-45 (n=191) | eGFR 15-30 (n=112) | eGFR <15 (n=25) |
|---|---|---|---|---|---|
| Age, mean (SD) | 68 (9.9) | 70.4 (9.2) | 70.4 (9.6) | 69.5 (9.6) | 61.3 (20.7) |
| Female, n (%) | 83 (28.8) | 50 (17.4) | 101 (35.1) | 49 (17) | 5 (1.7) |
| African American, n (%) | 20 (22) | 12 (13.2) | 21 (23.1) | 27 (29.7) | 11 (12.1) |
| Years of education, mean (SD) | 15.1 (2.6) | 14.4 (3) | 14.3 (2.6) | 13.3 (2.8) | 13.2 (2.5) |

## DISCUSSION

- Lower eGFR is associated with increased serum levels of bdTau.
- Associations of eGFR with bdTau are not explained by degree of cognitive impairment.
- Albumineria is also associated with increased serum levels of bdTau (results not shown).
- Kidney function needs to be considered when interpreting bdTau levels.

**Funding:** This project is supported by a pilot grant from the Alzheimer's Diagnosis in older Americans with Chronic Conditions (ADACC) Network (NIA U24 AG082930)