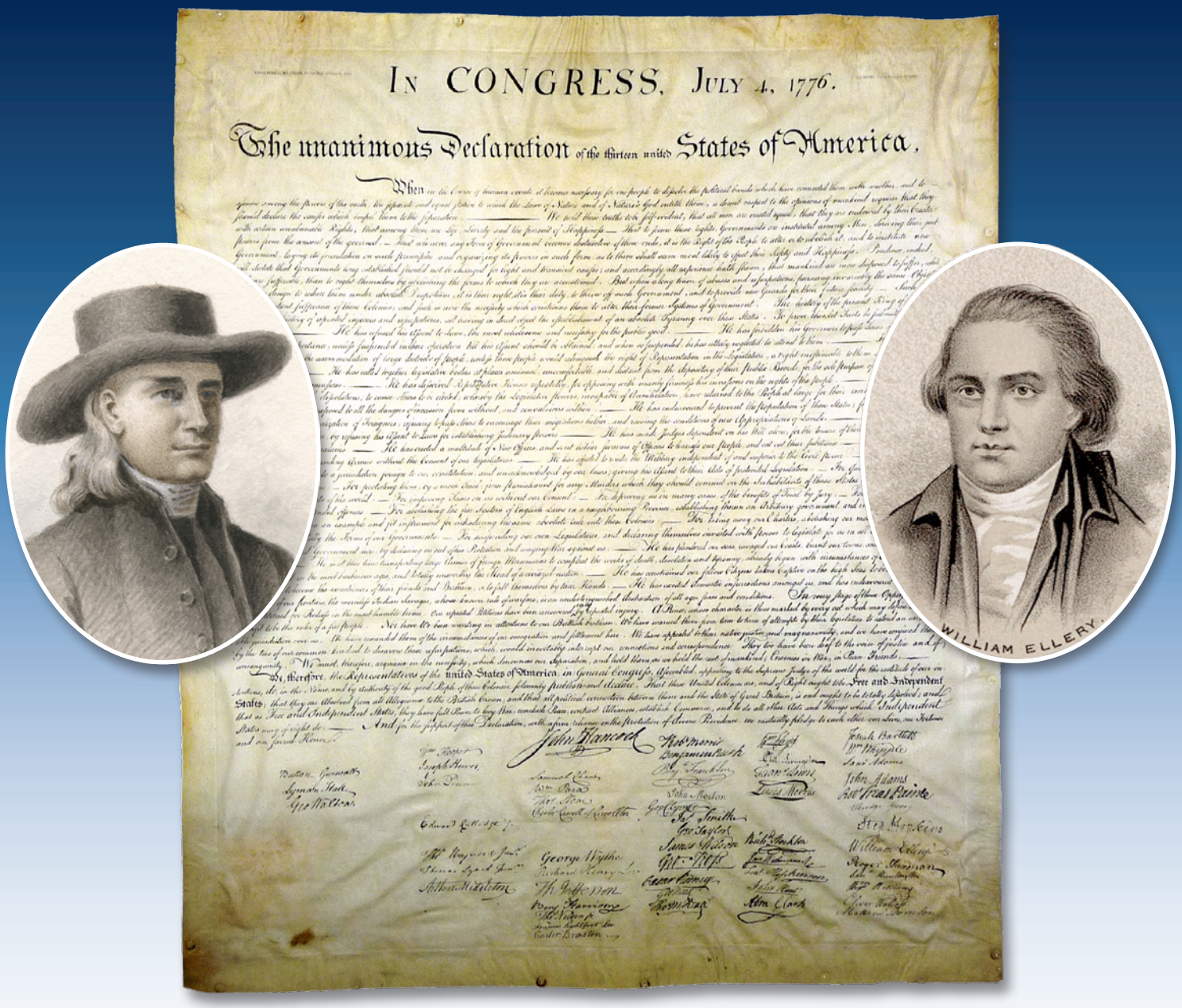
1917 2026 109

# RHODE ISLAND MEDICAL JOURNAL




**Rhode Island copy of the Declaration of Independence, and the two Rhode Island signers, Stephen Hopkins** (left) **and William Ellery** (right)

See Heritage, page 74

AUGUST 2026 VOLUME 109 • NUMBER 8 ISSN 2327-2228

# Are insurance costs affecting your bottom line?

As record setting malpractice verdicts occur with increasing frequency, insurance premiums for medical practices will continue to rise. It's critical to partner with an experienced insurance broker who can advocate on your behalf to secure the best coverage at the best price.

HUB can help. Our insurance and risk management specialists work with you to develop a strategy to manage your insurance costs — so you can continue to focus on patient care.

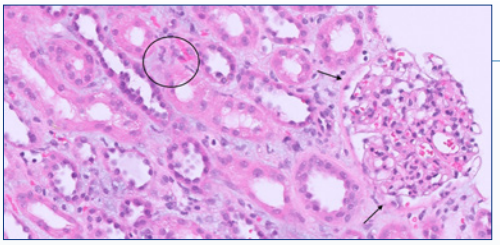
**hubinternational.com/rimed**

**Put our resources to work for you.**
Patrick Marra ○ 978-661-6203 ○ patrick.marra@hubinternational.com

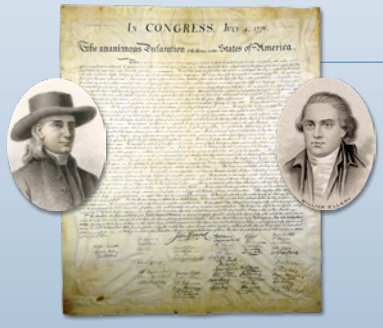
HUB

Risk & Insurance | Employee Benefits | Retirement & Private Wealth

RHODE ISLAND MEDICAL JOURNAL






**On the cover:**

Rhode Island copy of the Declaration of Independence, William J. Stone Printing, 1823, Rhode Island State Archives [HTTPS://SOSRI.ACCESS.PRESERVICA.COM/UNCATEGORIZED/IO_2D61B904-A7D2-4E05-AFB0-E3F96D5EB9CD]

William Ellery by Ole Erekson, engraver [HTTP://WWW.USHISTORY.ORG/DECLARATION/SIGNERS/ELLERY.HTM]

Stephen Hopkins [THE NEW YORK PUBLIC LIBRARY DIGITAL COLLECTIONS, HTTPS://DIGITALCOLLECTIONS.NYPL.ORG/ITEMS/10232FB0-C606-012F-F4A7-58D385A7BC34?CANVASINDEX=0]

AUGUST 2026
VOLUME 109 • NUMBER 8

# RHODE ISLAND MEDICAL JOURNAL



*RHODE ISLAND MEDICAL JOURNAL* (USPS 464-820), a monthly publication, is owned and published by the Rhode Island Medical Society, 225 Dyer Street, 2nd Floor, Providence RI 02903, 401-331-3207.  ISSN 2327-2228. 

## RESEARCH STUDIES



## PUBLIC HEALTH

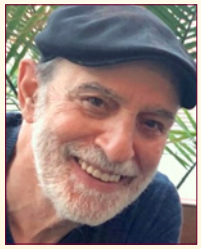
RHODE ISLAND MEDICAL JOURNAL




J. Abilheira, RN


J.A. Katarincic, MD


N. Quashie, PhD


E.R. Feller, MD


C.B. Kahn, MD


J.F. Padbury, MD

Favorite
Healthcare Staffing

# Rhode Island's Medical Staffing Experts

Favorite Healthcare Staffing provides a comprehensive range of staffing services at preferred pricing to RIMS members. Call today to see why we are the favorite choice of healthcare professionals and physician practices across the US!

401.354.7115

MedicalStaffing@FavoriteStaffing.com

Favorite Healthcare Staffing is a Valued Sponsor of the Rhode Island Medical Society

AA / EOE / M / F / V / D

# Flumazenil Use in Benzodiazepine-Induced Delirium Reversal

RIYA BHATTACHARYA, MD; ARIHANT SURANA, MD; ARUNAVA SAHA, MD; SANDEEP SASIDHARAN, MD; AKSHAT BANGA, MD; ERIN O'SHEA PAUDEL, MD

## ABSTRACT

Delirium is a frequent and serious complication in critically ill patients, associated with increased mortality, prolonged hospitalization, and long-term cognitive impairment. The hypoactive subtype is particularly underrecognized, missed in up to 75% of cases, and carries worse outcomes. Benzodiazepines (BZDs), though often used for sedation in the intensive care unit (ICU), can contribute to or exacerbate delirium due to their pharmacokinetics, especially in patients with renal or hepatic dysfunction. Flumazenil, a competitive benzodiazepine receptor antagonist, has been primarily utilized for acute overdose but may have an emerging role in reversing BZD-related delirium. We present a case in which flumazenil administration led to rapid neurological recovery in a critically ill patient with persistent hypoactive delirium following BZD exposure. This report highlights the importance of considering BZD-induced delirium in ICU patients and highlights flumazenil as a potential therapeutic strategy warranting further investigation.

**KEYWORDS:** Flumazenil; Benzodiazepines; Delirium; Intensive care unit; Benzodiazepine receptor antagonist

## INTRODUCTION

Delirium is common among patients admitted to the intensive care unit (ICU) and has been recognized as an independent factor associated with increased six-month mortality, extended ICU and hospital stays, and prolonged mechanical ventilation. The prevalence of delirium in adult ICU patients is approximately 64.6%, and the pooled prevalence of different subtypes of delirium is: hyperactive (4%), hypoactive (17%), and mixed (10%).[1,2] Notably, the prevalence of hypoactive delirium is substantially higher in patients with greater severity of illness (29%) and in mechanically ventilated populations (35%).[1] One study suggested a 10% increased risk of death for every additional day spent delirious in the ICU.[3] Although validated tools like the Confusion Assessment Method for the ICU (CAM-ICU) and the Intensive Care Delirium Screening Checklist (ICDSC) have facilitated delirium monitoring in the ICU,[4] delirium remains underrecognized, with rates of unrecognized delirium ranging from 55% to 70% in hospitalized patients; the hypoactive subtype is particularly prone to being missed and is linked to worse outcomes.[5] Hypoactive delirium is more common among older persons, often goes unrecognized, and is associated with higher rates of complications and mortality.[6] Early diagnosis and treatment of hypoactive delirium can reduce patient mortality.[7]

Benzodiazepines (BZDs) are often used in the ICU to manage anxiety, agitation, and to provide sedation, particularly in mechanically ventilated patients. BZDs work by enhancing the effect of the neurotransmitter gamma-aminobutyric acid (GABA) at the GABA(A) receptor in the central nervous system, which in turn leads to a decrease in neuronal excitability, producing sedative and anxiolytic effects.[8] BZDs are lipophilic drugs that get stored in adipose tissues, resulting in prolonged effects in individuals with higher body fat. Among the benzodiazepines commonly used in clinical practice, midazolam and diazepam are the most highly lipophilic. Midazolam is water-soluble in its acidic formulation but undergoes intramolecular reconfiguration at physiologic pH (7.4), becoming highly lipid-soluble in vivo.[9,10] BZDs are primarily cleared from the body through hepatic metabolism and renal excretion. Moreover, acute kidney injury has been shown to reduce the hepatic metabolism of midazolam in critically ill patients, which is metabolized by CYP 3A enzymes.[11]

We present a case that revolves around the treatment and reversal of benzodiazepine-induced hypoactive delirium with flumazenil, which is a competitive antagonist for the benzodiazepine-binding site.

## CASE DESCRIPTION

A 35-year-old man (Body mass index 26 kg/m$^2$) with a past medical history of HIV-AIDS with poor adherence to antiretroviral therapy and recurrent opportunistic infections in the past, including esophageal candidiasis and pneumocystis pneumonia, presented after an out-of-hospital cardiac arrest, likely due to an aspiration event. The exact downtime was unknown. He was intubated in the field emergently by emergency medical services (EMS) and started on a fentanyl drip for analgesia; no other sedating infusions were initiated at this time. He was stabilized in the emergency department and admitted to the Intensive Care Unit (ICU).

Initial laboratory evaluation [**Table 1**] demonstrated rhabdomyolysis and lactic acidosis. An echocardiogram revealed an ejection fraction of 60%. Imaging included a chest X-ray and CT chest with contrast which revealed a left, lower lung collapse; pulmonary embolism was excluded.

In the ICU, the patient was managed for aspiration pneumonia with IV antibiotics. Subsequently, he underwent a bronchoscopy with broncho-alveolar lavage (BAL) which revealed thick secretions without any obstructive mass. BAL was negative for bacteria, AFB, fungi, PCP, and malignant cells. His ICU course was also complicated by acute kidney injury requiring dialysis. Four days after admission to the ICU, due to ongoing persistent respiratory acidosis and electrolyte abnormalities, he developed non-sustained ventricular tachycardia, promptly followed by the onset of another cardiac arrest, consistent with pulseless electrical activity. CPR was initiated with the return of spontaneous circulation (ROSC) after 40 minutes. Post-arrest echo did not show any abnormalities or change in ejection fraction.

Following this, he was started on a midazolam drip, in addition to the fentanyl drip due to ventilator desynchrony. Gradually, his hemodynamic status improved, and his sedatives were weaned and stopped within 72 hours.

However, despite the termination of sedatives the patient remained unresponsive with absent neurological and brainstem reflexes. Routine labs did not reveal significant electrolyte derangements, hepatic injury, or hypoglycemia that would explain the persistent unresponsiveness [**Table 1**], and CT scan of the brain and MRI Brain revealed no intracranial abnormalities. He was empirically treated with ceftriaxone, vancomycin, and acyclovir for possible meningitis, which were eventually stopped when lumbar puncture ruled out any infectious etiology. Continuous EEG monitoring revealed diffuse cerebral slowing suggestive of encephalopathy but no epileptiform activity.

After four days without sedation, there was still no gross neurological improvement, but weak cough and gag reflexes were noted, findings inconsistent with brain death and prompting further investigation into reversible causes of unresponsiveness. A trial of naloxone yielded no improvement. Subsequently, the patient

**Table 1.** Routine labs and other investigations during hospital stay

| Labs | Day of admission | Before Flumazenil Administration | After Flumazenil Administration |
|---|---|---|---|
| **Complete Blood count** | | | |
| White blood cell count (x103/uL) | 5.7 | 11.2 with neutrophilic predominance | 10.3 |
| Hemoglobin (g/dL) | 16.3 | 8.7 | 8.6 |
| Hematocrit (%) | 47.4 | 27 | 27 |
| Platelets (x103/uL) | 242 | 236 | 230 |
| **Comprehensive Metabolic Panel** | | | |
| Sodium (mEq/L) | 138 | 135 | 137 |
| Potassium (mEq/L) | 5.6 | 4.1 | 4 |
| Chloride (mEq/L) | 101 | 92 | 94 |
| Bicarbonate (mEq/L) | 24 | 23 | 23 |
| Anion gap | 13 | 20 | 20 |
| Calcium (mg/dl) | 8.3 | 9.3 | 9.4 |
| Blood urea nitrogen (mg/dl) | 18 | 67 | 61 |
| Creatinine (mg/dl) | 1.09 | 8.7 | 8.05 |
| Glucose (mg/dl) | 100 | 108 | 114 |
| Alkaline Phosphatase (U/L) | 50 | 138 | 116 |
| ALT (SGPT) (U/L) | 60 | 27 | 24 |
| AST (SGOT) (U/L) | 103 | 33 | 28 |
| Total bilirubin (mg/dl) | 0.7 | 0.4 | 0.5 |
| Magnesium (mg/dl) | 2 | 2.9 | 2.7 |
| Phosphate (mg/dl) | 8.9 | 8.5 | 5.8 |
| Lactate (mmol/L) | 4.9 | 0.7 | - |
| Creatine Kinase (U/L) | 7,823 | — | — |
| Troponin (ng/ml) | 0.11 | — | — |
| Lactate Dehydrogenase (U/L) | 379 | — | — |
| Ammonia (ug/dl) | — | 59.7 | — |
| Arterial blood gas (pH/pCO2/pO2/bicarbonate) | 7.18/59.5/ 60.7/22 | 7.3/45/ 117/98 | — |
| **Thyroid Panel** | | | |
| TSH (uU/ml)/Free T4 (ng/dl) | 6.03/1.07 | — | — |
| **Toxicology Screen** | | | |
| Blood Ethanol and Urine drug screen | Negative | — | — |
| **HIV panel** | | | |
| CD4+ Helper cell # (/uL) | 89 | 161 | — |
| CD4+ Helper cell (%) | 9.9 | 10.7 | — |
| CD4/CD8 Ratio | 0.16 | — | — |
| HIV 1 RNA Quantitative copies/ml | 160 | — | — |
| Hepatitis B and C Panel | Negative | — | — |

was started on a trial of Flumazenil 0.5 mg bolus, followed by 0.2 mg hourly infusion, which resulted in significant improvement in sensorium. Within minutes of initiating the flumazenil bolus, the patient began opening his eyes spontaneously and demonstrating purposeful movements. By 12 hours, he was following simple commands, and by 24 hours, he was fully alert and oriented. After 24 hours, he was successfully extubated and eventually returned to his baseline mentation, leading to both the diagnosis and treatment of BZD-induced hypoactive delirium.

## DISCUSSION

This case report highlights the potential role of flumazenil in the management of benzodiazepine-induced delirium, particularly in a patient with the hypoactive subtype. Despite guideline recommendations to minimize benzodiazepine administration for sedation, they continue to be used in specific patient populations where alternative sedatives are contraindicated due to hemodynamic or pharmacologic considerations.[12] The prolonged half-life and bioaccumulation of benzodiazepines can result in persistent neurocognitive impairment, further complicating delirium management.[13] In this patient, acute kidney injury likely played a role in impaired drug clearance, leading to prolonged effects of the drug. In patients with acute renal failure, midazolam clearance is reduced (1.9 vs 2.8 mL/min/kg) and half-life is prolonged (7.6 vs 13 hours). Furthermore, the 1-hydroxy-midazolam glucuronide metabolite, which has substantial pharmacological activity, accumulates to approximately 10 times the parent drug level in renal failure and can cause prolonged sedation that is immediately reversible with flumazenil.[14,15]

It is important to note that the patient was receiving ongoing hemodialysis during the period when flumazenil was administered. No other sedating medications were initiated or discontinued during this time, supporting the hypothesis that the clinical improvement was attributable to flumazenil administration rather than other concurrent interventions.

Our case report supports the hypothesis that targeted reversal of benzodiazepines with flumazenil may provide clinical benefits in reducing delirium duration and further unnecessary work-up and intervention. Flumazenil is a competitive benzodiazepine receptor antagonist and has been primarily utilized in the acute reversal of benzodiazepine overdose. The observed improvement following flumazenil administration suggested that residual benzodiazepine played a significant role in the persistence of delirium. This aligns with prior studies indicating that benzodiazepines contribute to prolonged ICU stays, cognitive dysfunction, and increased mortality.[3]

A pilot, prospective, double-blinded, randomized placebo-controlled study investigated the use of flumazenil as a potential treatment for hypoactive delirium linked to benzodiazepine exposure.[2] Given flumazenil's relatively short half-life of approximately 60 minutes, a continuous infusion strategy was implemented to counteract the prolonged sedative effects of benzodiazepines. The study revealed that patients receiving flumazenil were 83% less likely to experience delirium by the end of the 72-hour infusion, with this beneficial effect persisting for an additional 24 hours after discontinuation. However, it is important to note that these results did not reach statistical significance, likely due to the study being underpowered with a small sample size. Additionally, ventilator-free days and ICU length of stay were similar between the flumazenil and placebo groups.[2] Despite these limitations, the study provides preliminary evidence supporting the potential benefit of flumazenil in this setting and highlights the need for larger, adequately powered trials.

Another study by Moore et al[16] observed a 79% positive response rate (calm and awake) using sequential flumazenil intravenous bolus dosing for reversal of benzodiazepine-associated delirium as a complication of treatment for patients with alcohol withdrawal. This retrospective review demonstrated that flumazenil administration was a low-risk yet highly effective intervention, significantly altering the course and management of delirium caused by over-sedation. This approach also minimized the need for further resource-intensive evaluations and unnecessary diagnostic workups for altered mental status.

Despite these promising findings, the use of flumazenil for this indication warrants cautious consideration. One of the primary concerns surrounding its administration is the risk of precipitating withdrawal symptoms or seizures, particularly in patients with chronic benzodiazepine use. The FDA label specifically cautions that flumazenil should be used with care in the ICU setting due to the risk of precipitating withdrawal seizures in patients physically dependent on benzodiazepines, and notes that seizures induced by flumazenil may be refractory to standard doses of first-line anticonvulsants.[17] In our case, no significant adverse events were observed, suggesting that careful patient selection and dosing strategies can mitigate these risks. Future research should focus on establishing optimal dosing protocols and identifying patient populations that are most likely to benefit from flumazenil therapy.

Additionally, the long-term effects of flumazenil administration on cognitive recovery and functional outcomes remain unknown. While our findings suggest that flumazenil contributes to delirium resolution, further studies are needed to assess whether this translates into improved long-term neurological function, reduced ICU length of stay, or lower mortality rates.[18] Prospective, randomized controlled trials with larger sample sizes will be essential in confirming the efficacy and safety of flumazenil in this context.

## CONCLUSION

In conclusion, our case report provides preliminary evidence supporting the use of flumazenil in a patient with persistent benzodiazepine-induced hypoactive delirium. While these findings are promising, further research is required to refine treatment protocols, assess long-term outcomes, and ensure patient safety with flumazenil use. Optimizing delirium management strategies in the ICU remains a critical priority, and targeted benzodiazepine reversal may represent a novel and effective approach in select patient populations.

### References


1. Krewulak KD, Stelfox HT, Leigh JP, Ely EW, Fiest KM. Incidence and Prevalence of Delirium Subtypes in an Adult ICU: A Systematic Review and Meta-Analysis. Crit Care Med. 2018 Dec;46(12):2029-2035. doi: 10.1097/CCM.0000000000003402. PMID: 30234569.
2. Schomer KJ, Duby JJ, Firestone RL, Louie EL, Sebat CM, Love DM, Cocanour CS, Albertson TE. Effect of Flumazenil on Hypoactive Delirium in the ICU: A Double-Blind, Placebo-Controlled Pilot Study. Crit Care Explor. 2020 Mar 24;2(3):e0085. doi: 10.1097/CCE.0000000000000085. PMID: 32259108; PMCID: PMC7098541.
3. Ely EW, Shintani A, Truman B, et al. Delirium as a predictor of mortality in mechanically ventilated patients in the intensive care unit. JAMA. 2004;291:1753–1762.
4. Stollings JL, Kotfis K, Chanques G, Pun BT, Pandharipande PP, Ely EW. Delirium in critical illness: clinical manifestations, outcomes, and management. Intensive Care Med. 2021 Oct;47(10):1089-1103. doi: 10.1007/s00134-021-06503-1. Epub 2021 Aug 16. PMID: 34401939; PMCID: PMC8366492.
5. Oh ES, Fong TG, Hshieh TT, Inouye SK. Delirium in Older Persons: Advances in Diagnosis and Treatment. JAMA. 2017; 318(12):1161-1174. doi:10.1001/jama.2017.12067.
6. Marcantonio ER. Delirium in Hospitalized Older Adults. N Engl J Med. 2017;377(15):1456-1466. doi:10.1056/NEJMcp1605501.
7. Lian F, Li F, Tang X, Yuan Y. Risk factors for hypoactive delirium in patients with nontraumatic ARDS: a prospective observational study. Sci Rep. 2024 Mar 24;14(1):6980. doi: 10.1038/s41598-024-57525-w. PMID: 38523173; PMCID: PMC10961304.
8. Goldschen-Ohm MP. Benzodiazepine Modulation of GABA_A Receptors: A Mechanistic Perspective. Biomolecules. 2022 Nov 30;12(12):1784. doi: 10.3390/biom12121784. PMID: 36551212; PMCID: PMC9775625.*
9. Reves JG, Fragen RJ, Vinik HR, Greenblatt DJ. Midazolam: Pharmacology and Uses. Anesthesiology. 1985;62(3):310-24.
10. Cohen LB, Delegge MH, Aisenberg J, et al. AGA Institute Review of Endoscopic Sedation. Gastroenterology. 2007;133(2):675-701. doi:10.1053/j.gastro.2007.06.002.
11. Kirwan CJ, MacPhee IA, Lee T, Holt DW, Philips BJ. Acute kidney injury reduces the hepatic metabolism of midazolam in critically ill patients. Intensive Care Med. 2012 Jan;38(1):76-84. doi: 10.1007/s00134-011-2360-8. Epub 2011 Oct 18. PMID: 22005822.
12. Boncyk CS, Hughes CG. Benzodiazepines and Hospital-Level sedation practices continue to impact outcomes. CHEST Critical Care. 2024;2(2):100052. https://doi.org/10.1016/j.chstcc.2024.100052
13. Peter JU, Dieudonné P, Zolk O. Pharmacokinetics, Pharmacodynamics, and Side Effects of Midazolam: A Review and Case Example. Pharmaceuticals (Basel). 2024 Apr 8;17(4):473. doi: 10.3390/ph17040473. PMID: 38675433; PMCID: PMC11054797.
14. Midazolam [package insert]. U.S. Food and Drug Administration; 2023.
15. Bauer TM, Ritz R, Haberthür C, et al. Prolonged sedation due to accumulation of conjugated metabolites of midazolam. Lancet. 1995;346(8968):145-7. doi:10.1016/s0140-6736(95)91209-6.
16. Moore PW, Donovan JW, Burkhart KK, et al. Safety and efficacy of flumazenil for reversal of iatrogenic benzodiazepine-associated delirium toxicity during treatment of alcohol withdrawal, a retrospective review at one center. J Med Toxicol. 2014;10:126–132.
17. Flumazenil [package insert]. U.S. Food and Drug Administration; 2020.
18. Saha A, Sasidharan S. 1384: Flumazenil: The Kiss of Life? Critical Care Medicine. January 2024;52(1):p S663, | DOI: 10.1097/01.ccm.0001003696.12253.f9


### Authors


Riya Bhattacharya, MD, Department of Medicine, Saint Vincent Hospital, Worcester, MA.

Arihant Surana, MD, Department of Medicine, Saint Vincent Hospital, Worcester, MA.

Arunava Saha, MD, Department of Pulmonology and Critical Care, Tulane University, New Orleans, LA.

Sandeep Sasidharan, MD, Department of Pulmonology and Critical Care, University of Florida, Jacksonville, FL.

Akshat Banga, MBBS, MD, Department of Internal Medicine, Mount Auburn Hospital, Harvard Medical School, Cambridge, MA.

Erin O'Shea Paudel, MD, Department of Pulmonology and Critical Care, Saint Vincent Hospital, Worcester, MA.


### Disclosures


**COI:** The authors have no conflicts of interest to report.

**Funding:** The author(s) did not receive any funding for this work.

**Ethical Approval:** Ethical approval was not required for this case report.

**Consent Approval:** Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

**Declaration of generative AI and AI-assisted technologies in the writing process:** No AI or AI-assisted technologies were used in the preparation of this article.


### Correspondence


Akshat Banga, MBBS, MD
bangaakshat1996@gmail.com

# Acute Interstitial Nephritis after Single Dose of Ketorolac

ISHAN JANI, MD; ARJUN SEKAR, MD; SERGEY BRODSKY, MD


## ABSTRACT

Acute interstitial nephritis (AIN) is an immunologically mediated cause of acute kidney injury (AKI), most often drug-induced, with NSAIDs being a leading culprit. We present a 39-year-old woman who developed biopsy-proven AIN following a single intramuscular dose of ketorolac, an exceptionally short latency likely due to prior sensitization. Despite lacking classic systemic features, she exhibited non-oliguric AKI that improved rapidly with corticosteroids. This case underscores that NSAID-induced AIN can occur even after minimal exposure, highlighting the importance of early recognition, drug withdrawal, and timely steroid therapy to optimize renal recovery.


**KEYWORDS:** Acute Interstitial Nephritis; AIN; NSAID; AKI; Nephrology

## INTRODUCTION

Acute Interstitial Nephritis (AIN) is an immunologically mediated response, characterized by inflammation and edema of the interstitium, leading to kidney injury. AIN is a common cause, with some studies suggesting that it is found in 15–35% of all kidney biopsies in patients with AKI. The most common cause of AIN is drugs, with B-lactams being on the top of the list, succeeded by NSAIDs. Studies have shown that patients develop AIN after being exposed to NSAIDs for a median of three months.[1,3] We report a case of a patient who developed AIN after a single dose of ketorolac 30 mg IM.

## CASE PRESENTATION

Our patient is a 39-year-old woman who presented to an urgent care clinic for evaluation of fatigue and back pain. She was given a dose of ketorolac 30 mg IM, and ondansetron for nausea and was discharged on the same day. Her symptoms did not resolve and she visited the emergency department (ED) five days later with the same complaints. Lab-work revealed a creatinine of 4.8 mg/dL up from her baseline of 0.8 mg/dL. Urinalysis revealed trace hematuria and proteinuria with no casts or dysmorphic RBCs on urine sediment exam; CT abdomen and pelvis (without contrast) was negative for renal calculi. In the ED, she received 1 liter of normal saline and was admitted to the hospital. Of note, she had a past medical history notable only for GERD and occasional migraines. She did not endorse any home medication use except occasional tylenol and rimegepant. She had a poor appetite for the last three days, but water intake was unchanged. She noted no change in urination. She did admit that she used to take NSAIDs occasionally in the past. However, it has been more than a year since she stopped them.

Further serological evaluation with ANCA, C3, C4 and hepatitis was negative. She remained non-oliguric but her

**Figure 1.** Creatinine Trend over time during hospitalization and follow-up

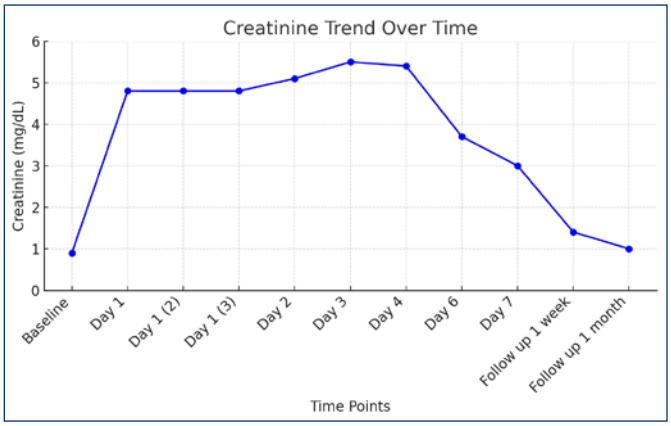
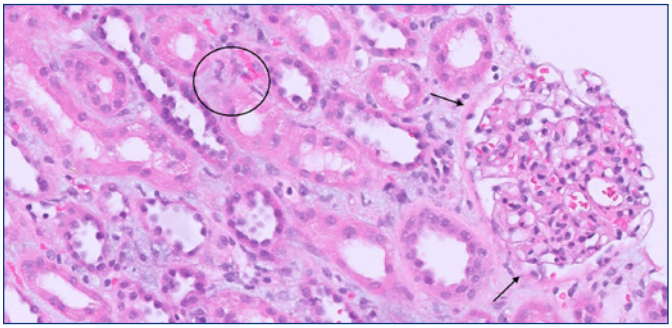



**Figure 2.** Biopsy showing unremarkable glomerulus, diffuse interstitial edema with active-appearing inflammatory cell infiltrates, acute tubular epithelial cell injury [H&E, x200]. Black circle represents interstitial inflammatory infiltrate. Arrows point towards a relatively preserved glomerulus.



kidney function continued to worsen with her creatinine reaching a ceiling at 5.4 on hospital day 4 after which it started to improve. A kidney biopsy was obtained. Morphologically, glomeruli were unremarkable, but there was acute tubular necrosis and diffuse interstitial edema with active-appearing interstitial inflammatory infiltrates, suggestive of acute interstitial nephritis. There was no evidence of immune complex deposition or monoclonal immunoglobulin deposition by immunofluorescence and electron microscopy.

She was started on a short course of oral steroids. This was for a total of five days as there was rapid improvement in renal function (likely due to withdrawal of NSAIDs). Three weeks later, creatinine was down to 1 mg/dL and she had no new complaints.

## DISCUSSION

We present a young woman who developed AIN-mediated AKI with a single dose of intramuscular ketorolac who had sporadic and remote NSAID use in the past. Even with prior sensitization, it is exceptionally rare to develop AIN after just one dose of precipitating medication.

While NSAID-induced AIN often follows weeks to months of therapy, there is evidence that latency can range from as short as one day to several months.[1] The minimum latency for new NSAID exposure in NSAID-induced AIN is typically 10–14 days,[1] but cases with shorter latency (as little as one day) can be possible, especially in previously sensitized individuals.[2] Given her remote history of NSAID use, it is plausible that prior sensitization primed the immune system, rendering her susceptible to an accelerated hypersensitivity response after re-exposure. Importantly, no alternative medications or systemic conditions known to cause AIN were identified, strengthening the causal link to ketorolac.

Clinical presentation of NSAID-induced AIN may be subtle, frequently lacking the classic triad of fever, rash, and eosinophilia, which is present in only about 10% of cases.[3,4] Our patient similarly presented without systemic allergic features and remained non-oliguric, underscoring the diagnostic challenge. Most patients present with nonspecific symptoms (malaise, nausea, vomiting) and non-oliguric AKI, as in our case. Kidney biopsy is needed for confirmatory diagnosis and was confirmed in our case with interstitial inflammation and preserved glomerular structure. Urinalysis findings can be nonspecific in AIN and very often the sediment is bland. The improvement of renal function after drug withdrawal and early corticosteroid initiation is consistent with prior studies demonstrating that timely steroids, particularly when administered within seven days of diagnosis, can improve recovery and reduce the risk of progression to chronic kidney disease. Use of steroids is controversial in AIN. However, there may be stronger evidence when NSAIDs are thought to be the culprit for AIN.[5] The mainstay of treatment is withdrawal of the culprit agent.

An important learning objective which can be identified here is that AIN should be considered in the differential diagnosis of AKI even after a single dose of an NSAID, particularly in patients with prior sensitization, and that early withdrawal of the offending agent and timely initiation of corticosteroids may improve and hasten renal recovery.

### References


1. Porile JL, Bakris GL, Garella S. Acute interstitial nephritis with glomerulopathy due to nonsteroidal anti-inflammatory agents: a review of its clinical spectrum and effects of steroid therapy. J Clin Pharmacol. 1990 May;30(5):468-75. doi: 10.1002/j.1552-4604.1990.tb03487.x. PMID: 2189904.
2. Raghavan R, Shawar S. Mechanisms of Drug-Induced Interstitial Nephritis. Adv Chronic Kidney Dis. 2017 Mar;24(2):64-71. doi: 10.1053/j.ackd.2016.11.004. PMID: 28284381.
3. Muriithi AK, Leung N, Valeri AM, et al. Biopsy-proven acute interstitial nephritis, 1993-2011: a case series. Am J Kidney Dis. 2014 Oct;64(4):558-66. doi: 10.1053/j.ajkd.2014.04.027. Epub 2014 Jun 11. PMID: 24927897.
4. Praga M, González E. Acute interstitial nephritis. Kidney Int. 2010 Jun;77(11):956-61. doi: 10.1038/ki.2010.89. Epub 2010 Mar 24. PMID: 20336051.
5. González E, Gutiérrez E, Galeano C, et al; Grupo Madrileño De Nefritis Intersticiales. Early steroid treatment improves the recovery of renal function in patients with drug-induced acute interstitial nephritis. Kidney Int. 2008 Apr;73(8):940-6. doi: 10.1038/sj.ki.5002776. Epub 2008 Jan 9. PMID: 18185501.


### Authors


Ishan Jani, MD, Dept. of Internal Medicine, Rochester General Hospital, Rochester, NY.

Arjun Sekar, MD, Dept. of Nephrology, Rochester General Hospital, Rochester, NY.

Sergey Brodsky, MD, Dept. of Pathology, Ohio State University Medical Center, Columbus, Ohio.


### Correspondence


Ishan Jani, MD

Ishan.jani@rochesterregional.org

# When Psychiatric Disease is Not What it Seems: History Taking Uncovers Steroid-Induced Delirium Following Intra-Articular Injections

CLARE NIMURA, BA; ZACHARY SHAW, MD; SARAH FREEMAN, MD

**KEYWORDS:** Delirium; hallucination; psychosis; corticosteroid injection; geriatric

## BACKGROUND

Acute neuropsychiatric symptoms in older adults are often multifactorial and diagnostically challenging. This case describes an 87-year-old woman with mild cognitive impairment who developed episodic insomnia and hallucinations following intra-articular corticosteroid injections for osteoarthritic pain. While neuropsychiatric adverse effects are well recognized with systemic corticosteroids, they can also occur after local administration, particularly in older adults with baseline cognitive impairment.[1,2]

Corticosteroids are widely used anti-inflammatory agents delivered via systemic or local routes, including intra-articular injections for osteoarthritis. Although intra-articular therapy is generally considered safe, systemic absorption can occur, occasionally leading to adverse effects.[3,4] Neuropsychiatric manifestations range from mood changes and sleep disturbance to delirium with hallucinations and delusions, with heightened risk in older adults due to pharmacokinetic variability, age-related blood-brain barrier changes, and polypharmacy.[5,6] Symptoms may emerge within days of exposure, sometimes after a single injection. Acute delirium and hallucinations following intra-articular corticosteroid injections have been reported in older adults, though the incidence of these neuropsychiatric complications is uncertain and underrecognized.[2,7,8]

When evaluating acute psychotic symptoms, it is important to distinguish delirium from psychotic disorder. As defined by the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5), criteria for substance/medication-induced psychotic disorder include prominent hallucinations or delusions developing during or shortly after medication exposure, symptoms not better explained by a primary psychotic disorder, and disturbances that do not occur exclusively during delirium. Functional impairment or distress is also required, and persistence of symptoms beyond typical medication half-life may suggest an independent psychotic disorder.[9]

This case highlights the importance of considering intra-articular corticosteroid exposure as a potential trigger for acute delirium with prominent hallucinations and delusions in older adults and underscores the importance of a complete history.

## CASE PRESENTATION

An 87-year-old woman with mild cognitive impairment, a prior diagnosis of a recurrent unspecified delusional disorder, hypothyroidism, and osteoarthritis presented from her assisted living facility with acute insomnia and auditory and visual hallucinations. Her medication history included levothyroxine, atorvastatin, vitamin D3, and famotidine. Notably, she had received two intra-articular corticosteroid knee injections one day prior to symptom onset. Her daughter reported that she was found wandering the halls of her assisted living facility overnight, conversing aloud and responding to apparent internal stimuli; she had not slept for approximately 36 hours by the time she presented to the hospital. During this period, she also made several phone calls to her daughter with confabulation regarding recent events. Prior to presentation, she was in her usual state of health and performing all activities of daily living independently.

On admission, she was afebrile and hemodynamically stable. She was alert and oriented to person and time but disoriented to place and recent events; there was no evidence of auditory or visual hallucinations at the time of initial evaluation. Her thought process was linear and goal-directed, without delusions. Physical examination revealed no neurological deficits. A complete blood count, metabolic panel, thyroid function tests, and urinalysis were unremarkable, and a CT scan of the head was normal. Urine toxicology screening and ammonia level had been negative on prior similar admissions but were not obtained during this hospitalization.

Further history from the patient's daughter revealed that over the preceding year, she had experienced similar episodes every few months, characterized by acute, transient auditory and visual hallucinations and delusional beliefs that others were overly infatuated with her, with spontaneous resolution of symptoms and complete return to baseline mental status within 48 to 72 hours. Several episodes were

empirically treated with antibiotics for presumed urinary tract infection, though no consistent infectious etiology was identified. She underwent extensive outpatient evaluation by geriatric psychiatry, neurology, and neuropsychology, including comprehensive laboratory testing, electroencephalography, brain MRI, and vision screening, all of which were unrevealing. She was ultimately diagnosed with mild cognitive impairment with suspected unspecified episodic delusional/psychotic disorder and started on quetiapine.

Review of records and additional history revealed a consistent temporal relationship between psychotic episodes and intra-articular corticosteroid injections. Each prior episode had occurred within days of an injection, and associated neuropsychiatric symptoms consistently resolved within several days with or without medical intervention. Given this temporal relationship, her advanced age, baseline cognitive impairment, and the recurrent, transient nature of her symptoms, her presentation most likely represented delirium with prominent hallucinations and delusions, rather than a primary late onset delusional disorder. She did not meet DSM-5 criteria for a substance/medication-induced psychotic disorder, as her psychotic symptoms occurred exclusively in the context of delirium rather than as an isolated or persistent psychotic syndrome. The inpatient psychiatry consultation service concurred with this assessment. By the morning after admission, her mental status had returned to baseline without intervention; she was alert and oriented to person, place, and time, with intact recall of events during hospitalization.

At discharge, recommendations were made to the outpatient geriatric psychiatry team to consider dose reduction or discontinuation of standing antipsychotic therapy, and to her outpatient orthopedic provider to limit future intra-articular corticosteroid injections by reducing either injection frequency or the number of joints treated concurrently.

## DISCUSSION

This case illustrates the value of thorough medication history. The differential diagnosis for acute delirium with hallucinations and delusions in older adults is broad and includes metabolic or endocrine derangements, infection-related delirium, primary CNS infections, substance intoxication or withdrawal, dementia-related neuropsychiatric symptoms, primary psychiatric disorders, medication-induced psychotic disorder, and medication-induced delirium.[1,2] In this patient, a comprehensive metabolic, endocrine, and infectious evaluation was unrevealing, excluding significant metabolic or infectious etiology. A urine toxicology screen would have strengthened the assessment for substance involvement, although urine toxicology screens obtained in earlier presentations were negative, lowering suspicion for substance involvement.

The recurrent, transient nature of her symptoms initially raised concern for a late-onset primary psychotic disorder; however, detailed history revealed a consistent temporal relationship with intra-articular corticosteroid injections. Neuropsychiatric complications of corticosteroids include insomnia, mood changes, mania, and delirium with hallucinations and delusions, occurring in up to 18% of patients receiving systemic corticosteroids.[10-12] Intra-articular injections can also result in clinically significant systemic absorption,[3,4] and several case reports describe steroid-induced delirium or hallucinations following local injections in older adults.[2,7,8] Pharmacokinetic studies demonstrate that systemic absorption after intra-articular corticosteroid injection can be both rapid and prolonged. Methylprednisolone acetate, for example, reaches peak plasma levels at approximately four hours post-injection, with detectable levels persisting for at least 96 hours,[13] whereas triamcinolone acetonide extended-release formulations produce lower peak concentrations but sustained exposure for up to 20 weeks.[14] Risk factors for neuropsychiatric complications include high corticosteroid dose, number of joints injected, solubility of the preparation, advanced age, baseline cognitive impairment, and polypharmacy.[1,15] This phenomenon remains underreported, leading to likely misattribution of symptoms to primary psychiatric illness, minor metabolic derangements, or asymptomatic bacteriuria.

Management of delirium begins with recognition and discontinuation of possible offending agents. While supportive measures are first line treatment, short-term antipsychotic therapy may be considered if symptoms are severe or pose a safety risk to the patient or others, but should be used cautiously in older adults due to potential adverse effects.[11,16] In this case, careful history and interdisciplinary collaboration prevented misdiagnosis and unnecessary chronic antipsychotic therapy and antibiotic therapy. Recognition of the potential for intra-articular corticosteroid injections to precipitate delirium with hallucinations and delusions is increasingly important as the use of these injections increases among older adults.[17,18]

## CONCLUSION

Systemic absorption of intra-articular corticosteroids can precipitate acute delirium with prominent hallucinations and delusions in older adults, particularly those with cognitive impairment or polypharmacy. Failure to recognize these episodes may result in inappropriate psychiatric diagnoses and unnecessary antipsychotic therapy. This case underscores the importance of considering all forms of corticosteroid exposure as potential triggers for acute delirium and highlights the critical role of thorough history and careful clinical evaluation in identifying modifiable medication-related etiologies.

## References


1. Manzo C, Serra-Mestres J, Castagna A, Isetta M. Behavioral, Psychiatric, and Cognitive Adverse Events in Older Persons Treated with Glucocorticoids. Medicines. 2018; 5(3):82.
2. Samala RV, Ciocon JO. Steroid-induced hallucination following intra-articular administration: a case report and brief review. J Am Med Dir Assoc. 2011;12(6):451–453.
3. Bilsborough Smith C, Baker D, Botchu R, et al. Corticosteroid injections for non-spinal musculoskeletal conditions: consideration of local and systemic adverse drug reactions. New Zealand Journal of Physiotherapy. 2023;51(1).
4. Stout A, Friedly J, Standaert CJ. Systemic Absorption and Side Effects of Locally Injected Glucocorticoids. PM&R. 2019; 11(4):409-419.
5. Dubovsky AN, Arvikar S, Stern TA, Axelrod L. The neuropsychiatric complications of glucocorticoid use: steroid psychosis revisited. Psychosomatics. 2012;53(2):103-115.
6. Parasher A, Bez J. Steroid-induced psychiatric adverse effects: an overview of risk factors, clinical features and management. International Journal of Research in Medical Sciences. 2020; 8(7):2508–2513.
7. Lally L, McCarthy G, Meehan K. Hyperactive delirium following administration of intra-articular corticosteroid. BMJ Case Rep. 2017; bcr2016217483.
8. Robinson DE, Harrison-Hansley E, Spencer RF. Steroid psychosis after an intra-articular injection. Ann Rheum Dis. 2000; 59(11):927.
9. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders* (5th ed.); 2013.
10. Ross DA, Cetas JS. Steroid psychosis: a review for neurosurgeons. J Neurooncol. 2012;109(3):439-447.
11. Huynh G, Reinert JP. Pharmacological Management of Steroid-Induced Psychosis: A Review of Patient Cases. J Pharm Technol. 2021;37(2):120-126.
12. Warrington TP, Bostwick JM. Psychiatric adverse effects of corticosteroids. Mayo Clin Proc. 2006;81(10):1361-1367.
13. Steer JH, Ma DT, Dusci L, Garas G, Pedersen KE, Joyce DA. Altered leucocyte trafficking and suppressed tumour necrosis factor alpha release from peripheral blood monocytes after intra-articular glucocorticoid treatment. *Ann Rheum Dis*. 1998; 57(12):732-737.
14. Kraus VB, Conaghan PG, Aazami HA, et al. Synovial and systemic pharmacokinetics (PK) of triamcinolone acetonide (TA) following intra-articular (IA) injection of an extended-release microsphere-based formulation (FX006) or standard crystalline suspension in patients with knee osteoarthritis (OA). *Osteoarthritis Cartilage*. 2018;26(1):34-42.
15. Knox EG, Aburto MR, Clarke G, Cryan JF, O'Driscoll CM. The blood-brain barrier in aging and neurodegeneration. Mol Psychiatry. 2022;27(6):2659-2673.
16. Oh ES, Fong TG, Hshieh TT, Inouye SK. Delirium in Older Persons: Advances in Diagnosis and Treatment. JAMA. 2017; 318(12):1161-1174.
17. Kamel SI, Rosas HG, Gorbachova T. Local and Systemic Side Effects of Corticosteroid Injections for Musculoskeletal Indications. AJR Am J Roentgenol. 2024;222(3):e2330458.
18. Koenig KM, Ong KL, Lau EC, et al. The Use of Hyaluronic Acid and Corticosteroid Injections Among Medicare Patients With Knee Osteoarthritis. J Arthroplasty. 2016;31(2):351-355.


## Authors


Clare Nimura, BA, The Warren Alpert Medical School of Brown University, Providence, Rhode Island.

Zachary Shaw, MD, The Warren Alpert Medical School of Brown University, Division of General Internal Medicine, Providence, Rhode Island.

Sarah Freeman, MD, Division of General Internal Medicine, Rhode Island Hospital, Providence, Rhode Island.


## Disclosures


This research did not receive external funding.


**Ethical Approvals:** The patient provided informed consent at the time of hospital admission for the use of de-identified case information for educational and research purposes. No identifying information is included in this report.

## Correspondence


Clare Nimura, BA
222 Richmond St.
Providence, RI 02903
Clare_nimura@brown.edu

# Myoclonus Due to Acute-On-Chronic Hypercarbic Respiratory Failure

MARINA HILARIO BRUGUÉS, MD, MBA; DECHEN TULADHAR, DO; ALISA MEROLLI, MD; MAURICIO F. VILLAMAR, MD

**KEYWORDS:** Hypercarbia; Myoclonus; Asterixis; Chronic obstructive pulmonary disease; Respiratory failure

## INTRODUCTION

Hypercarbic respiratory failure is defined by an elevation in the partial pressure of carbon dioxide in the blood and occurs when one or more elements of the respiratory system fail.[1] Intrinsic lung disease is the leading cause of hypercarbic respiratory failure and, within this category, chronic obstructive pulmonary disease (COPD) is the most common etiology. Hypercarbia is known to cause a wide array of neurological symptoms, ranging from somnolence to seizures, coma, and death. Therefore, identifying this diagnosis early in its course is essential.[2,3] In the appropriate clinical scenario, myoclonus may be a clue suggesting the presence of hypercarbic respiratory failure.[4]

## CASE PRESENTATION

A 73-year-old man had history of COPD (on 3–4L of supplemental oxygen), myocardial infarction, heart failure with reduced ejection fraction, implantable cardioverter-defibrillator, atrial fibrillation, hypertension, and untreated obstructive sleep apnea. He presented to the emergency department with complaints of worsening dyspnea, generalized weakness, and tremors. On initial physical examination he was tachycardic and tachypneic, with shallow and diminished breath sounds throughout both lung fields. The patient was somnolent and exhibited psychomotor slowing. Prominent positive and negative myoclonus was appreciated in his bilateral upper > lower extremities, also involving the face and trunk [**Video, Part 1**].

Venous blood gases were consistent with acute-on-chronic hypercarbic respiratory failure (pH 7.26, pCO2 102 mmHg, HCO3 45.7 mmol/L, pO2 45 mmHg). Testing for SARS-CoV-2 was negative. Computed tomography of the chest demonstrated bibasilar consolidations/infiltrates and underlying chronic changes in the lung, without pleural effusion. Computed tomography of the head revealed no significant abnormalities.

Positive pressure non-invasive ventilation was initiated, and the patient was admitted to the step-down unit. Antibiotics, steroids, and nebulizer treatments were administered. Overnight he responded appropriately to ventilation, and the following day the patient was awake, oriented, and interactive. Myoclonus had fully resolved [**Video, Part 2**]. Repeat venous blood gas demonstrated a pH of 7.44, pCO2 of 60 mmHg, HCO3 of 40.8 mmol/L, and pO2 of 26.1 mmHg.

Click image to view video parts 1 and 2 on Vimeo
https://vimeo.com/1189470556 [1:13]


**Video part 1. Pre-treatment examination**
Myoclonus in a patient with acute-on-chronic hypercarbic respiratory failure. The patient had both positive and negative myoclonus (asterixis) that preferentially involved the upper > lower extremities, but were also seen in his face and trunk.

**Video part 2. Post-treatment examination**
Following delivery of positive pressure non-invasive ventilation and improvement in hypercarbia, the patient's myoclonus resolved.

## DISCUSSION

Myoclonus is a hyperkinetic, involuntary movement disorder that can be characterized by sudden, brief, lightning-like muscle contractions (positive myoclonus) or by abrupt cessation of muscle tone (negative myoclonus).[4] Asterixis represents a specific form of negative myoclonus that typically occurs in toxic-metabolic encephalopathies, most commonly hepatic and uremic encephalopathy, though it has also been reported in hypercapnic respiratory failure. The distribution of myoclonus may be generalized, focal, or multifocal.[4,5]

Among hospitalized patients, toxic-metabolic derangements are a common cause of myoclonus. Acute processes that may be associated with the development of myoclonus, and asterixis in particular, include uremic and hepatic encephalopathies, electrolyte abnormalities, or certain drug toxicities. Hypoxic-ischemic encephalopathy is another process that frequently leads to the development of myoclonus. Correctly identifying the etiology of myoclonus leads to physiology-based treatment.[6]

Hypercarbia is one often overlooked cause of both positive and negative myoclonus. Furthermore, there is a paucity of video cases in the literature illustrating the phenomenology of myoclonus in the context of hypercarbia. The pathophysiology of hypercarbia-associated myoclonus is incompletely understood. One theory is that elevated CO2 levels may lead to depressed afferent transmission and altered synaptic function between type Ia fibers of the muscle spindle and the alpha motor neuron, affecting neuromuscular function.[7] Additionally, hypercapnia-induced acidosis may modulate neuronal excitability through pH-dependent mechanisms, including inhibition of voltage-gated sodium and calcium channels, modulation of adenosine and adenosine triphosphate signaling pathways, and effects on GABAergic inhibitory circuits, which collectively influence cortical excitability and synaptic transmission.[8]

In addition to some of the more "classical" toxic-metabolic processes, the presence of myoclonus should prompt timely evaluation for possible CO2 retention and acute respiratory failure, as this can be potentially life-threatening. In this context, correction of hypercarbia should lead to gradual improvement in myoclonus. Hence, clinical examination of myoclonus may also assist in monitoring a patient's respiratory status and response to treatment.

## References


1. Lagina M, Valley TS. Diagnosis and Management of Acute Respiratory Failure. Critical Care Clinics. 2024;40(2):235-253. PMID: 38432694
2. Sutter R, Ristic A, Rüegg S, Fuhr P. Myoclonus in the critically ill: Diagnosis, management, and clinical impact. Clin Neurophysiol. 2016 Jan;127(1):67-80. doi: 10.1016/j.clinph.2015.08.009. Epub 2015 Aug 29. PMID: 26428447.
3. Stahl CM, Frucht SJ. An Update on Myoclonus Management. Expert Rev Neurother. 2019 Apr;19(4):325-331. doi: 10.1080/14737175.2019.1592676. Epub 2019 Mar 20. PMID: 30874443.
4. Dijk JM, Tijssen MA. Management of patients with myoclonus: available therapies and the need for an evidence-based approach. Lancet Neurol. 2010 Oct;9(10):1028-36. doi: 10.1016/S1474-4422(10)70193-9. PMID: 20864054.
5. Pal G, Lin MM, Laureno R. Asterixis: a study of 103 patients. Metab Brain Dis. 2014 Sep;29(3):813-24. doi: 10.1007/s11011-014-9514-7.
6. Pena AB, Caviness JN. Physiology-Based Treatment of Myoclonus. Neurotherapeutics. 2020 Oct;17(4):1665-1680. doi: 10.1007/s13311-020-00922-6. PMID: 32910414; PMCID: PMC7851206.
7. Beekley MD, Cullom DL, Brechue WF. Hypercapnic impairment of neuromuscular function is related to afferent depression. Eur J Appl Physiol. 2004 Jan;91(1):105-10. doi: 10.1007/s00421-003-0936-x. Epub 2003 Sep 4. PMID: 12955522.
8. Dulla CG, Dobelis P, Pearson T, Frenguelli BG, Staley KJ, Masino SA. Adenosine and ATP link PCO2 to cortical excitability via pH. Neuron. 2005 Dec 22;48(6):1011-23. doi: 10.1016/j.neuron.2005.11.009.


## Authors


Marina Hilario Brugués, MD, MBA, Kent Hospital, Brown University Internal Medicine Program, Warwick, RI.

Dechen Tuladhar, DO, Kent Hospital, Brown University Internal Medicine Program, Warwick, RI.

Alisa Merolli, MD, Kent Hospital, Department of Internal Medicine, Warwick, RI.

Mauricio F. Villamar, MD, Kent Hospital, Department of Internal Medicine, Warwick, RI; Department of Neurology, The Warren Alpert Medical School of Brown University, Providence, RI. ORCID ID: M. F. Villamar: 0000-0003-4503-8152


## Disclosures


**Study sponsorship/funding:** No targeted funding for this manuscript. M.F. Villamar is the recipient of a Faculty Career Development Award from Brown Physicians, Inc.

**Declaration of conflicting interests:** Drs. Hilario Brugues, Tuladhar, and Merolli have no conflicts of interest to declare. Dr. Villamar has no conflicts of interest that are relevant to this manuscript. He has served as a consultant for Ceribell, Inc. and is recipient of a Career Development Award from Brown Physicians, Inc.

**Acknowledgments:** The authors thank the patient for consenting to this publication.


## Correspondence


Marina Hilario Brugués, MD, MBA
Kent Hospital, Brown University Internal Medicine Program
455 Toll Gate Road Warwick, RI 02886
401-487-8917
marina_hilario_brugues@brown.edu

# A Decade of Pathways to Medicine: Program Evaluation and Lessons Learned in Implementing a Local Health-Professions Outreach Program

RAJEEV J. KANT, PhD; DAVID F. PAINTER, MD; LUCKSON OMOAREGBA, MS, MPH; KYLA DEWAR, MD; JOSEPH A. DIAZ, MD

## ABSTRACT

Pathway programs provide structured opportunities for students to explore healthcare careers and develop familiarity with educational pathways into the health professions. Ongoing evaluation of such programs is essential to gauge their success and inform iterative improvement. In 2013, The Warren Alpert Medical School of Brown University launched the Pathways to Medicine program in partnership with local health professions' schools to provide Rhode Island high school students with structured educational experiences, mentorship, and career exploration opportunities in healthcare fields. Herein we describe the design and structure of the Pathways to Medicine program and summarize internal program evaluation data from 2013–2022 related to participant engagement and post-program educational trajectories. Insights from participant feedback and program metrics informed targeted modifications, including expanded partnerships and enhanced support structures. These findings illustrate how iterative, systematic program evaluation can guide the evolution of pathways initiatives and support continuous improvement in program design and delivery.

**KEYWORDS:** educational pathways; medical education; career; mentorship

## INTRODUCTION

Awareness of health careers and familiarity with educational pathways are important components of a student's career exploration. However, significant systemic and contextual factors can shape the accessibility of learning opportunities for many youths, both in Rhode Island and nationally.[1–3] In medicine, commonly cited challenges to the pursuit of a career in healthcare include prohibitive costs, escalating expectations for academic and extracurricular preparation, and variable access to mentorship and pre-medical experiential opportunities.[4,5] Similar challenges persist across other health professions' training pathways, including physician assistant,[6,7] pharmacy,[8] and nursing programs.[9] These barriers yield downstream consequences for the healthcare workforce, contributing to persistent gaps in the development of future clinicians. One important manifestation is the rapidly widening disparity between the need and availability of primary care physicians (PCPs), both locally and nationally.[10] In Rhode Island, there will be an estimated shortage of approximately 100 PCPs by 2030 (roughly 11% of the current workforce), which is attributed to a mismatch in new graduates entering the healthcare workforce in Rhode Island compared to the expected retirement of existing PCPs and population growth.[11,12] These patterns, observed both regionally and nationally, have prompted increasing institutional attention toward educational strategies that broaden knowledge of and access to health professions and strengthen early-career development. Pathway programs have emerged as a promising solution to this issue, offering structured exposure to support students' interest in, and understanding of, support for healthcare careers.[13,14]

Instituted in 2013, Pathways to Medicine ("Pathways") is a mentorship program hosted by The Warren Alpert Medical School of Brown University that provides structured opportunities, individualized mentorship, and early career exploration of the health professions for Rhode Island high school students.[15] Pathways leaders at Brown University have collaborated with numerous other graduate-level healthcare programs in Rhode Island to represent a cross-section of the myriad healthcare professions. Collaborating professional schools include the physician assistant (PA) programs at Johnson & Wales University and Bryant University, the nursing schools at the University of Rhode Island and Rhode Island College, and the pharmacy school at the University of Rhode Island. Additionally, Pathways is internally supported by faculty from the center for community engagement and pathways programming at The Warren Alpert Medical School.

Each summer, a student leadership team advertises and promotes the Pathways to Medicine program via a dedicated website, information sessions, and outreach emails distributed to Rhode Island high schools, fostering longitudinal partnerships across diverse public school communities. Interested students apply through a brief application describing their interests and goals, while mentors from participating health professions' schools are recruited through a parallel application process. Mentors and participants are selected based on application merit, with the number of accepted students determined by available mentors to maintain at least a 1:1 mentor-to-participant ratio and ensure

consistent, individualized engagement. Each participant is paired with a health-professions' student mentor for longitudinal guidance. Pathways to Medicine is led by four to six second-year medical students from The Warren Alpert Medical School, all former mentors, with additional student liaisons from partnering institutions, supporting interschool and interprofessional coordination and collaboration.

Monthly sessions held in the Fall semester of each academic year cover topics including an introduction to acquiring vital signs, exposure to the cadaver lab,[16] skills workshops such as suturing and ultrasound, and college/career preparatory panels. The program culminates in a final poster presentation, in which participants create an academic poster based on a healthcare topic of their choice and present it during a final symposium. Participants are also provided with opportunities to connect with healthcare professionals and engage in shadowing opportunities at local Rhode Island physician practices, further establishing their network and exposure to healthcare careers. Here, we describe a retrospective evaluation of the Pathways to Medicine program in its first decade, with the goals of characterizing program development to understand participant trajectories following high school graduation, and identifying areas for refinement to improve future program iterations.

## EVALUATION METHODS

### Data Sources

Participant information was collated across Pathways cohorts from 2013 to 2022, using participant application forms from routine program enrollment and optional post-program assessments, including focus groups and surveys. All collected information was anonymized and saved on a secure institutional, cloud-storage service. Participants were excluded from analysis if they did not complete the entire program, defined as greater than three absences and/or failure to submit the final presentation. If a student participated in Pathways more than once (n = 4), only data from their initial participation was included.

To characterize post-program educational and career trajectories, publicly available information was reviewed using online sources including LinkedIn, institutional webpages, news articles, and other publicly accessible online profiles. Searches were conducted between May 2024 and February 2025 using names provided in program applications, and when available, additional contextual information (e.g., high school attended, graduation year, and hometown). A participant was considered "locatable" if their cross-matched profile contained at least one additional piece of information relevant to educational or career trajectory analysis, including, but not limited to, current occupation or university matriculation. Participants with cross-referenced profiles but no additional information relevant to evaluation were excluded from further analysis (n = 209).

Although rigid metrics were employed to minimize incorrect participant profile identification for analysis, no contact was made with participants, their families, faculty, or staff from participating high schools, or any other institutional entities to verify any data. This work was conducted as a program evaluation of an existing educational initiative. All data were collected as part of routine program operations or obtained from publicly available sources. No additional data collection, intervention, or participant contact occurred for research purposes. In accordance with institutional policy, this evaluation did not meet the definition of human subjects research and was exempt from Institutional Review Board review.

### Data Analysis

Health-related degrees and careers were defined as any degree, major, or job related to patient care or human health, including, but not limited to, physical therapy, counseling, research, clinical trial coordinator, psychology, and medical assistant. Health professions' careers were defined as a subset of health-related careers, including those represented by the Pathways program: medicine (MD/DO), pharmacy (PharmD and pharmacy technician), physician assistant (PA), and nursing (degree and certificate programs). Of note, demographic information, including self-reported race/ethnicity, was not collected prior to 2020 and was therefore excluded from this initial evaluation.

All collected data were anonymized by assigning an arbitrary number to each Pathways participant. Data were compiled in Prism 10 (GraphPad Software, Boston, MA, USA) and plotted to identify trends across years.

## RESULTS

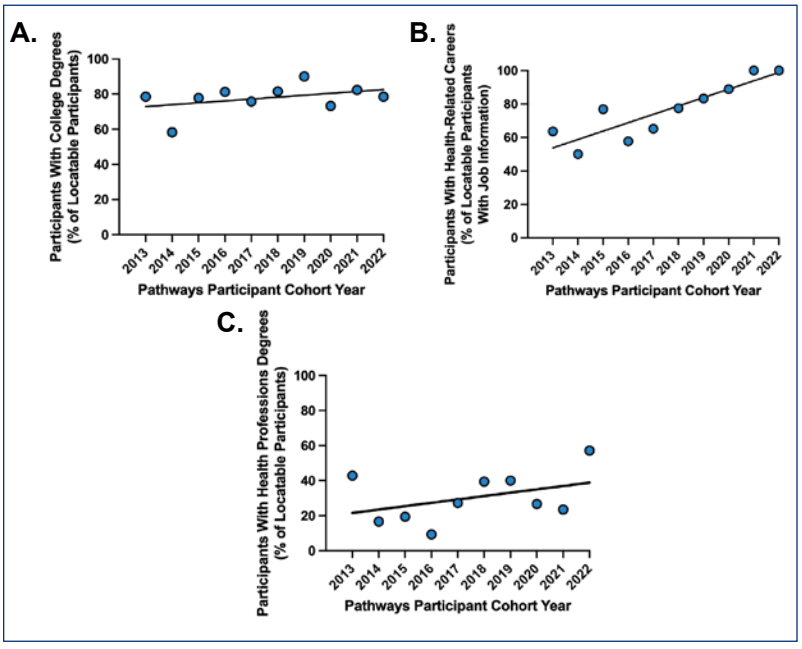
Pathways to Medicine has hosted students from 26 high schools across Rhode Island since 2013, including public schools (n = 21, one of which is online), private schools (n = 2), and public technical career schools (n = 3). A total of 455 participants enrolled in Pathways to Medicine over this time, representing an average annual cohort of 46 participants [**Table 1**]. Participants hailed from many communities across Rhode Island, including, but not limited to, Barrington, Bristol, Coventry, Central Falls, Cranston, Cumberland, East Providence, Johnston, Lincoln, North Smithfield, North Providence, Pawtucket, Providence, Riverside, Smithfield, Warren, Warwick, West Warwick, and Woonsocket. Participants were supported by 507 mentors across the six health professional schools, representing an average annual cohort of 51 mentors per year, with a mentor-participant ratio of 1.1:1. Among the 455 participants, 246 (54.1%) were locatable via our online search strategy and were therefore included in analysis.

Overall, 193 (78.5%) of the 246 locatable participants have earned a college degree or are enrolled in a degree-granting

**Table 1.** Pathways participant and mentor demographics

| | # | % Participants | % Locatable Participants |
|---|---|---|---|
| Participating Health Professions' Programs | 6 | — | — |
| Participating High Schools | 26 | — | — |
| Mentors | 507 | — | — |
| Average Mentor Cohort Size | 51 | — | — |
| MD Mentors (The Warren Alpert Medical School) | 249 | — | — |
| PA Mentors (Bryant, JWU) | 97 | — | — |
| Pharmacy Mentors (URI) | 118 | — | — |
| Nursing Mentors (URI, RIC) | 43 | — | — |
| Participants | 455 | — | — |
| Average Participant Cohort Size | 46 | — | — |
| Mentor:Participant Ratio | 1.1 | — | — |
| Locatable Participants | 246 | 54.1 | — |
| Post-Secondary Education | 193 | 42.4 | 78.5 |
| Advanced/Terminal Degrees | 25 | 5.5 | 10.2 |
| Participants in Health-Related Careers | 118 | 25.9 | 48.0 |
| Participants in Health Professions | 70 | 15.4 | 28.5 |

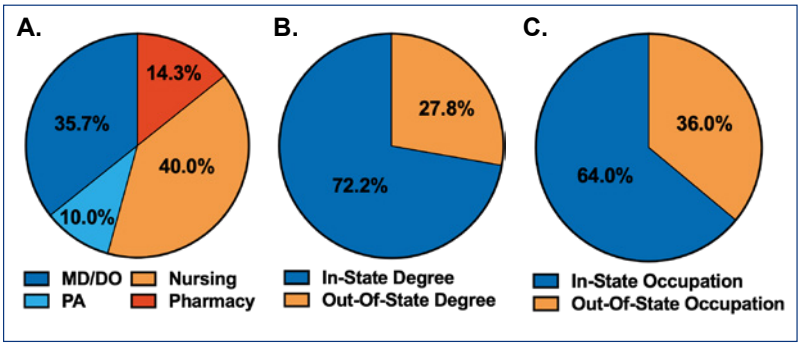
**Figure 1.** [**A**] Annual percentage of Pathways participants who earned or are currently enrolled in a college degree program (Associate's or Bachelor's). [**B**] Annual percentage of Pathways participants involved in health-related careers, or [**C**] health professions (defined as professions represented by Pathways partner institutions, i.e., medical doctor, physician assistant, pharmacy, and nursing).




institution, representing a consistent rate of Pathways participants earning their first degree each year over the last decade [**Figure 1A**]. Of participants with an undergraduate degree, 25 (10.2%) went on to earn, or are expected to earn, an advanced degree, including, but not limited to, Master of Science (MS), Master of Physician Scientist Studies (MPAS), Master of Health Science, Master of Nursing, Doctor of Jurisprudence (JD), Doctor of Pharmacy (PharmD), Doctor of Allopathic Medicine (MD), and Doctor of Osteopathic Medicine (DO). Out of all locatable participants with current job information, 118 (48.0%) pursued health-related careers after high school graduation. From 2013–2022, our data show longitudinal increases across cohorts in the number of participants who pursued health-related careers [**Figure 1B**]. At least 70 (28.5%) locatable participants (59.3% of participants with health-related careers) pursued health professional careers represented by our partner programs. Program-evaluation data further shows consistent entry or intended entry of participants into the health professions [**Figure 1C**], inclusive of current health professions' students, pre-professional students, and non-degree health professions (certified nursing assistant or pharmacy technician).

Of the participants involved in the health professions, 28 (40.0%) entered or plan to enter nursing programs, 25 (35.7%) pursued or plan to pursue an MD/DO degree, 10 (14.3%) enrolled or plan to enroll in pharmacy programs, and 7 (10.0%) completed or plan to complete a PA degree [(**Figure 2A**]. As of this evaluation, 36 (51.4%) of the health professions' students were currently enrolled in or had completed a terminal health professions' degree, 31 (44.3%) were pre-professional students preparing to apply into one of the health professions' programs, and 3 (4.2%) did not earn a post-secondary degree but were working in a related health professions career. Of the 36 health professions' students/degree holders, 26 (72.2%) remained in-state for their degree, and 10 (27.8%) went out-of-state [**Figure 2B**]. Based on current occupation information regarding the subset of 25 participants who already completed their health professions degree or did not pursue one, 16 (64.0%) remained in or returned to Rhode Island to work in their profession, and 9 (36.0%) left or remained out-of-state [**Figure 2C**].

**Figure 2.** [**A**] Total percentage of locatable participant involvement in the subset of health professions represented by Pathways (n = 70 participants). [**B**] Percentage of health professions' participants who pursued their degree within or outside of Rhode Island (n = 36 participants). [**C**] Percentage of health professions' participants with current occupation data whose occupations are within or outside of Rhode Island (n = 25 participants).




## DISCUSSION

Findings from our program evaluation suggest that Pathways participants over the last decade consistently enrolled in higher education and healthcare careers after completing the Pathways program. A substantial portion of participants who pursued health-related careers did so in the health professional fields represented by Pathways program mentors, suggesting alignment between the program content and participants' educational and professional trajectories.

### Participant Impact and Educational Pathways

Pathways to Medicine emphasizes broad exposure to the healthcare professions and aims to nurture scientific passion and instill confidence in participants so they can successfully pursue careers in healthcare. For students interested in pursuing a career in healthcare, mentorship, encouragement, and support are crucial factors in successfully pursuing these interests and achieving their goals. Much of what Pathways participants learn throughout the program is translatable to academic and career success in high school, college, and beyond. To that end, a particular metric of interest is the number of high school students who, after participating in Pathways, receive a college degree (Associate's or beyond). Our data indicate that high school students participating in Pathways to Medicine pursue higher education at an overall rate of 78%, higher than the estimated state average of 39.2%.[17]

While many factors influence college enrollment, our program data suggest that Pathways may support students' exposure to healthcare careers, access to information about higher education, and connections with mentors who are willing to guide students through the application process. It is also encouraging to see longitudinal increases in locatable participants entering health-related fields following high school. Our findings also suggest that a substantial proportion of participants who enter the health professions remain in Rhode Island for both education (72.2%) and early-career placement (64.0%). This retention may be supported in part by networking facilitated by Pathways mentors and events. While state-level retention data exists for physicians after residency (38.5% to 77.5% nationally and 42.9% in Rhode Island from 2013 to 2022),[18] comparable data are not available for the other health professional programs included in our evaluation. Although direct comparisons are limited, the observed in-state retention among Pathways participants may indicate a positive influence of the program on career trajectory and local workforce development.

Although these findings cannot be attributed to program impact alone, they highlight the importance of education surrounding the many options for those interested in pursuing a healthcare-related career and underscore differences between program participants and broader population benchmarks.[19,20] Qualitative feedback from surveys and post-program focus groups has further contextualized these findings. Participants frequently expressed appreciation for sessions outlining and differentiating between healthcare professions, individual mentorship time, and skill development relevant to higher education, including workshops covering college application tips, resume writing, research involvement, and scientific poster creation.

### Mentor Experience and Program Structure

For program mentors, Pathways to Medicine offers an opportunity for local community outreach and educational engagement with a diverse group of Rhode Island high school students, in addition to interprofessional collaboration. Mentor feedback frequently praised the program's mentorship model, specifically regarding the opportunities for sustained and individualized interaction with assigned participants, in addition to the structured group-based learning activities. Mentors also relayed benefits associated with teaching experience, professional development, and exposure to interdisciplinary perspectives. Constructive feedback from mentors has helped shape session development, program reach, and mentor recruitment strategy, including the designation of student liaisons for each participating health professional school. Implementation of post-program meetings with outgoing student leaders, professional school liaisons, graduating student participants, and incoming program leaders (for future program iterations) have facilitated program continuity and iterative improvement. This underscores the role of interdisciplinary mentorship in shaping program implementation on a year-to-year basis.[21,22]

### Limitations

Several limitations should be considered when interpreting these findings. Reliance on publicly available information may result in incomplete or outdated representations of participants' educational or professional histories. Additionally, the voluntary nature of program participation and application-based selection process may introduce selection effects that influence observed patterns. It is also important to acknowledge that the impact of Pathways on participant trajectories may be confounded by the program's inherent selection of students who may already be more likely to enroll in college and pursue health-related careers.

### Future directions

Despite these limitations, our program evaluation highlights opportunities for continued curricular development, including standardizing feedback mechanisms to capture actionable insights and support longitudinal program monitoring, addressing logistical barriers such as transportation, and strengthening existing institutional partnerships. In parallel, ongoing efforts aim to cultivate new relationships with other regional, health professional education programs to expand interprofessional engagement. Broadening these partnerships will foster shared curricular initiatives, promote sharing of limited educational resources like simulation equipment, and facilitate collaborative learning experiences. Collectively, these strategies aim to enhance program implementation and long-term sustainability, refine tracking of program performance for iterative improvements, and ultimately maximize the program's impact on participants.

## CONCLUSIONS

Pathways to Medicine is a Rhode Island-based, multi-institutional program that provides structured opportunities for healthcare career exploration among high school students. This retrospective evaluation of the program's first decade describes promising patterns in participant engagement, educational trajectories toward health professions, and identifies areas for ongoing program refinement based on iterative feedback. Our findings illustrate how systematic program evaluation can support the evolution of pathways initiatives within academic institutions. Continued attention to program structure, feedback processes, and institutional collaboration will further inform future iterations of Pathways to Medicine and contribute to the sustained development of educational programming in health professional pathways for future generations of Rhode Island students.

### References


1. Williams JS, Walker RJ, Egede LE. Achieving Equity in an Evolving Healthcare System: Opportunities and Challenges. *Am J Med Sci.* 2016;*351*(1):33–43. https://doi.org/10.1016/j.amjms.2015.10.012.
2. Gomez LE, Bernet P. Diversity Improves Performance and Outcomes. *J Natl Med Assoc.* 2019;*111*(4):383–392. https://doi.org/10.1016/j.jnma.2019.01.006.
3. Arvizo C, Garrison E. Diversity and Inclusion: The Role of Unconscious Bias on Patient Care, Health Outcomes and the Workforce in Obstetrics and Gynaecology. *Curr Opin Obstet Gynecol.* 2019;*31*(5):356–362. https://doi.org/10.1097/GCO.0000000000000566.
4. Tello C, Goode CA. Factors and Barriers That Influence the Matriculation of Underrepresented Students in Medicine. *Front Psycho.l* 2023;*14*:1141045. https://doi.org/10.3389/fpsyg.2023.1141045.
5. Rinderknecht FAB, Kouyate A, Teklu S, Hahn M. Antiracism in Action: Development and Outcomes of a Mentorship Program for Premedical Students Who Are Underrepresented or Historically Excluded in Medicine. *Prev Chronic Dis.* 2023;*20*:E49. https://doi.org/10.5888/pcd20.220362.
6. Bradley-Guidry C, Burwell N, Dorough R, Bester V, Kayingo G, Suzuki S. An Assessment of Physician Assistant Student Diversity in the United States: A Snapshot for the Healthcare Workforce. *BMC Med Educ.* 2022;*22* (1):680. https://doi.org/10.1186/s12909-022-03717-9.
7. Kibe LW, Schrode KM, Paik S, Frias-Sarmiento D. Underrepresentation of Black Men in Physician Assistant and Associate Training. *JAMA Netw Open.* 2024;7(10), e2441531. https://doi.org/10.1001/jamanetworkopen.2024.41531.
8. Alonzo N, Bains A, Rhee G, Htwe K, Russell J, De Vore D, Chen XL, Nguyen M, Rajagopalan V, Schulte M, Doroudgar S. Trends in and Barriers to Enrollment of Underrepresented Minority Students in a Pharmacy School. *Am J Pharm Educ.* 2019;*83* (7):6925. https://doi.org/10.5688/ajpe6925.
9. Akintade B, González J, Idzik S, Indenbaum-Bates K. Topic: Intentional Diversity in Academia: Recruiting, Admitting, Enrolling, and Retaining Underrepresented Students in Nursing Programs. *J Prof Nurs.* 2023;*45*:21–28. https://doi.org/10.1016/j.profnurs.2023.01.004.
10. GlobalData Plc. The Complexities of Physician Supply and Demand: Projections From 2021 to 2036; 2024. https://www.aamc.org/media/75236/download?attachment.
11. Petterson SM, Cai A, Moore M, Bazemore A. State-Level Projections of Primary Care Workforce, 2010-2030; 2013.
12. Borkan J, Coppa D, Flanagan P, Hurwitz D, Saal A, Bowes Y, Nicolella E, Hollmann P. Primary Care Access for All: A Roadmap for Addressing the Primary Care Crisis in Rhode Island. *R I Med J (2013).* 2024;*107*(4):40–44.
13. Brottman MR, Char DM, Hattori RA, Heeb R, Taff SD. Toward Cultural Competency in Health Care: A Scoping Review of the Diversity and Inclusion Education Literature. *Acad Med.* 2020;*95*(5):803–813. https://doi.org/10.1097/ACM.0000000000002995.
14. Smith SG, Nsiah-Kumi PA, Jones PR, Pamies RJ. Pipeline Programs in the Health Professions, Part 1: Preserving Diversity and Reducing Health Disparities. *J Natl Med Assoc.* 2009;*101*(9):836–840, 845–851. https://doi.org/10.1016/s0027-9684(15)31030-0.
15. Gibson J, Bay A, Omoaregba L, Diaz JA. Pathways to Medicine. *R I Med J.* 2024;*107*(7): 28–30.
16. Painter D, Dewar K. Early Cadaver Lab Exposure Increases Motivation to Pursue Medical Careers in High School Students. *R I Med J.* 2023;*10*(9):57–58.
17. United States Census Bureau. *S1501: Educational Attainment-Census Bureau Table*. https://data.census.gov/table/ACSST1Y2023.S1501?g=040XX00US44 (accessed 2025-02-09).

18. *Physician Retention in State of Residency Training, by State*. AAMC. https://www.aamc.org/data-reports/students-residents/data/report-residents/2023/table-c6-physician-retention-state-residency-training-state (accessed 2026-03-21).
19. Zavattieri L, D'Anna S, Maillet JO. Evaluation of High-School Health Science Careers Program Impact on Student Retention and Careers. *J Allied Health.* 2007;*36*(2):81–87.
20. Winkleby MA. The Stanford Medical Youth Science Program: 18 Years of a Biomedical Program for Low-Income High School Students. *Acad Med.* 2007;*82*(2):139–145. https://doi.org/10.1097/ACM.0b013e31802d8de6.
21. Coe C, Piggott C, Davis A, Hall MN, Goodell K, Joo P, South-Paul JE. Leadership Pathways in Academic Family Medicine: Focus on Underrepresented Minorities and Women. *Fam Med.* 2020;*52*(2):104–111.https://doi.org/10.22454/FamMed.2020.545847.
22. Bonifacino E, Ufomata EO, Farkas AH, Turner R, Corbelli JA. Mentorship of Underrepresented Physicians and Trainees in Academic Medicine: A Systematic Review. *J Gen Intern Med.* 2021;*36*(4):1023–1034. https://doi.org/10.1007/s11606-020-06478-7.

## Authors

Rajeev J. Kant, PhD, The Warren Alpert Medical School of Brown University, Providence, Rhode Island.

David F. Painter, MD, The Warren Alpert Medical School of Brown University, Providence, Rhode Island.

Luckson Omoaregba, MS, Office of Belonging, Equity, Diversity & Inclusion, The Warren Alpert Medical School of Brown University, Providence, Rhode Island.

Kyla Dewar, MD, Division of General Internal Medicine, The Warren Alpert Medical School of Brown University, Providence, Rhode Island.

Joseph A. Diaz, MD, MPH, Division of General Internal Medicine, The Warren Alpert Medical School of Brown University, Providence, Rhode Island.

## Disclosures

The authors declare no conflicts of interest.

**Funding:** The programs described are supported in part by a grant from The Warren Alpert Foundation: SMART Plus Pathways: School Health Model for Academics Reaching All Transforming Lives Plus a Health Professions Pathways Program for Rhode Island.

## Correspondence

Rajeev J. Kant
rajeev_kant@brown.edu

# Characteristics and Management of Xylazine-Associated Wounds: A Systematic Review of Published Cases

CATHERINE M. CALL, MD; CHRISTOPHER J. LAMA, MD; SEAN L. AGRODNIA, BA; JONATHAN LIU, MD; JULIA A. KATARINCIC, MD; JOSEPH A. GIL, MD

## ABSTRACT

**BACKGROUND:** The rise in xylazine-adulterated fentanyl and heroin has been designated as an emerging public health threat due to a devasting pattern of xylazine-associated wounds associated with its injection. This study was undertaken to systematically characterize patient and wound characteristics, treatment strategy, and outcomes of xylazine-associated wounds reported in the literature.

**METHODS:** A systematic review was conducted in December 2025 according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, and PubMed, Scopus, EMBASE, and Cochrane Review databases were queried. In total, 17 studies were included, describing 277 patients.

**RESULTS:** The mean age was 39.0 years (±8.38), and 43.0% of the patients were women. Wounds were reported on the upper extremity (83.0%), lower extremity (53.4%), and trunk (0.04%). Of the 275 patients with treatment reported, 14.9% were treated with just local wound care; surgical interventions utilized included irrigation and debridement only (9.8%), skin graft (9.8%) and flap coverage (5.1%); 9.5% of patients required amputation. Discharge against medical advice was reported in 42.2% of cases. Of the published literature, 240 of all cases were published in 2025, and 259 of all cases were reported in Pennsylvania, confirming a growing public health threat with a regional epicenter.

**CONCLUSIONS:** This study reports on the demographic, medical, and social characteristics of patients with xylazine-associated wounds and investigates the wound attributes, treatment strategies, and reported outcomes of affected individuals. Such findings can inform identification, management, and research of xylazine-associated wounds, with the goal to minimize the morbidity of this emerging public health issue.

**KEYWORDS:** Xylazine; Tranq; soft-tissue necrosis; intravenous drug use (IVDU); Xylazine-associated necrotic (XAN) wounds; people who inject drugs (PWID)

## INTRODUCTION

Xylazine, also known as "tranq", is a non-opioid veterinary tranquilizer that has infiltrated the illicit drug supply within the United States.[1,2] Initially reported among people who inject drugs (PWID) around 2001 in Puerto Rico, it is now increasingly detected in fentanyl-containing street drug supplies, particularly in the Northeast.[1,3] Deaths involving xylazine and fentanyl are also on the rise, having increased more than 3000% between 2018 and 2021,[4] leading the White House Office of National Drug Control Policy to designate fentanyl associated with xylazine as an emerging threat to national health.[5]

Added to street opioids (e.g., heroin and fentanyl) in an effort to prolong the euphoric effects, xylazine, as an alpha-2 agonist, can cause acute central nervous system depression.[6,7] Alarmingly, xylazine does not respond to conventional opioid overdose reversal agents, and is increasingly implicated in the development of a distinct pattern of severe, necrotic, soft-tissue wounds.[1,6,8,9] While the exact mechanism underlying the observed tissue injury remains unclear, peripheral injections of xylazine are thought to cause local vasoconstriction, which subsequently results in soft-tissue hypoxia and necrosis.[2,10] Reported xylazine-associated extremity wounds can be devastating, and pose considerable treatment challenges to clinicians. To date, no review of available literature on the musculoskeletal manifestations and care options of xylazine-associated wounds has been performed. We undertook this systematic review to describe the presentation, clinical findings, treatment, and outcomes of all published cases addressing xylazine-associated wounds to inform identification and management of this growing public health threat.

## MATERIALS AND METHODS

### Eligibility Criteria and Search Strategy

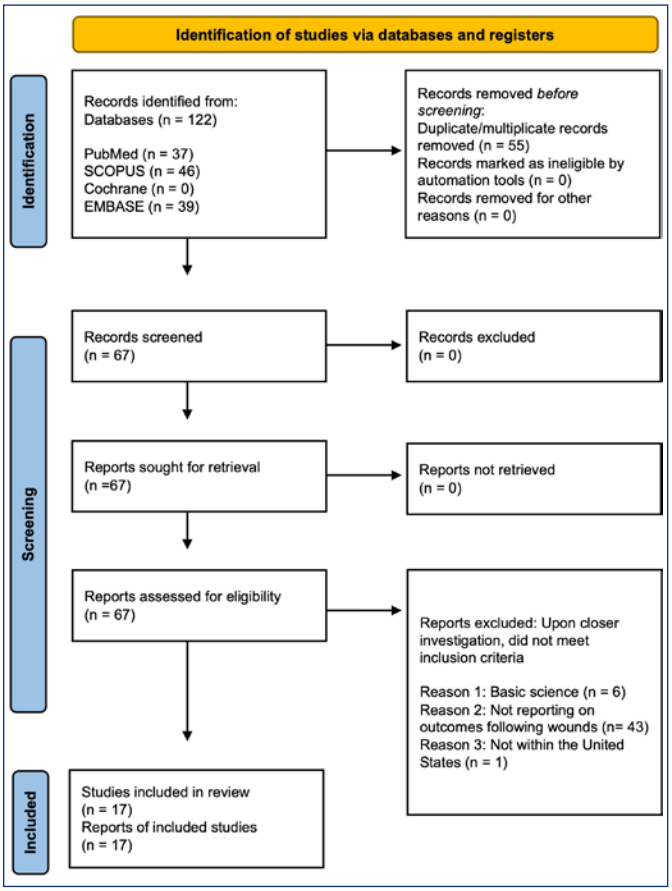
A comprehensive literature review was conducted on December 20, 2025 according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines,[11] using PubMed, EMBASE, Scopus, and Cochrane Review databases. English-language articles examining xylazine-related wounds in human subjects were considered eligible if they met the following criteria: (1) the study employed a prospective or retrospective cohort, case control, or case

series design; (2) patients were aged 18 years or older and receiving treatment for xylazine-related wounds at a healthcare facility within the United States; and (3) the authors reported on any of the following: characteristics, treatment, or outcome of patient(s) related to their xylazine-related wounds. Conference articles, book chapters, and published abstracts were excluded. Because our focus was on clinical outcomes, not basic science, filters for research on human subjects were employed when available, including utilization of the 'human' filters in PubMed and EMBASE. Within Scopus, where a human filter was unavailable, search results for the subject area were limited to "medicine" or "health professions." The comprehensive search strategy employed was comprised of relevant keywords. For each included article, the cited references were reviewed to evaluate for inclusion of publications that were not captured in the initial search. Articles deemed eligible were published between January 1, 1990, and December 20, 2025.

## Study selection

This search yielded 122 publications, of which 67 were unique and subsequently screened for inclusion [**Figure 1**]. Duplicates (55) were identified by one author (CMC) using Rayyan (Rayyan Systems, Cambridge, MA) software.[12] Resulting articles were independently evaluated by either of two authors (CMC and SLA) using Rayyan,[12] based on title and abstract. Any discrepancies were noted by reviewers and discussed to come to agreement regarding inclusion. Studies reporting on xylazine wounds on patients outside of the United States (1), or on basic science topics (6) otherwise nonapplicable to the study question (43) were excluded, leaving 17 potentially eligible articles that underwent full-text review by one author (CMC) and were determined fit for study inclusion.

**Figure 1.** PRISMA 2020 flow diagram displaying the systematic review of search strategy.[11]




## Assessment of Quality

The quality of evidence of included case reports and case series was assessed by one author (SLA) using a checklist created by Murad et al specifically designed to assess risk of bias within case reports and case series.[13] Questions 5 and 6 of this questionnaire were omitted as irrelevant, as they addressed cases reporting adverse drug events. The quality of each case report was assessed as 'good' if 'yes' was scored greater than four times, 'moderate' for a score of two or three, and 'poor' if score was less than one. All eligible reports were included, irrespective of methodological quality.

## Data Collection and Analysis

Data collected included the following when available: patient age, sex, reported drug use, wound location, reported injection drug use into the wound, wound duration at time of presentation, wound staging, treatment, outcome, and comorbid medical and psychosocial comorbidities, including Human Immunodeficiency Virus (HIV) and hepatitis C (HCV) positive status, any psychiatric diagnosis, unhoused status, and if mentioned, left care against medical advice (AMA). Wound staging was based on documented stage if reported; wounds without a stage reported were staged by one author (SLA) based on the written and photographic description available in the study utilizing the framework adapted from Retrouvey et al, which defined ulcers as stage 1: 'ulcer involving skin and/or soft tissue' to stage 4: 'ulcer involvement of all critical structures (neurovascular structures, tendon, muscle, bone)'.[14] Year and location of each study were also recorded. Data storage and analysis occurred within Microsoft Excel (Microsoft, Inc., Seattle, WA). A statistical comparison of outcomes was not performed. Meta-analysis was not attempted due to the heterogeneity across the pooled study data and lack of available control group.

# RESULTS

A total of 17 studies met inclusion criteria[14-30]; According to the checklist of Murad et al,[13] 58.8% (n=10) of the studies were of 'good' methodological quality. Each study reported on one to 82 cases of xylazine-associated wounds, identifying a total of 277 patients with this condition. Search

methodology is outlined in **Figure 1**. **Tables 1** and **2** present the characteristic data of the entire group. The mean age of included patients was 39.0 years (±8.38); 43.0% (119/277) of the patient population was female. All studies reported location of wound(s); 83.0% (230/277) had a wound present to the upper extremity, 53.4% had a wound present to the lower extremity (148/277), and just 0.04% (11/277) had a wound to the trunk. Just 15 of 277 cases included

**Table 1.** Summary of reported cases, manuscripts 1 through 8 by publication date

| First author, year | Murad [13] rating | Patient age, sex | IVDU at wound site | Wound location | Wound duration | Wound stage | Treatment |
|---|---|---|---|---|---|---|---|
| Ehrman-Dupre, 2022[15] | Good | 29F | Yes | LE | 8 mos | 1 | Wound care |
| Malayala, 2022 [26] | Mod | 37F | Yes | LE | Few wks | 3 | Wound care |
| Dowton, 2023 [16] | Good | 69M;<br>37M;<br>54F | Yes | UE | 3 yrs;<br>16 mos;<br>13 mos | 1;<br>1;<br>2 | Wound care;<br>Wound care;<br>Fasciotomy then graft |
| O'Neil, 2023 [27] | Mod | 32M | Yes | Trunk | 1 mos | 4 | Flap |
| Rengifo, 2023 [30] | Good | 35M | Yes | UE | — | 2 | Graft |
| Rose, 2023 [28] | Good | 30sF;<br>40sM | Yes | LE | 5 d;<br>1 wk | 1;<br>1 | Wound care |
| Soderquist, 2023 [29] | Mod | 3 M and 5 F,<br>avg. age 34 | — | UE | — | 4 | Amputation |
| Naidu, 2024 [18] | Mod | 43F;<br>33F;<br>43F;<br>37F;<br>32M | Yes | UE | 4 mos;<br>5 mos;<br>—<br>Multiple yrs;<br>— | 4;<br>4;<br>2;<br>4;<br>4 | Graft and flap to amputation;<br>Fasciotomies and allograft to amputation;<br>Wound care with outpatient fingertip amps;<br>Graft and flaps;<br>Thrombectomies, fasciotomies and carpal tunnel release, repeat thrombectomies to amputation |

**Table 2.** Summary of reported cases, manuscripts 9 through 17 by publication date

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Retrouvey, 2024 [14] | Mod | 43M;<br>38M;<br>35M;<br>31F;<br>33M;<br>20sF;<br>48M | — | UE | 2 yrs;<br>2 yrs;<br>—;<br>2 mos;<br>—;<br>5 d | 3;<br>4;<br>4;<br>—;<br>2;<br>2;<br>2 | Bone reconstruction;<br>Amputation;<br>Amputation;<br>No care;<br>Graft;<br>Graft;<br>I&D |
| Sun, 2024 [19] | Mod | 30F;<br>40F;<br>34M | Yes | UE | 1.5 yrs;<br>Several mos;<br>— | 2;<br>2;<br>2 | Graft;<br>I&D (left before graft);<br>Graft |
| Warp, 2024 [17] | Good | 43F | Yes | LE, UE | — | 1 | Wound care |
| Yeung, 2024 [20] | Good | 28F;<br>32F;<br>40F;<br>33F | Yes;<br>—;<br>Yes;<br>— | LE;<br>LE, UE;<br>UE;<br>LE, UE | — | 3;<br>2;<br>3;<br>2 | I&D;<br>Fasciotomy, I&D;<br>Wound care;<br>Grafts |
| Arango, 2025 [21] | Good | 47 M and 35 F,<br>avg. age 40.3 | — | 43 LE,<br>82 UE,<br>3 trunk | — | 68 with stage 3 or 4 | 51 total surgeries: 7 flaps, 9 grafts, 11 amputations, 2 carpal tunnel releases, 1 fasciotomy, 21 I&Ds only |
| Johnsen, 2025 [24] | Good | 26 M and 29 F,<br>avg. age — | — | 19 LE,<br>55 UE | — | — | 33 wound care,<br>9 graft/allograft, 4 flaps, 7 amputations, 2 I&D only |
| Khaddage, 2025 [22] | Mod | 33F | Yes | LE | — | — | Wound care |
| Novick, 2025 [23] | Good | 55 M and 18 F,<br>avg. age 40.8 | — | 50 LE,<br>35 UE | — | — | — |
| Lutz, 2025 [25] | Good | 15 M and 14 F,<br>avg. age — | — | 26 LE,<br>27 UE,<br>1 trunk | — | 5 with stage 3 or 4 | 3 I&D only; additional treatments not mentioned |

**Table 3.** Summary of compiled data

| Characteristic | Average (SD) or percentage (N of total) | Reporting |
|---|---|---|
| **Age** (years) | 39.0 (8.38) | 274 of 277 reported |
| **Sex** | | 277 of 277 reported |
| Male | 57.0% (158/277) | |
| Female | 43.0% (119/277) | |
| **Area affected by wounds** | | 277 of 277 reported |
| Upper extremity | 83.0% (230/277) | |
| Lower extremity | 53.4% (148/277) | |
| Trunk | 0.040% (11/277) | |
| **Reported wound duration** (months) | 10.7 (10.9) | 15 of 277 reported |
| **Wound stage** | 2.78 (1.17) | 36 of 277 reported |
| 1 | 2.2% (6/277) | |
| 2 | 4.0% (11/277) | |
| 3 | 1.4% (4/277) | |
| 4 | 5.4% (15/277) | |
| Unable to assess | 87.0% (241/277) | |
| **Treatment** | | 275 of 277 reported |
| Wound care only | 14.9% (41/275) | |
| Surgical irrigation and debridement only | 9.8% (27/275) | |
| Skin graft | 9.8% (27/275) | |
| Flap | 5.1% (14/275) | |
| Amputation | 9.5% (26/275) | |
| Care not able to be provided | 0.73% (2/275) | |
| Other: Fasciotomy, thrombectomy, carpal tunnel release, bone reconstruction | 4.0% (11/275) | |
| **Named IVDU** | | N as listed reporting |
| Fentanyl and/or heroin | 44.0% (122/277) | |
| Benzodiazepines | 11.9% (33/277) | |
| Cocaine | 41.5% (114/277) | |
| Methamphetamine/ amphetamine | 13.4% (37/277) | |
| **Reported IDVU at site of wound(s)** | 7.58% (21/277) | N as listed reporting |
| **HIV positive** | 3.6% (10/277) | N as listed reporting |
| **HCV positive** | 39.0% (108/277) | N as listed reporting |
| **Psychiatric condition** | 12.3% (34/277) | N as listed reporting |
| **Unhoused** | 24.5% (68/277) | N as listed reporting |
| **Left AMA** | 42.2% (117/277) | N as listed reporting |

**Table 4.** Study information

| Characteristic | Number of studies (% of total) | Number of patients (% of total) |
|---|---|---|
| **Year of publication** | | |
| 2022 | 2 (11.8%) | 2 (0.72%) |
| 2023 | 5 (29.4%) | 15 (5.42%) |
| 2024 | 5 (29.4%) | 20 (7.2%) |
| 2025 | 5 (29.4%) | 240 (86.6%) |
| **Study location** | | |
| Unable to determine | 1 (5.9%) | 1 (0.36%) |
| Philadelphia, PA | 10 (58.8%) | 259 (93.5%) |
| Hershey, PA | 1 (5.9%) | 3 (1.1%) |
| New Haven, CT | 1 (5.9%) | 3 (1.1%) |
| Columbus, OH | 1 (5.9%) | 2 (0.72%) |
| Chicago, IL | 1 (5.9%) | 1 (0.36%) |
| Denver, CO | 1 (5.9%) | 7 (2.5%) |
| Miami, FL | 1 (5.9%) | 1 (0.36%) |

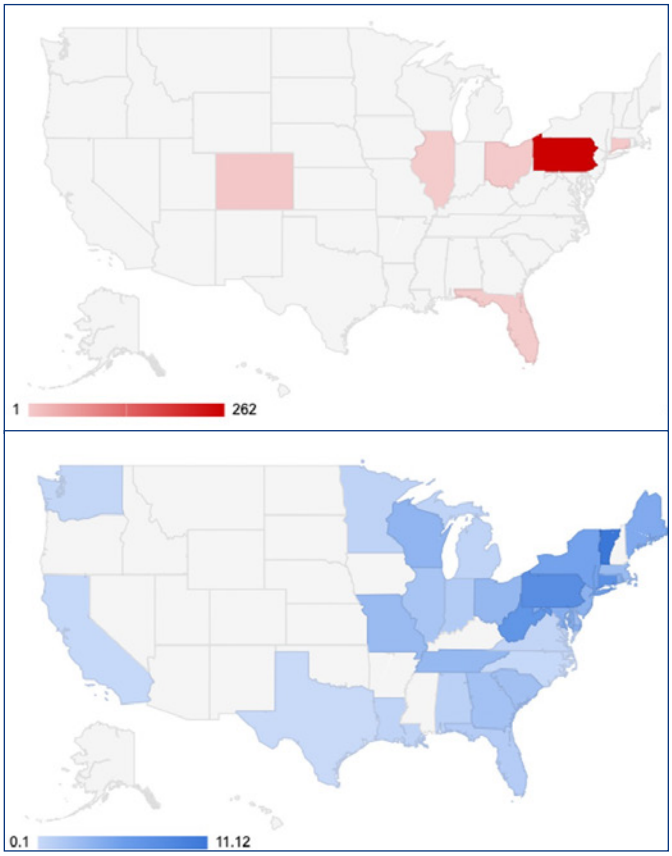
patient-reported wound duration; the average reported wound duration was 10.7 months (±10.9), and ranged from five days to three years. Wound stage was determinable for 36 of 277 patients, utilizing either the case's reported stage or evaluated by the authors using description and/or clinical imaging based on the guidelines established by Retrouvey et al.[14] Of this group, average stage was 2.78 (SD 1.17). Some form of treatment was reported for the majority of patients (275/277). Treatments included local wound care, surgical irrigation and debridement (I&D) only, and additional surgical procedures, including skin graft, flap, and amputation. Additional surgical procedures reported included fasciotomy, thrombectomy, carpal tunnel release, and bone reconstruction.

All included patients were reported to have consumed illicit drugs. Fentanyl or heroin use specifically was reported for 44.0% (122/277) of included patients. Additional substances consumed included benzodiazepines, cocaine, and methamphetamines/amphetamines. Intravenous drug use (IVDU) with injection into the wound site specifically was mentioned in 21/277 patient cases (7.58%). Medical comorbidities mentioned included HIV (10/277; 3.6%), HCV (108/277; 39.0%), and psychiatric diagnosis (34/277; 12.3%). A total of 68 of 277 patients (24.5%) were mentioned to be unhoused, and 117 of 277 (42.2%) were stated to have left the healthcare facility Against Medical Advice (AMA) [**Table 3**].

All included studies were published within the past four years, with 240 of 277 patients (86.6%) identified from studies published in 2025 [**Table 4**]. The temporal trend of recent publications on xylazine-associated wounds is mirrored in the overall publishing data, with review of PubMed-indexed publications on the topic demonstrating the subject matter is receiving increasing attention. Notably, 11 of the

17 included studies were published by institutions within Pennsylvania; these studies accounted for 259 of the 277 total patients (93.5%) [**Table 4**]. Such patient distribution grossly aligns with the 2023 fentanyl-xylazine overdose mortality rates per capita reported by Zhou et al [**Figure 2**].[31]

**Figure 2. [A]** Heat map (red) showing the distribution of all patients represented in this review by state, with highest population density in Pennsylvania. [**B**] Heat map (blue) showing the crude death rate (95% CI) per 100,000 people due to fentanyl-xylazine overdose death in 2023 by state, with highest density in the mid-Atlantic states.[31]




## DISCUSSION

Xylazine, as a street drug adulterant, is increasingly recognized as a growing public health threat due to its association with fatal overdose and distinct pattern of severe, necrotic, soft-tissue wounds.[3] We report on the 277 cases published in 17 studies identified in our systematic review of the literature. Our findings highlight several distinctive features of xylazine-associated wounds. The degree of soft-tissue necrosis xylazine can elicit, especially when injected synergistically with other street drugs, poses a serious threat to limb viability.[32] The wounds most commonly affect the upper extremities and tend to present in advanced stages with a prolonged, festering appearance by the time patients seek medical care.[25] Because of this, local wound care is often insufficient, and many patients require operative intervention and, in some cases, amputation. Collectively, these findings illustrate the significant morbidity of xylazine-associated wounds and emphasize the importance of recognizing this emerging clinical phenomenon.

The clinical patterns identified in this review are consistent with prior literature demonstrating xylazine's destructive and chronic role in the development of soft-tissue injury. Though the exact mechanism by which xylazine elicits tissue injury is not fully understood, evidence suggests a multifactorial etiology. As an alpha-2 adrenergic agonist, it is known that xylazine causes potent vasoconstriction, which predisposes soft tissues to impaired perfusion, local ischemia, and eventual necrosis.[6,7,32] In addition, the high acidity of illicit drug preparations has been proposed to compound xylazine-mediated vasoconstriction, resulting in substantial vascular injury and downstream ischemic damage.[32] Recent research suggests xylazine may also promote systemic effects in the peripheral vasculature, offering a plausible explanation for the wounds that develop distant from the site of injection.[6,9,14,25] Patients report immediate burning sensations and loss of venous access upon injection, leading to repeated injection attempts, use of larger central veins and frequent subcutaneous "skin popping," all of which contribute to xylazine's clinical cascade of wound development.[32]

Taken together, there is a characteristic wound phenotype described across studies that is consistent with our review. There is a predilection for the upper extremity (83.0% in this review) due to its thin dermal layers, especially the extensor surfaces, a common area of injection drug use.[25] Wound beds are often devitalized and form large confluent areas of eschar, slough, and necrosis. Given that wounds tend to be chronic and progressive with an average duration of 10.54 months, involvement of the deep structures, including tendon and bone, can occur in approximately 9–20% of cases.[25,33]

The spectrum of xylazine-associated wounds spans a wide range of severity, chronicity, and depth of involvement, underscoring the utility to reference a standardized disease-specific classification system. Similar to existing frameworks designed for pressure injuries, diabetic ulcers, or burns, deeper wounds often prompt consideration of more aggressive intervention. The staging system proposed by Retrouvey et al for xylazine-associated wounds offers tailored severity stratification based off depth of tissue involvement.[14] In theory, this would facilitate consistency in clinical description and communication across multidisciplinary teams. However, xylazine-associated wounds differ in their early necrosis, lack of blister formation typical of burns, and absence of gangrenous features seen in diabetic foot ulcers. Recent literature attempts to move beyond simple depth. The recently proposed HEAL-X classification system by Terraccino et al represents an emerging tool for xylazine-associated wounds that uses five assessment

domains—History, Extent, Appearance, Location, and Xylazine-specific features, including proximity to injection sites, disproportionately low pain relative to tissue damage severity, absence of surrounding infection, and involvement of underlying structures.[34] This thorough, xylazine-specific, descriptive and organizational tool may be useful to contextualize disease severity, facilitate communication, and improve comparability across future studies, as an extension of the framework established by Retrouvey et al [**Table 1**].[14]

Notably, affected patients were reported to have multiple comorbidities, including HCV, HIV, and psychiatric conditions. Multiple studies mentioned patients were unhoused, and almost half of patients were reported to have left AMA at least once during their treatment. Given the publication bias towards cases with adequate follow-up, it is likely that this reported rate of AMA (42.4%) undercounts the clinical occurrence of this event. The high burden of medical and psychosocial comorbidities among patients with xylazine-associated wounds reflects the profound marginalization and structural vulnerabilities affecting this unique population. It is well established that people who inject drugs face multiple barriers to healthcare access when attempting to seek medical care.[35] On top of the stigma within healthcare, and particularly the fear of judgement by clinicians, there are competing priorities related to substance abuse and mental health needs, including shelter, avoiding withdrawal, transportation, long wait times, and fear of criminalization.[36] Addressing these barriers requires a multifaceted approach. Given that patients with xylazine-associated wounds often show up late and intermittently, low-threshold access care models that prioritize wound stabilization in active users over long-term compliance requirements helps patients who may have been denied care in previously rigid structures. Acknowledging ongoing drug use and providing harm reduction services and safe practices while integrated wound management can lessen the xylazine-associated burden over time. Most importantly, a culture of nonjudgemental, patient-centered care around these therapeutic initiatives is essential for success, especially given the rate of AMA seen in this review. Proactive engagement strategies and a nonpunitive approach to patients who leave against AMA are essential to maintaining continuity of care and preventing further xylazine-associated morbidity.

Such findings that all included studies on xylazine-specific wounds have been published in the past four years, with 86.6% of all cases from manuscripts published in 2025, highlight the recency of this threat, and the need for comprehensive characterization of this condition to address it going forward. Almost all reported patients (93.5%) and most published studies (11 of 17) originated in Pennsylvania. Philadelphia was among the first U.S. cities to document widespread xylazine adulteration in the illicit drug supply, with xylazine detected in less than 2% of fatal heroin/fentanyl overdoses between 2010 and 2015, yet rising to 31% (262 of 858 cases) by 2019.[37] By 2021, xylazine was detected in 91% of all Philadelphia heroin and fentanyl samples, further affirming the city as the epicenter for xylazine-associated harm.[38] However, recent, state-level data from 2022 showed that xylazine-involved overdose death rates were highest in Vermont (10.5 per 100,000 residents) and Connecticut (9.8 per 100,000 residents), suggesting that xylazine's impact has intensified in surrounding northeastern states. While Philadelphia and Pennsylvania remain heavily affected, xylazine is now a nationwide problem, with 43 states reporting at least one xylazine-related overdose death by 2022, and the Northeast demonstrating the highest concentration.[39] Xylazine-related overdose death has now even been reported in Europe.[40]

## Suggestions for Management

Thorough history, exam, and adjunct studies can play important roles in establishing the diagnosis of xylazine-associated wounds.[14,28] History can assess IVDU, injection into wound sites, known xylazine use, and/or travel to a location where the street drug supply is contaminated with xylazine. Physical exam and imaging studies can assess the presence of wounds, depth of tissue involvement, and any characteristic necrotic components. Laboratory investigation that includes toxicology screening with formal xylazine testing, infectious workup, and inflammatory marker review can help confirm diagnosis and trend improvement. Lastly, wound biopsy can help rule out vasculitis or concurrent necrotizing soft tissue infection, if suspected. Once a diagnosis of xylazine-associated wound has been established, management can be guided by clinical stability of patient and depth of soft-tissue involvement.[14] Multidisciplinary care involving infectious disease, psychiatry, addiction medicine, social work, plastic and/or burn surgery, and orthopedic surgery teams is recommended, given the extensive comorbidities affecting the patient population presenting with xylazine-associated wounds and need for close follow-up and continued medical care to optimize outcome. Care must be taken to manage patient expectations, with the understanding that delay of treatment poses limb-threatening consequences.

## Potential Limitations

Since there are few comparative studies, the present review consists primarily of case series and case reports, which are considered low-quality research prone to the impact of publication bias. We have assessed the articles on quality using the checklist by Murad et al to minimize this limitation.[13] Published studies originated within the orthopedic surgery, plastic surgery, addiction medicine, and pharmacy literature; as such, characteristics reported varied based on study focus and readership interest, and not all variables assessed were reported for each case. Conclusions drawn are limited by lack of a control population. Generalizing findings, suggesting treatment, and inferring causality remain inappropriate

in the setting of small sample size and the heterogeneity of reported cases. Follow-up data is limited by both the case report/series structure and the psychosocial factors that impact the PWID patient population. Nonetheless, we find this summary of all reported cases necessary to summarize what is currently known about xylazine-associated wound presentation and treatment to guide future research and policy, and help clinicians identify and manage the xylazine-associated wounds affecting this extremely vulnerable patient population appropriately.

## SUMMARY

As xylazine use increases, the prevalence of xylazine-associated wounds is also expected to increase, with devasting consequences and increasing need for multidisciplinary management. This article presents the results of all 277 published cases reporting on xylazine-associated wounds to offer a perspective on the demographic, psychosocial, and medical factors of affected patients and report on treatment strategies and outcomes. Early intervention, multidisciplinary care, and increased awareness are essential to help mitigate the morbidity of this growing public health threat.

### References


1. Friedman J, Montero F, Bourgois P, et al. Xylazine spreads across the US: a growing component of the increasingly synthetic and polysubstance overdose crisis. *Drug Alcohol Depend*. 2022;233:109380.
2. Nunez J, DeJoseph ME, Gill JR. Xylazine, a veterinary tranquilizer, detected in 42 accidental fentanyl intoxication deaths. *The American Journal of Forensic Medicine and Pathology*. 2021;42(1):9-11.
3. Gupta R, Holtgrave DR, Ashburn MA. Xylazine—medical and public health imperatives. *N Engl J Med*. 2023;388(24):2209-2212.
4. Spencer MR, Cisewski JA, Warner M, Garnett MF. Drug overdose deaths involving xylazine: United States, 2018–2021; 2023.
5. Policy OoNDC. Biden-Harris administration designates fentanyl combined with xylazine as an emerging threat to the United States; 2023.
6. Ruiz-Colón K, Chavez-Arias C, Díaz-Alcalá JE, Martínez MA. Xylazine intoxication in humans and its importance as an emerging adulterant in abused drugs: a comprehensive review of the literature. *Forensic Sci Int*. 2014;240:1-8.
7. D'Orazio J, Nelson L, Perrone J, Wightman R, Haroz R. Xylazine adulteration of the heroin–fentanyl drug supply: a narrative review. *Ann Intern Med*. 2023;176(10):1370-1376.
8. Perrone J, Haroz R, D'Orazio J, et al. National Institute on Drug Abuse Clinical Trials Network meeting report: managing patients exposed to xylazine-adulterated opioids in emergency, hospital and addiction care settings. *Ann Emerg Med*. 2024;84(1):20-28.
9. Bishnoi A, Singh V, Khanna U, Vinay K. Skin ulcerations caused by xylazine: A lesser-known entity. *J Am Acad Dermatol*. 2023;89(2):e99-e102.
10. Alexander RS, Canver BR, Sue KL, Morford KL. Xylazine and overdoses: trends, concerns, and recommendations. *Am J Public Health*. 2022;112(8):1212-1216.
11. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *International journal of surgery*. 2021;88:105906.
12. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. *Systematic Reviews*. 2016:1:210. doi:10.1186/s13643-016-0384-4
13. Murad MH, Sultan S, Haffar S, Bazerbachi F. Methodological quality and synthesis of case series and case reports. *BMJ Evid Based Med*. Apr 2018;23(2):60-63. doi:10.1136/bmjebm-2017-110853
14. Retrouvey H, Meyer MA, Ipaktchi K, Maertens A, Folchert M, Lauder A. Management of Xylazine-Induced Soft-Tissue Necrosis: A Review of 20 Cases. *J Am Acad Orthop Surg*. 2024;32(23):e1219-e1225. doi:10.5435/JAAOS-D-24-00125
15. Ehrman-Dupre R, Kaigh C, Salzman M, Haroz R, Peterson L-K, Schmidt R. Management of xylazine withdrawal in a hospitalized patient: a case report. *J Addict Med*. 2022;16(5):595-598.
16. Dowton A, Doernberg M, Heiman E, et al. Recognition and Treatment of Wounds in Persons Using Xylazine: A Case Report from New Haven, Connecticut. *J Addict Med*. 2023;17(6):739-741. doi:10.1097/ADM.0000000000001198
17. Warp PV, Hauschild MH, Serota DP, et al. A confirmed case of xylazine-induced skin ulcers in a person who injects drugs in Miami, Florida. *Harm Reduction Journal*. 2024;21(1)64. doi:10.1186/s12954-024-00978-z
18. Naidu K, Morales CZ, Card EB, Lin IC. Increasing Prevalence of Xylazine and Worsening Upper-Extremity Wounds in Injection Drug Use: A Local Phenomenon With National Implications. Review. *J Hand Surg Am*. 2024;49(11):1129-1135. doi:10.1016/j.jhsa.2024.07.017
19. Sun A, Borusiewicz M, Johnson TS. Radial nerve palsy in patients presenting with fentanyl/xylazine wounds of the dorsal forearm: A case series. *Orthoplastic Surgery*. 2024;15:15-20. doi:10.1016/j.orthop.2024.01.004
20. Yeung HM, Worrilow WM. Treatment of Xylazine-Associated Injection Skin Injuries. *Case Reports in Dermatological Medicine*. 2024;(1)8618440. doi:10.1155/2024/8618440
21. Arango SD, Flynn JC, Zeitlin JH, Weir TB, Miller AJ. Xylazine-Associated Necrotic Upper-Extremity Wounds: A Single Hospital System's Experience with 82 Patients and 125 Wounds. *J Bone Joint Surg*. 2025;107(3):279-286. doi:10.2106/JBJS.24.00534
22. Khaddage S, Schultz K, Le T. The XYZs of xylazine: Management of withdrawal and complications. *Am J Health Syst Pharm*. 2025;83(8). DOI:10.1093/ajhp/zxaf325
23. Novick E, Seval N, Coppock D, et al. Clinical and Demographic Characteristics of Hospitalized Patients With Xylazine-related Wounds. *J Addict Med*. 2024;10.1097.
24. Johnsen P, Morway GR, Jackson A, et al. The Management of Upper-Extremity Xylazine-Associated Wounds. *J Hand Surg Am*. 2025;50(3):331-339. doi:10.1016/j.jhsa.2024.11.017
25. Lutz L, McFadden R, Xu L, et al. Wound characteristics among patients exposed to xylazine. *JAMA dermatology*. 2025;161(1):75-80.
26. Malayala SV, Papudesi BN, Bobb R, Wimbush A. Xylazine-induced skin ulcers in a person who injects drugs in Philadelphia, Pennsylvania. *Cureus*. 2022;14(8).
27. O'Neil J, Kovach S. Xylazine-associated skin injury. *N Engl J Med*. 2023;388(24):2274-2274.
28. Rose L, Kirven R, Tyler K, Chung C, Korman AM. Xylazine-induced acute skin necrosis in two patients who inject fentanyl. *JAAD Case Reports*. 2023;36:113-115.
29. Soderquist M, Delgado G, Abdelfattah H, Thoder J, Solarz M. Necrotic upper-extremity infections in people who inject drugs: a case series. *The Journal of Hand Surgery*. 2024;49(5):459-464.
30. Rengifo S, Ilyas AM, Tosti R. Upper extremity soft tissue wound related to xylazine-laced fentanyl intravenous (IV) drug abuse: a case report. *SurgiColl*. 2023;1(1).

31. Zhu DT, Cano M. Fentanyl-xylazine overdose deaths in the USA, 2018–2023. *Inj Prev*. 2025:ip-2024-045596. doi:10.1136/ip-2024-045596
32. Ciccarone D, Karandinos G, Krotulski A, et al. Tranq burn: Exploring the etiology of xylazine-related soft tissue injuries. *International Journal of Drug Policy*. 2025;142104830. doi:10.1016/j.drugpo.2025.104830
33. Makhoul AT, Morales CZ, Card EB, et al. Surgical Management of Xylazine-Associated Wounds: A Retrospective Review and Algorithmic Approach. *Ann Plast Surg*. 2025;10:1097.
34. Terracciano DJ, Steinhauser SF, Introcaso CE, et al. HEAL-X: A Novel Classification System for Xylazine Associated Wounds. *Int Wound J*. 2025;22(9):e70758. doi:10.1111/iwj.70758
35. Jawa R, Blakemore S, Murray S, et al. Wound Care Capacity of the Addiction Workforce in the Setting of Xylazine. *J Addict Med*. 2024;18(6):723-726. doi:10.1097/ADM.0000000000001352
36. Attwood LO, Schroeder SE, Vujovic O, et al. Qualitative analysis of barriers and facilitators to healthcare engagement for people with injecting-related invasive infections using a social ecological framework. *Addiction*. 2025;120(12):2476-2488.
37. Johnson J, Pizzicato L, Johnson C, Viner K. Increasing presence of xylazine in heroin and/or fentanyl deaths, Philadelphia, Pennsylvania, 2010-2019. *Inj Prev*. Aug 2021;27(4):395-398. doi:10.1136/injuryprev-2020-043968
38. Bettigole C, Franklin F, Hom J. Health alert: risks of xylazine use and withdrawal in people who use drugs in Philadelphia. Philadelphia Department of Public Health, Health Commissioner's Office; 2022.
39. Cano M, Daniulaityte R, Marsiglia F. Xylazine in Overdose Deaths and Forensic Drug Reports in US States, 2019-2022. *JAMA Network Open*.2024;7(1):e2350630-e2350630.doi:10.1001/jamanetworkopen.2023.50630
40. Rock KL, Lawson AJ, Duffy J, Mellor A, Treble R, Copeland CS. The first drug-related death associated with xylazine use in the UK and Europe. Article. *J Forensic Leg Med*. 2023;97102542. doi:10.1016/j.jflm.2023.102542



## Authors

Catherine M. Call, MD, Brown University Department of Orthopaedics, Providence, RI.

Christopher J. Lama, MD, Brown University Department of Orthopaedics, Providence, RI.

Sean L. Agrodnia, BA, Tufts University School of Medicine, Boston, MA.

Jonathan Liu, MD, Brown University Department of Orthopaedics, Providence, RI.

Julia A. Katarincic, MD, Brown University Department of Orthopaedics, Providence, RI.

Joseph A. Gil, MD, Brown University Department of Orthopaedics, Providence, RI.



## Disclosures

The authors declare no disclosures.

**Conflict of Interests:** The authors declare no conflicts of interest.

**Acknowledgments:** The authors declare no acknowledgments.



## Correspondence

Catherine M. Call, MD
Brown University Department of Orthopaedics
2 Dudley Street
Providence, RI 02905
Catherine_call@brown.edu

# Shotgun Metagenomics Identify Unique Changes of the Intestinal Microbiome in Pediatric Survivors of Acute Lymphoblastic Leukemia

ROMA BHUTA, DO, MPH; THOMAS KUNTZ, PhD; BRADLEY DENARDO, MD; XOCHITL MORGAN, PhD; JASON SHAPIRO, MD


## ABSTRACT

**BACKGROUND:** Intestinal microbiota plays an important role in human health and metabolism. Microbial dysbiosis has been observed in various chronic conditions, many of which are late effects of leukemia treatment. We previously observed significant differences in the gut microbiome of pediatric ALL survivors compared to healthy sibling controls. Shotgun metagenomic analyses were completed to better characterize the durability and metabolic implication of these changes.

**PROCEDURE:** Shotgun metagenomic sequencing was completed on DNA extracted from stool samples obtained from nine survivors of childhood acute lymphoblastic leukemia (ALL) and 10 healthy sibling controls.

**RESULTS:** Beta diversity (dissimilarity between samples) was significant with survivors' microbiomes becoming more similar to siblings further from treatment. The functional potential of gluconate-5-dehydrogenase enzyme (Ga5DH) decreased significantly with time from treatment. Relative abundance of *Faecalibacterium prausnitzii* was identified as the major contributor to differential Ga5DH expression within subjects.

**CONCLUSIONS:** Time from treatment has a significant effect on functional microbial recovery in ALL. Increased time from chemotherapy corresponds to microbiomes becoming more similar to sibling controls in select dyads. More significant differences were noted in patients closer to treatment. Additional, prospective studies will focus on deeper characterization of these findings and further investigate the functional role of Ga5DH in ALL survivors.


**KEYWORDS:** Metagenomics; gut microbiome; pediatric; children; cancer

## INTRODUCTION

The treatment of pediatric acute lymphoblastic leukemia (ALL) has progressed over the last several decades with 5-year survival rates now above 90%.[1] With improved risk stratification and targeted therapy resulting in increased overall survival, minimizing late effects of treatment and decreasing survivorship-related mortality represent vital aspects of long-term care. Fifty percent of survivors of childhood ALL report at least once chronic medical condition and are 2.8 times more likely than siblings to describe having multiple chronic medical conditions.[2] Late effects of therapy include subsequent malignancy as well as musculoskeletal, cardiovascular, and neurologic diseases.[2,3]

Durable alterations of the intestinal microbiota may contribute to some of the late effects seen in survivors of childhood ALL. The gut microbiome is an integral part of maintaining human health through its impact on metabolic homeostasis and immune function.[4] It is impacted by a variety of factors, many of which overlap with standard pediatric ALL therapy, including diet, medications, environmental exposures, and infection.[5,6] Microbial dysbiosis, or imbalance of the gut microbiota following intestinal disruption, can contribute to a variety of pathologies, including cardiovascular disease, gastrointestinal disease, neurologic disease, endocrinopathies, and malignancy.[7,8]

We previously reported on 16S rRNA gene sequencing performed on gut microbiome samples from nine survivors of ALL compared to 10 healthy sibling controls. A significant difference was seen in the composition of the gut microbiome of pediatric ALL survivors compared to healthy siblings. This observation supports the hypothesis that ALL treatment regimens may result in durable changes of the gut microbiome which can contribute to the long-term health complications often observed in this population.[9]

Shotgun metagenomic sequencing is able to assess cumulative DNA within a sample and provide additional information regarding microbial gene content compared to targeted sequencing of 16S rRNA gene hypervariable regions. Such analyses allow for improved taxonomic resolution and provide a more detailed understanding of functional profiles.[10,11] We sought to better understand the functional implications of our initial findings in survivors of pediatric ALL via shotgun metagenomic analyses.

## MATERIALS AND METHODS

Gut microbiome shotgun metagenomic sequencing was completed on DNA samples obtained from a previously completed, approved institutional review board, single-center cohort study.[9] Stool samples were collected to assess the gut microbiome composition of survivors of pediatric and

adolescent pre-B-cell ALL compared to their siblings. Eligible patients were between the ages of 3 and 30, had a history of pre-B-cell ALL currently in remission, and were at least six months from the completion of therapy. All participants were required to have at least one biological sibling who lived in the same home full-time. Exclusion criteria included history of bone marrow transplant and known autoimmune conditions or inflammatory bowel disease. Individuals with use of antibiotics or a diagnosis of gastrointestinal illness (defined as vomiting and/or diarrhea) within 30 days of enrollment were excluded, as well as those taking medications known to impact the gut microbiome, such as immunosuppressive agents, nonsteroidal anti-inflammatory drugs, and proton pump inhibitors. Three stool samples were collected from each study participant, each a minimum of 24 hours apart via a standardized method. Detailed description of methods and results from these analyses were previously published.[9]

Metagenomic sequencing was completed by Novogene Corporation, Inc. for quality control of the DNA samples, library construction, and sequencing. Sequencing libraries were generated using NEBNext® Ultra™DNA Library Prep Kit for Illumina (NEB, USA) and sequenced on an Illumina HiSeq platform, following manufacturer's recommendations. Sequencing data was processed using the bioBakery meta'omics workflow, using the standard pipeline with default parameters.[12] KneadData v0.12.0 was used for quality control of raw reads, including trimming, adapter removal, and removal of off-target reads from the default hg37 and human contamination database. No samples fell under a 10 million final read, quality-control cutoff. Species-level taxonomic profiles were generated using MetaPhlAn v3.0.14 and the CHOCOPhlAn v30 database.[13] Functional profiling was performed using HUMAnN v3.0.0 with UniRef gene families grouped into enzyme commission number (EC) for downstream analysis.[14]

Data was analyzed using R 4.3.0. The vegan package was used for calculation of ecological diversity measurements and whole-community statistical tests. Alpha and beta diversity were quantified as Shannon diversity and Bray-Curtis dissimilarity, respectively. Permutation-based ANOVA was performed using the adonis2 function. The MaAsLin2 v1.18.0 package was used for linear modeling, for which species were filtered at a threshold of minimum 0.1% relative abundance in over 10% of samples.[15] Total sum scaling was used, and species were log-transformed with a pseudocount of half the minimum non-zero value for variance stabilization. Resulting p-values from linear modeling were adjusted for false discovery using the Benjamini and Hochberg method via the p.adjust function in R, and q-values <0.25 were reported as significant. Sequencing data is deposited in Sequencing Read Archive as BioProject PRJNA1235679.

## RESULTS

### Patient Information

Nine survivors of ALL and 10 siblings were enrolled [**Table 1**].[9] All survivors had a history of pre B cell ALL and were treated according to standard chemotherapy protocols at the time of diagnosis. There was a fairly equal sex distribution (4 females, 5 males). At the time of stool collection, the median age of survivors was 11 years (4–19 years), and the median age of siblings was 12.5 years (5–19). Fifty-seven stool samples were collected. Median time from end of leukemia therapy to stool collection was 24 months (6.5–114 months).

### Species Composition

A total of 247 species were initially identified by Meta PhlAn v3.0.14.[13] The 15 species with highest mean relative abundance were plotted and inspected to assess the sample microbial compositions and its consistency between replicates [**Figure 1**]. Four samples were omitted from analyses. Sample RB48 (one stool sample from patient 10) had a taxonomic composition vastly different from the other two samples from the same patient, suggesting a quality issue. The taxonomic composition of three stool samples from Patient 1 was an extreme outlier compared to all other samples, possibly due to underlying diagnosis of Down Syndrome. Thus, sample RB48 and the samples from Patient 1 and their corresponding sibling were omitted from subsequent analyses. A principal coordinate analysis (PCoA) plot was created to demonstrate the relationship between survivor and sibling samples [**Figure 2**].

**Table 1.** Patient Demographics

| Survivor ID | Sex of Survivor | Age of Survivor at Time of Stool Collection (years) | Age at Diagnosis (years) | NCI Risk stratification | Time from End of Therapy (months) | Age of Sibling at Time of Stool Collection (years) |
|---|---|---|---|---|---|---|
| 1 | F | 7 | 4 | SR | 6.5 | 5 |
| 2 | M | 11 | 6 | VHR | 24 | 12 |
| 3 | F | 10 | 1 | SR | 71 | 11 |
| 4 | M | 15 | 10 | SR | 38 | 17 |
| 5 | F | 15 | 11 | HR | 24 | 13 |
| 6 | M | 9 | 4 | SR | 38.5 | 14, 11 |
| 7 | M | 19 | 16 | HR | 23 | 15 |
| 8 | F | 4 | 1 | SR | 8.5 | 7 |
| 9 | M | 17 | 4 | SR | 114 | 19 |

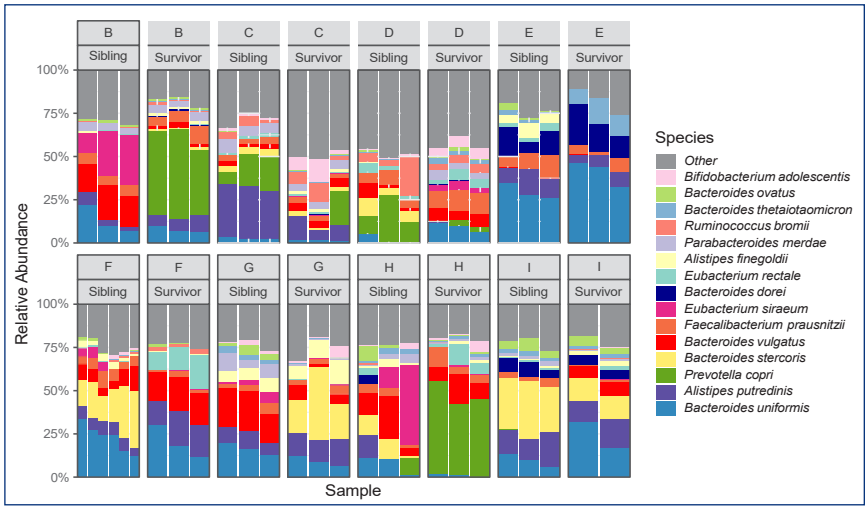
Nine survivors of childhood ALL and 10 siblings were enrolled on this study. Median time from end of therapy was 24 months. NCI= National Cancer Institute, F= female, M= male

## Alpha and Beta Diversity

Alpha diversity, or within sample evenness and richness, was assessed using the inverse Simpson index. There was no significant difference between survivors and siblings when tested by linear model, controlling for subject and family as random effects ($p = 0.635$). Time from treatment also did not significantly affect alpha diversity among survivors ($p = 0.309$). Beta diversity, or between-sample dissimilarity, was quantified using Bray-Curtis dissimilarity. Survivor vs. sibling status did not significantly affect beta diversity in a model controlling for family and permuting metadata blocked by subject ($R^2 = 0.034$, $p = 0.832$, permutation-based ANOVA).[16] Within survivors, time elapsed since chemotherapy was significant ($R^2 = 0.249$, $p = 0.019$, permutation-based ANOVA). Bray-Curtis dissimilarity between survivors and siblings within the same family was used as a metric of the degree of dysbiosis of survivor microbiomes. Linear modeling was used to assess the relationship between time since chemotherapy and difference between survivor and sibling microbiomes (coef = –0.0021, p = 5.36e-05). There was a downward trend, indicating that survivors' microbiomes were more similar to siblings at time points further from treatment [**Figure 3**]. While a robust measure of expected familial dissimilarity within healthy controls was not available, one pair of siblings in a single family had a mean dissimilarity of 0.36, which is comparable to the samples with the longest elapsed time since chemotherapy.

**Figure 1. Taxonomic composition of samples**

Bacterial separation based on taxonomic family level are represented by color variation. One hundred twenty-two species and 60 genera were present after basic filtering. The 15 species with the highest mean relative abundance were plotted for each stool sample.




## Taxonomic and functional associations

The association between survivor status and the relative abundance of each microbiome feature (i.e., species and EC) was tested using the MaAsLin2 framework. Linear mixed models were constructed with patient ID and family ID as random effects to account for repeated sampling. No significant associations were observed.

When analyzing months from chemotherapy in survivors, the functional potential of gluconate-5-dehydrogenase enzyme (Ga5DH) was found to decrease significantly with time since treatment (q = 0.025) [**Figure 4**]. The species *Faecalibacterium prausnitzii* was identified as the major

**Figure 2. PCoA plot of survivors of ALL and their siblings**

Samples largely cluster by survivor and family with small separations between points from the same subject, which is expected from the bar plots and experimental design.

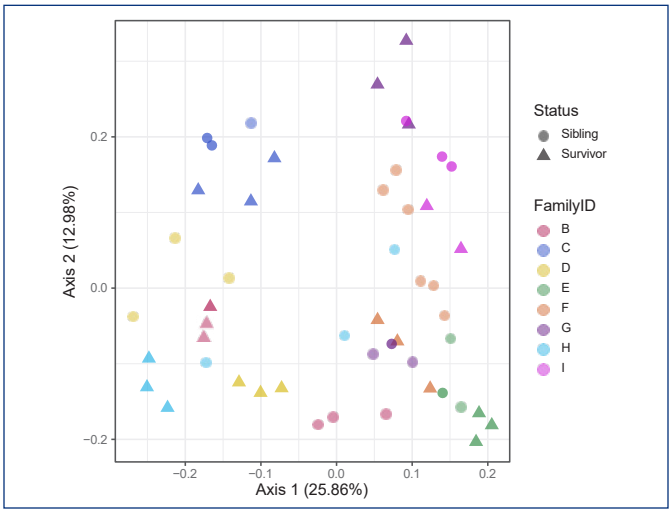



**Figure 3. Beta diversity between survivors and siblings within families**

The downward trend indicated microbiomes of survivors were more similar to siblings at times further from healthy siblings.

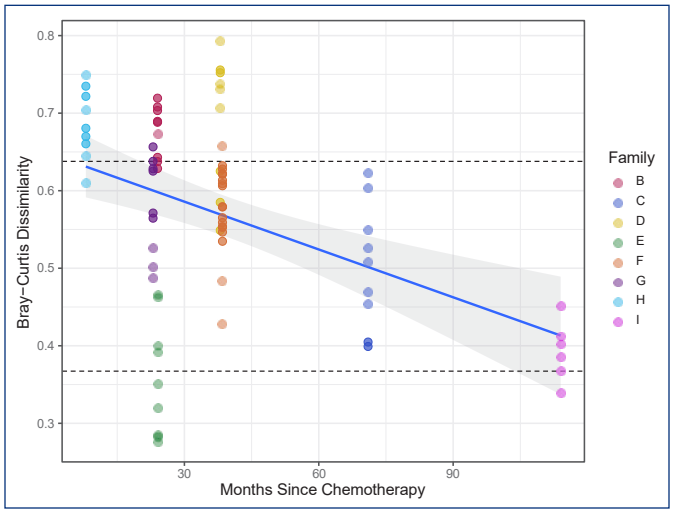


**Figure 4. Abundance of Gluconate-5-dehydrogenase enzyme in survivors, as a function of time since chemotherapy**

The functional potential of gluconate-5-dehydrogenase in survivors decreases the further away from chemotherapy.

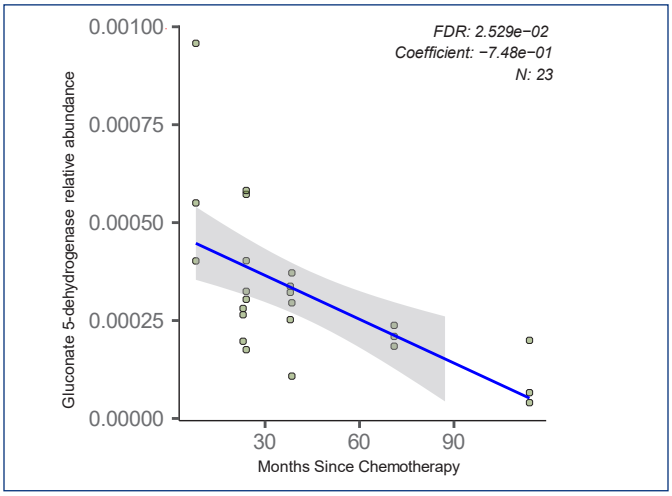
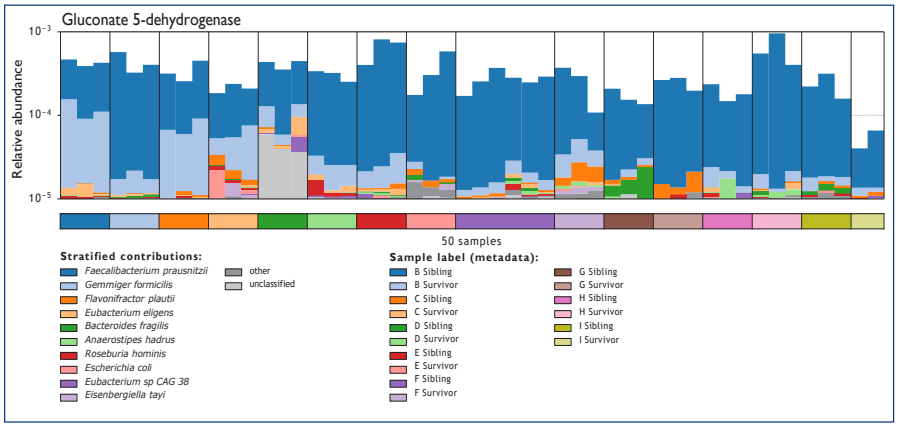



**Figure 5. Contributions of microbial species to measured gluconate-5-dehydrogenase, stratified by subjects**

The species Faecalibacterium prausnitzii was identified as the major contributor in most samples to the relative abundance of Ga5DH in subjects.




contributor in most samples to the relative abundance of Ga5DH in subjects [**Figure 5**]. However, the overall abundance of *Faecalibacterium prausnitzii* was not associated with time from treatment (p = 0.08).

## DISCUSSION

This study compared the intestinal microbiota of pediatric ALL survivors and healthy siblings via next generation sequencing with shotgun metagenomic analysis. Prior studies have been limited and relied on 16S rRNA sequencing to demonstrate that certain gut microbiome changes can be seen in ALL survivors.[17-19] Thomas et al found that members of *Ruminococcaceae, Lachnospiraceae,* and *Faecalibacterium* were significantly depleted in survivors compared to siblings.[17] Chua et al also reported a decrease in *Faecalibacterium* and alterations in immune regulation in survivors of ALL.[19] Our previous work added to these studies and demonstrated a significant difference in alpha and beta diversity in ALL survivors compared to healthy sibling controls.[9]

Shotgun metagenomic sequencing allowed for better understanding of the differences between our two cohorts with higher species resolution, assessment of functionality, and improved accuracy due to less amplification during library preparation. While survivor status alone was not a significant predictor of overall microbiome community signatures, there was evidence that time from treatment had a significant effect on recovery. For within-family comparisons, the Bray-Curtis dissimilarities for each survivor sample against each sibling sample were used as an approximation of deviation from a baseline state. Previous work has established that shared environment and kinship exert a stronger influence than genetics on microbial similarity amongst family members.[20] Therefore, large differences between survivors and siblings may indicate treatment-induced dysbiosis.[21] Upper and lower reference points were established by comparing unrelated study participants and a pair of untreated siblings, respectively. Our study demonstrated that longer duration from chemotherapy exposure is associated with increasing similarity of subjects' microbiome composition compared to their siblings. Only two families had sample pairs as similar as untreated siblings, one of which was the survivor sampled furthest from treatment. For select survivors closer to treatment, the difference between sibling microbiomes was approximately as large as the difference between unrelated study participants. This supports the notion that microbial dysbiosis may persist for years following completion of chemotherapy.[22]

Microbiome feature associations with time within the survivor cohort should provide reasonable estimates of longitudinal trends, particularly if a feature is relatively conserved across healthy subjects. This is more likely to be observed in functional profiles rather than species.[23] Using sibling comparators as a survivor baseline in interaction models was precluded by limited sample size. The relative abundance of Ga5DH enzyme was found to have a significant negative association with time from end of therapy. Ga5DH catalyzes a reversible reduction of 5-ketogluconate to D-gluconate.[24] D-gluconate is an important source of carbon for many microorganisms and may play a role in bacterial survival and virulence.[25] Additional studies are needed to

verify a within-patient decrease in Ga5DH and investigate its role in the gut microbiome in survivors of ALL. Further work will be needed to better understand if there are clinical implications of Ga5DH disruption in survivors of ALL.

Our study had several strengths and limitations. Our design pairing survivors with healthy siblings allowed for the control of various factors known to impact the gut microbiome such as genetics, environment, and diet. By usings siblings as the comparator group, a per-patient microbiome baseline could be created where one would expect the microbiome of survivors to regress to over time after treatment. Collecting three different samples from each participant also allowed for better assessment of outliers and technical artifacts. Shotgun metagenomic sequencing allowed for more precise taxonomic assignments than previous 16S rRNA studies, as well as functional profiling. Our primary limitation was sample size precluding further powered analyses to expand on some of the perturbations seen. Samples from one patient (patient 1) in our survivorship cohort were removed due to a significant difference in the taxonomic composition compared to other participants, likely due to underlying Down Syndrome. Their corresponding sibling was also removed from analyses. One sample from patient 10 (labeled RB48) was also omitted from analyses as its taxonomic composition varied significantly compared to the other samples from that same patient, raising concern for a technical or experimental error as such variations would not be expected in samples collected within one month of one another. By allowing samples to be taken at different times after the completion of chemotherapy, we were less powered to see consistent associations between subjects and treatment history at specific time points. Conversely, this allowed for better assessment of treatment recovery, albeit not as well as true longitudinal sampling. General aspects of microbiome recovery from chemotherapy are not currently well described because of the difficulty of sample acquisition. Longitudinal designs require a long sampling time so many studies are either ongoing or utilize older microbiome sequencing and analysis methodologies. Increasing sample size and length of time from end of therapy to stool collection will be critical to better understand the changes demonstrated in our study.

While the cure rate of pediatric ALL is high in children, the multimodal treatment regimen needed to maximize survival is intense and associated with long-term effects. Microbial dysbiosis from various treatment exposures may represent a pathologic mechanism for the development of long-term side effects of such therapy. The microbiome is known to have important clinical implications, especially with regards to immune development and function. Early life perturbations in the microbiome have been demonstrated to have long lasting effects, so disruptions are particularly concerning if recovery of the microbiome is slow compared to conditions such as illness and antibiotic usage.[26] Furthermore, survivors' microbiomes might never return to their pre-treatment state, instead developing a new equilibrium that is either more or less healthy.[27] Additional studies are required to understand how microbial dysbiosis is associated with specific multi-modal ALL treatment and whether interventions can be utilized to support microbiome recovery during and following treatment. The current results are a strong step in determining this relationship and will serve as the basis for prospective research in survivors of childhood ALL.

## References


1. Inaba H, Mullighan CG. Pediatric acute lymphoblastic leukemia. *Haematologica.* 2020 Nov 1;105(11):2524-2539. doi: 10.3324/haematol.2020.247031. PMID: 33054110.
2. Mody R, Li S, Dover DC, Sallan S, Leisenring W, Oeffinger KC, Yasui Y, Robison LL, Neglia JP. Twenty-five-year follow-up among survivors of childhood acute lymphoblastic leukemia: a report from the Childhood Cancer Survivor Study. *Blood.* 2008 Jun 15;111(12):5515-23. doi: 10.1182/blood-2007-10-117150. Epub 2008 Mar 11. PMID: 18334672.
3. Liu W, Cheung YT, Conklin HM, Jacola LM, Srivastava D, Nolan VG, Zhang H, Gurney JG, Huang IC, Robison LL, Pui CH, Hudson MM, Krull KR. Evolution of neurocognitive function in long-term survivors of childhood acute lymphoblastic leukemia treated with chemotherapy only. *J Cancer Surviv*. 2018 Jun;12(3):398-406. doi: 10.1007/s11764-018-0679-7. Epub 2018 Feb 27. PMID: 29484542.
4. Hou K, Wu ZX, Chen XY, Wang JQ, Zhang D, Xiao C, Zhu D, Koya JB, Wei L, Li J, Chen ZS. Microbiota in health and diseases. *Signal Transduct Target Ther*. 2022 Apr 23;7(1):135. doi: 10.1038/s41392-022-00974-4. PMID: 35461318.
5. Duerkop BA, Vaishnava S, Hooper LV. Immune responses to the microbiota at the intestinal mucosal surface. *Immunity.* 2009 Sep 18;31(3):368-76. doi: 10.1016/j.immuni.2009.08.009. PMID: 19766080.
6. Kostic AD, Xavier RJ, Gevers D. The microbiome in inflammatory bowel disease: current status and the future ahead. *Gastroenterology.* 2014 May;146(6):1489-99. doi: 10.1053/j.gastro.2014.02.009. Epub 2014 Feb 19. PMID: 24560869.
7. de Vos WM, Tilg H, Van Hul M, Cani PD. Gut microbiome and health: mechanistic insights. *Gut.* 2022 May;71(5):1020-1032. doi: 10.1136/gutjnl-2021-326789. Epub 2022 Feb 1. PMID: 35105664.
8. Valdes AM, Walter J, Segal E, Spector TD. Role of the gut microbiota in nutrition and health. *BMJ.* 2018 Jun 13;361:k2179. doi: 10.1136/bmj.k2179. PMID: 29899036.
9. Bhuta R, DeNardo B, Wang J, Atoyan J, Zhang Y, Nelson D, Shapiro J. Durable changes in the gut microbiome in survivors of childhood acute lymphoblastic leukemia. *Pediatr Blood Cancer.* 2021 Dec;68(12):e29308. doi: 10.1002/pbc.29308. Epub 2021 Aug 31. PMID: 34467651.
10. Durazzi F, Sala C, Castellani G, Manfreda G, Remondini D, De Cesare A. Comparison between 16S rRNA and shotgun sequencing data for the taxonomic characterization of the gut microbiota. *Sci Rep*. 2021 Feb 4;11(1):3030. doi: 10.1038/s41598-021-82726-y. PMID: 33542369.
11. Peterson D, Bonham KS, Rowland S, Pattanayak CW; RESONANCE Consortium; Klepac-Ceraj V. Comparative Analysis of 16S rRNA Gene and Metagenome Sequencing in Pediatric Gut Microbiomes. *Front Microbiol*. 2021 Jul 15;12:670336. doi: 10.3389/fmicb.2021.670336. PMID: 34335499.
12. Beghini F, McIver LJ, Blanco-Míguez A, Dubois L, Asnicar F, Maharjan S, Mailyan A, Manghi P, Scholz M, Thomas AM, Valles-Colomer M, Weingart G, Zhang Y, Zolfo M, Huttenhower C, Franzosa EA, Segata N. Integrating taxonomic, functional,

and strain-level profiling of diverse microbial communities with bioBakery 3. *Elife*. 2021 May 4;10:e65088. doi: 10.7554/eLife.65088. PMID: 33944776.

13. Truong DT, Franzosa EA, Tickle TL, Scholz M, Weingart G, Pasolli E, Tett A, Huttenhower C, Segata N. MetaPhlAn2 for enhanced metagenomic taxonomic profiling. *Nat Methods*. 2015 Oct;12(10):902-3. doi: 10.1038/nmeth.3589. Erratum in: Nat Methods. 2016 Jan;13(1):101. PMID: 26418763.
14. Franzosa EA, McIver LJ, Rahnavard G, Thompson LR, Schirmer M, Weingart G, Lipson KS, Knight R, Caporaso JG, Segata N, Huttenhower C. Species-level functional profiling of metagenomes and metatranscriptomes. *Nat Methods*. 2018 Nov;15(11):962-968. doi: 10.1038/s41592-018-0176-y. Epub 2018 Oct 30. PMID: 30377376.
15. Mallick H, Rahnavard A, McIver LJ, Ma S, Zhang Y, Nguyen LH, Tickle TL, Weingart G, Ren B, Schwager EH, Chatterjee S, Thompson KN, Wilkinson JE, Subramanian A, Lu Y, Waldron L, Paulson JN, Franzosa EA, Bravo HC, Huttenhower C. Multivariable association discovery in population-scale meta-omics studies. *PLoS Comput Biol*. 2021 Nov 16;17(11):e1009442. doi: 10.1371/journal.pcbi.1009442. PMID: 34784344.
16. Lloyd-Price J, Arze C, Ananthakrishnan AN, Schirmer M, Avila-Pacheco J, Poon TW, Andrews E, Ajami NJ, Bonham KS, Brislawn CJ, Casero D, Courtney H, Gonzalez A, Graeber TG, Hall AB, Lake K, Landers CJ, Mallick H, Plichta DR, Prasad M, Rahnavard G, Sauk J, Shungin D, Vázquez-Baeza Y, White RA 3rd; IBDMDB Investigators; Braun J, Denson LA, Jansson JK, Knight R, Kugathasan S, McGovern DPB, Petrosino JF, Stappenbeck TS, Winter HS, Clish CB, Franzosa EA, Vlamakis H, Xavier RJ, Huttenhower C. Multi-omics of the gut microbial ecosystem in inflammatory bowel diseases. *Nature*. 2019 May;569(7758):655-662. doi: 10.1038/s41586-019-1237-9. Epub 2019 May 29. PMID: 31142855.
17. Thomas R, Wong WSW, Saadon R, Vilboux T, Deeken J, Niederhuber J, Hourigan SK, Yang E. Gut microbial composition difference between pediatric ALL survivors and siblings. *Pediatr Hematol Oncol*. 2020 Sep;37(6):475-488. doi: 10.1080/08880018.2020.1759740. Epub 2020 May 19. PMID: 32427521.
18. Chua LL, Rajasuriar R, Lim YAL, Woo YL, Loke P, Ariffin H. Temporal changes in gut microbiota profile in children with acute lymphoblastic leukemia prior to commencement-, during-, and post-cessation of chemotherapy. *BMC Cancer*. 2020 Feb 24;20(1):151. doi: 10.1186/s12885-020-6654-5. PMID: 32093640.
19. Chua LL, Rajasuriar R, Azanan MS, Abdullah NK, Tang MS, Lee SC, Woo YL, Lim YA, Ariffin H, Loke P. Reduced microbial diversity in adult survivors of childhood acute lymphoblastic leukemia and microbial associations with increased immune activation. *Microbiome*. 2017 Mar 20;5(1):35. doi: 10.1186/s40168-017-0250-1. PMID: 28320465.
20. Valles-Colomer M, Bacigalupe R, Vieira-Silva S, Suzuki S, Darzi Y, Tito RY, Yamada T, Segata N, Raes J, Falony G. Variation and transmission of the human gut microbiota across multiple familial generations. *Nat Microbiol*. 2022 Jan;7(1):87-96. doi: 10.1038/s41564-021-01021-8. Epub 2021 Dec 30. PMID: 34969979.
21. Zhao L, Chen W, Ge Y, Lv X, Wang Y, Yu H, Liu Y, Wu D, Jiao N, Wu Y, Lv D, Zhang G, Xue F, Xu X, Gai Z, Zhu R, Zhang L, Zhao G. Putative Familial Transmissible Bacteria of Various Body Niches Link with Home Environment and Children's Immune Health. *Microbiol Spectr*. 2021 Dec 22;9(3):e0087221. doi: 10.1128/Spectrum.00872-21. Epub 2021 Dec 8. PMID: 34878304.
22. Elvers KT, Wilson VJ, Hammond A, Duncan L, Huntley AL, Hay AD, van der Werf ET. Antibiotic-induced changes in the human gut microbiota for the most commonly prescribed antibiotics in primary care in the UK: a systematic review. *BMJ Open*. 2020 Sep 21;10(9):e035677. doi: 10.1136/bmjopen-2019-035677. PMID: 32958481.
23. Human Microbiome Project Consortium. Structure, function and diversity of the healthy human microbiome. *Nature*. 2012 Jun 13;486(7402):207-14. doi: 10.1038/nature11234. PMID: 22699609.
24. Zhang Q, Peng H, Gao F, Liu Y, Cheng H, Thompson J, Gao GF. Structural insight into the catalytic mechanism of gluconate 5-dehydrogenase from Streptococcus suis: Crystal structures of the substrate-free and quaternary complex enzymes. *Protein Sci*. 2009 Feb;18(2):294-303. doi: 10.1002/pro.32. PMID: 19177572.
25. Shi Z, Xuan C, Han H, Cheng X, Wang J, Feng Y, Srinivas S, Lu G, Gao GF. Gluconate 5-dehydrogenase (Ga5DH) participates in Streptococcus suis cell division. *Protein Cell*. 2014 Oct;5(10):761-9. doi: 10.1007/s13238-014-0074-8. Epub 2014 Jun 11. PMID: 24916441.
26. Saeed NK, Al-Beltagi M, Bediwy AS, El-Sawaf Y, Toema O. Gut microbiota in various childhood disorders: Implication and indications. *World J Gastroenterol*. 2022 May 14;28(18):1875-1901. doi: 10.3748/wjg.v28.i18.1875. PMID: 35664966.
27. Vangay P, Ward T, Gerber JS, Knights D. Antibiotics, pediatric dysbiosis, and disease. *Cell Host Microbe*. 2015 May 13;17(5):553-64. doi: 10.1016/j.chom.2015.04.006. PMID: 25974298.

## Authors

Roma Bhuta, DO, MPH, Division of Pediatric Hematology-Oncology, Hasbro Children's, The Warren Alpert Medical School of Brown University, Providence, RI.

Thomas Kuntz, PhD, Harvard Chan Microbiome Analysis Core, Department of Biostatistics, Harvard TH Chan School of Public Health, Boston, MA.

Bradley DeNardo, MD, Division of Pediatric Hematology-Oncology, Hasbro Children's, The Warren Alpert Medical School of Brown University, Providence, RI.

Xochitl Morgan, PhD, Harvard Chan Microbiome Analysis Core, Department of Biostatistics, Harvard TH Chan School of Public Health, Boston, MA.

Jason Shapiro, MD, Division of Pediatric Gastroenterology, Hasbro Children's, Nutrition and Liver Diseases, The Warren Alpert Medical School of Brown University, Providence, RI.

## Disclosures

The authors have no conflicts of interest. The authors have no financial disclosures relevant to this manuscript.

**Ethics:** Ethical approval for this research was obtained from the Rhode Island Hospital Institutional Review Board.

**Acknowledgments:** We acknowledge the work of David Nelson, PhD; Ying Zhang, PhD; Jing Wang, PhD; and Janet Atoyan, MS, at the Rhode Island Genomics and DNA Sequencing Center and the University of Rhode Island Department of Cell and Molecular Biology for assistance with initial stool sample processing, DNA extraction, and 16S analysis.

## Correspondence

Roma Bhuta, DO, MPH
539 Eddy St., Providence, RI 02903
401-444-5171
Fax 401-444-8845
roma_bhuta@brown.edu

# Evaluation of Emergency Department Visits by Refugee Children in Rhode Island

GIOVANNA DELUCA, MD, MS; TIMMY LIN, MPH; JANETTE BAIRD, PhD; CAROL LEWIS, MD; KYLE MARTIN, MD, MPH; SARA JLILATI, MBBS, MPH; SURAIYA HAMIDZADA, MPH; SERAPHINA NEGASH, MPH; ALIZEH SHAMSHAD; SIRAJ AMANULLAH, MD, MPH

## ABSTRACT

Children constitute 40% of the world's refugees and often have complex medical needs. This retrospective chart review examined Emergency Department (ED) utilization by pediatric refugees (aged 0–18) within a state-level healthcare system to understand the healthcare needs of this population. Pediatric refugee patients were defined as under the age of 18 years with the presence of the ICD-10 code "refugee health exam" in their electronic medical record (EMR). Between 2015–2023, 483 encounters were identified. Descriptive analysis was conducted on characteristics of these encounters. Arabic, Swahili, and Pushto were the most common primary languages of the 22 total languages identified. Most patients resided near the pediatric and adult tertiary care ED, but notably there was one ZIP code outside of the city that represented only 3.3% of all encounters but contributed to 10.6% of traumatic incidents. Medium-low acuity triage levels predominated (79.5%) with 87.8% of patients discharged. The highest percentage of medical (36%) and trauma (28%) visits were by Arabic speakers. Swahili and Spanish speakers had the highest percentage of mental health visits (50%, 36%). Although Arabic speakers had most patient encounters, they had no mental health visits. This study underscores the importance of exploring cultural, spatial, and social influences on ED visits, especially for trauma and mental health-seeking behavior in the pediatric refugee population.

**KEYWORDS:** refugee health; pediatric refugees; pediatric emergency medicine

## BACKGROUND

By the end of 2022, the number of refugees was estimated to be 34.6 million worldwide.[1] Each year the number of refugees welcomed into the United States (U.S.) fluctuates. There were 22,491, 30,000, and 11,411 refugees resettled into the U.S. in 2018, 2019, and 2021 respectively.[2] Additionally, since mid-2021 the U.S. has welcomed 90,000 Afghan evacuees as part of Operations Allies Welcome.[3] Nearly 40% of the world's refugees are children. These children have experienced a long road to resettlement and often have faced violence, housing, and food insecurity.[1]

Newly arrived refugee and migrant children have a high burden of unintentional injuries, nutritional deficiencies, hematologic disorders, infections, and psychological trauma.[4-13] Additionally, there are systemic barriers within the healthcare community that impact the healthcare needs of this population.[12,14,15] Emergency Department (ED) visits provide important data on health care access, types of illness, mental health, and trauma.[16] Although there have been studies in Europe, Canada, and Australia involving ED visits of refugee children, there are limited recent studies looking at ED utilization for pediatric refugee patients in the U.S. Furthermore, there have been even fewer studies taking place after the arrival of the most recent refugees within the past five years. Due to the high volume of refugee children in the U.S. and the influx of Afghan evacuees in 2021, it is important to identify the characteristics of ED presentations of this population.

Rhode Island receives between 100 to 345 refugees per year, and all newly resettled refugee children have an initial health screening through Hasbro Children's Hospital (HCH) Pediatric Refugee Health Program.[17] The initial intake provider becomes the child's primary care provider (PCP). Consequently, most pediatric refugees have the same PCP and are in one medical home leading to a close-knit medical community. Understanding the characteristics of ED visits within this community is essential for identifying gaps and guiding meaningful interventions and improvements. Only one study assessed ED-related visits for pediatric refugees in Rhode Island, and this was done more than a decade ago.[18] Our study aims to evaluate more recent ED utilization and detailed visit characteristics. This deeper insight into the healthcare requirements of this population will provide information for the ED, the medical home and the Department of Health to make meaningful interventions.

## METHODS

This was a retrospective, observational study of ED utilization by pediatric refugee patients in a single health system between April 1st, 2015, and July 31st, 2023. Four EDs, including a level 1 trauma center, were included in the study. Pediatric refugee patients were defined as under the age of 18 years with the presence of the ICD-10 code "refugee health exam" in their electronic medical record (EMR). This

ICD code was assigned during their initial health screening at HCH Pediatric Refugee Health Program upon arrival in Rhode Island.

The primary objective of this study was to explore ED visits by pediatric refugee patients seeking emergency care in Rhode Island. Data extraction was performed via EMR by cross-referencing ED visits and the ICD 10 code "refugee health exam". Patient identifiers were then removed and an analysis file for subsequent descriptive and comparative analyses was created.

Patient and visit-related variables were collected including primary language, age, gender, ZIP code of residence, chief complaints, Emergency Severity Index (ESI), disposition, and discharge diagnosis.

The initial data analysis employed descriptive techniques. Furthermore, the number of ED visits by pediatric refugee patients for injury, illness, or mental health reasons was calculated. Patient encounters were divided into these three categories based on their final ICD code and disposition diagnosis. Comparative analyses were conducted to discern differences in these ED visit reasons by patient language spoken, providing an understanding of the emergency healthcare experiences of pediatric refugee patients in Rhode Island during the specified timeframe. Statistical inferences were not drawn from the comparative analysis due to small counts across several groups. This study was approved by the local Institutional Review Board.

## RESULTS

Between April 2015 to July 2023, we were able to identify a total of 483 ED visits by pediatric refugee patients. The annual number of ED visits began with nine in 2015, reaching a peak of 85 visits in 2017, with notable fluctuations observed in subsequent years. Notably, the second lowest visits were in 2020 with a total of 35 annual visits that year. Although the exact pediatric refugee population in Rhode Island during these years is unknown, 1,271 refugees (adults and children) arrived in the state between 2015 to 2023. The average was about 141 arrivals per year, but this number dropped to as low as 47 in 2021 and as high as 337 in 2016. We were unable to find how many of these refugees were adults vs children; however, on average, children make up about 40% of the world's refugees.[1] **Figure 1** details the number of pediatric emergency department visits from 2016-2022 compared with the overall refugee arrivals from 2016-2022. The years 2015 and 2023 were not included because we only had partial data from each of these years.

Of the ED encounters, 37.1% were by children aged 10–18 years and 33.5% by those aged 5–10 years [**Table 1**]. Younger children aged two to five years accounted for 21.9% of visits, while infants younger than two years comprised 7.4%. Infants under one month had no reported ED visits. There was a balanced gender distribution among pediatric refugees utilizing ED services, with females representing 50.7% of the patients. This cohort exhibited a diverse primary language preference. Among the 22 preferred languages, Arabic speakers accounted for 34.8% of the cohort [**Table 1**]. Most patients resided in Providence, the capital city of Rhode Island, representing 88.4% of all ED visits [**Figure 2**]. Only 15.9% of patients arrived by ambulance, and most patients

**Figure 1.** Emergency department encounters of pediatric refugees from 2016–2023 compared with overall refugee arrivals in Rhode Island from 2016–2023

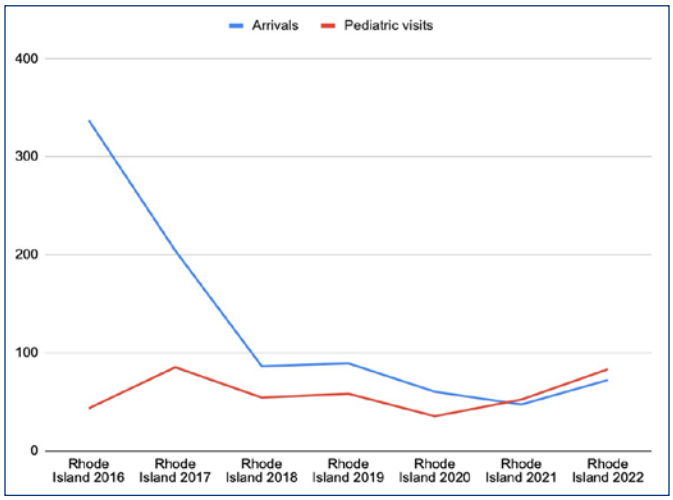
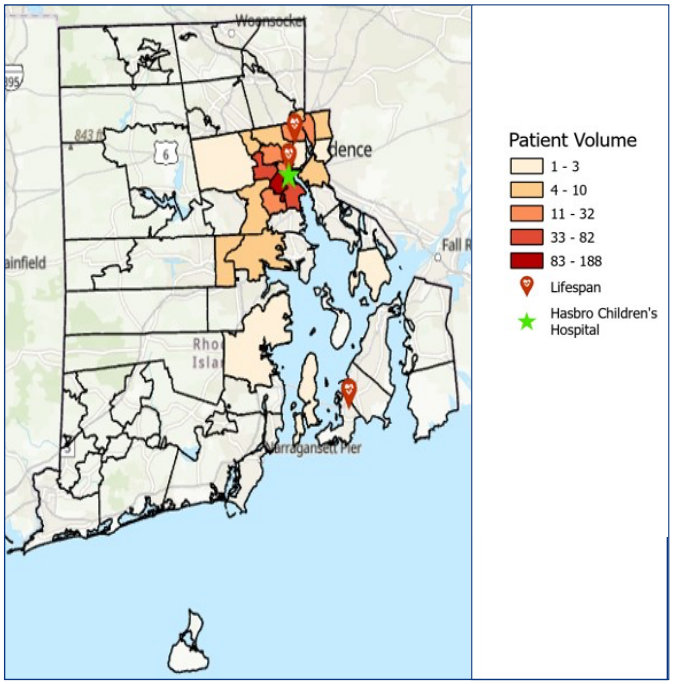



**Table 1.** The age, gender, and language distribution of pediatric refugee ED visits

| Demographics | The total number from the year 2015–2023 n (%) |
|---|---|
| **Age** | |
| Under 1 month | 0 (0%) |
| 1 month–1 year | 4 (0.8%) |
| 1 year–2 years | 32 (6.6%) |
| 2 years–5 years | 106 (21.9%) |
| 5 years–10 years | 162 (33.5%) |
| 10 years–18 years | 179 (37.1%) |
| **Gender** | |
| Male | 238 (49.3%) |
| Female | 245 (50.7%) |
| **Preferred Language** | |
| Arabic | 168 (34.8%) |
| Swahili | 87 (18.0%) |
| Pushto | 47 (9.7%) |
| English | 34 (7.0%) |
| Spanish | 29 (6.0%) |
| Other | 118 (24.5%) |

*Other languages included Burmese, Dari, Haitian Creole, Kinarwanda, Kirundi, Kpelle, Kunama, Lingala, Nepali, Person, Rundi, Russian, Somali, Tigrinya, Ukrainian, Urdu

**Figure 2.** Distribution of pediatric refugee ED patient volume by zip code




were discharged (87.8%), with only two percent experiencing a bounce back within 72 hours [**Table 2**].

Only one encounter was categorized as level 1 on the Emergency Severity Index (ESI), 19% as ESI 2, with the majority (79.5%) triaged as medium-to-low acuity (ESI 3-5). Medical reasons accounted for the majority (64.8%) of ED visits,

**Table 2.** Bounce back visits within 72 hours of discharge

| | NO | YES | Total |
|---|---|---|---|
| All Visits | 473 | 10 | 483 |
| **Age** | | | |
| Under 1 month | 0 | 0 | 0 |
| 1 month–1 year | 3 | 1 | 4 |
| 1 year–2 years | 32 | 0 | 32 |
| 2 years–5 years | 102 | 4 | 106 |
| 5 years–10 years | 157 | 5 | 162 |
| 10 years–18 years | 179 | 0 | 179 |
| **Gender** | | | |
| Male | 229 | 9 | 238 |
| Female | 244 | 1 | 245 |

**Table 3.** The ED utilization by diagnosis

| | Trauma | Non-Trauma | Mental Health/Behavioral Health | Other | Total |
|---|---|---|---|---|---|
| All Visits | 85 (17.6%) | 313 (64.8%) | 14 (2.9%) | 71 (14.7%) | 483 |
| **Age** | | | | | |
| Under 1 month | 0 | 0 | 0 | 0 | 0 |
| 1 month–1 year | 0 | 4 | 0 | 0 | 4 |
| 1 year–2 years | 3 | 24 | 0 | 5 | 32 |
| 2 years–5 years | 20 | 63 | 0 | 23 | 106 |
| 5 years–10 years | 22 | 118 | 2 | 20 | 162 |
| 10 years–8 years | 40 | 104 | 12 | 23 | 179 |
| **Preferred Language** | | | | | |
| Arabic | 24 | 113 | 0 | 31 | 168 |
| Burmese | 1 | 8 | 0 | 0 | 9 |
| Dari | 4 | 12 | 0 | 0 | 17 |
| English | 7 | 19 | 1 | 7 | 34 |
| Kinyarwanda | 8 | 8 | 0 | 4 | 20 |
| Kunama | 0 | 3 | 0 | 3 | 6 |
| Lingala | 0 | 4 | 0 | 1 | 5 |
| Other* | 5 | 12 | 0 | 3 | 20 |
| Persian | 4 | 7 | 0 | 0 | 11 |
| Pushto | 6 | 38 | 1 | 2 | 47 |
| Somali | 2 | 10 | 0 | 9 | 21 |
| Spanish | 2 | 17 | 5 | 5 | 29 |
| Swahili | 19 | 56 | 7 | 5 | 87 |
| Tigrinya | 3 | 6 | 0 | 0 | 9 |

*Other languages include: Haitian Creole (4), Kirundi (1), Kpelle (1), Nepali (3), Rundi (3) Russian (3), Ukrainian (3), Urdu (1), Unknown (1)

followed by trauma (17.6%) [**Table 3**]. Mental health-related visits constituted approximately three percent, while 14.7% were attributed to other reasons, such as patients with unclear diagnosis, those who left without being seen, and individuals with unclear pain.

Arabic speakers had the highest percentage of medical (36.1%) and trauma (28.2%) visits, while Swahili speakers exhibited the highest percentage of mental health visits (50%), followed by Spanish-speaking patients (35.7%). While Arabic-speaking patients account for the highest number of all ED visits, they had no visits for mental health concerns. Spanish speakers, who made up only six percent of all ED visits, made up 35.7% of mental health visits.

## DISCUSSION

In this study, we analyzed 483 ED visits by 216 refugees aged 18 years or younger across the state of Rhode Island. Our findings demonstrated a notable difference in healthcare utilization among patients with different primary languages. Arabic was the most common language spoken by patients, followed by Swahili, Pushto, English, and Spanish. Further studies are needed to see if this directly reflects the refugee demographics of the area or if there are a disproportionate amount of ED visits by certain communities and populations. Examining language-specific patterns, Arabic speakers exhibited the highest percentage of medical (36.1%) and trauma (28.2%) visits, while Swahili speakers demonstrated the highest percentage of mental health-related visits (50%), closely followed by Spanish-speaking patients (35.7%).

Regarding mental health visits, Arabic speakers, who represent the highest number of overall ED encounters, had no recorded visits related to mental health. Conversely, Spanish speakers, constituting only six percent of all visits, accounted for 35.7% of mental health-related encounters, presenting a noteworthy disproportionality in these linguistic groups. These disparities warrant a further detailed assessment as previous studies have also shown large disparities in mental health visits by race, country of origin, and refugee status. While previous studies have shown that five percent of pediatric ED visits are related to mental health, there has been a significant increase over the years in mental health complaints and a significantly greater number in Black and Hispanic children when compared to their White peers.[19-21] It is particularly important to understand these trends as refugee children have been shown to have higher rates of depression and post-traumatic stress disorder when compared to non-refugee children, yet refugee children attend less appointments for and are more likely to drop out of mental health treatment for these conditions. Where a prior study showed that trauma represented half of all presentations by pediatric refugees,[18] our study showed that trauma was much less common and only constituted 17.59% of encounters. Additionally, our study shows that Arabic speakers constituted the highest number of traumatic encounters, closely followed by Swahili speakers, aligning proportionally with the overall visitation rates of these populations. Notably, Kinyarwanda speakers emerged as the third-highest group for trauma, comprising 9.1% of all traumatic visits despite constituting only four percent of overall visits, although the overall sample size was low. Additionally, Spanish speakers accounted for six percent of all ED visits but represented only about two and a half percent of traumatic encounters, highlighting variations in trauma and trauma-related healthcare-seeking behaviors among different linguistic groups.

While most traumatic encounters (88.4%) were reported by patients residing in the city of Providence, one residential ZIP code, situated just north of the city, exhibited a distinct pattern. Although constituting only about three percent of all encounters, this ZIP code contributed to 10.6% of traumatic encounters. This prompts further exploration into potential factors influencing the prevalence of traumatic incidents in this specific residential area, offering insight for further exploration and targeted healthcare interventions, and community-based trauma prevention strategies.

According to our findings, there were fluctuations in annual visits to the ED, starting with nine visits in 2015 and peaking at 85 visits in 2017. Factors contributing to these variations could include changes in refugee arrivals to the state, healthcare accessibility and community health initiatives. Notably, other than 2015, 2020 witnessed the fewest ED visits (35 total), potentially linked to the global pandemic and a heightened fear of hospitals during that period.

The residential distribution showed 88.4% of all ED visits were attributed to patients residing in Providence. Notably, the residential zones surrounding the major pediatric tertiary care center account for the highest concentration of patient visits. This can be seen in **Figure 2**. This phenomenon may be influenced by the possibility that a significant number of refugees reside in this area, or the possible impact of proximity to the major pediatric tertiary care hospital on healthcare utilization. Most reside around the tertiary care center, intentionally housed there by resettlement agencies to promote access to the resettlement agencies, medical care, and governmental agencies. As housing becomes more limited and unaffordable, we see a shift to areas north of the city.

## LIMITATIONS

This study had several limitations. First, all the data was collected from one healthcare system; consequently, pediatric refugees who sought care at other institutions may have been missed. Second, refugee status was identified through documentation of a "refugee health exam" in their chart. Refugee children who did not have this documented in their chart would not have been captured within our data. Third, language spoken as a proxy for cultural background is an imperfect measure and may not accurately reflect a patient's community, ethnicity, or migration history. Fourth, the overall sample size, particularly relating to mental health

encounters, was low; this limits our ability to make clear associations. Finally, there are challenges in interpreting mental health presentations in different populations. Mental health issues in children often manifest as somatic complaints and ED coding may reflect these physical symptoms rather than the psychological distress. As a result, the prevalence of mental health concerns in this population may be underrepresented in our findings.

## CONCLUSION

This analysis of pediatric refugee ED visits in the state of Rhode Island shines a light on the complex dynamics involving demographic, linguistic, and geographic factors that influence ED utilization. The identified disparities among this population, particularly in mental health and trauma encounters, underscore the need for future research. This study identifies areas for further investigation to understand causal associations and contextual factors contributing to unique patterns of mental health and trauma encounters. This ongoing research will enhance our understanding of the distinctive healthcare needs of refugee children and inform the development of policies aimed at improving care delivery and fostering community-based health initiatives.

### References


1. United Nations High Commissioner for Refugees. Global Trends: Forced Displacement in 2022. Geneva: UNHCR; 2023.
2. United Nations High Commissioner for Refugees. Refugee Resettlement Facts. Washington (DC): U.S. Department of State; July 2022.
3. U.S. Department of State, Bureau of Population, Refugees, and Migration. Afghan arrivals under the U.S. Refugee Admissions Program. Washington (DC): U.S. Department of State; 2022.
4. Fritschi N, et al. Pediatric tuberculosis disease during years of high refugee arrivals: a 6-year national prospective surveillance study. Respiration. 2021;100(11):1050-1059.
5. Dundar I, Buyukavci MA. Nutritional rickets in Turkish and refugee children aged 0–2 years: an increasing problem despite vitamin D prophylaxis. Turk J Pediatr. 2023;65(3):406-415.
6. Eiset AH, Wejse C. Review of infectious diseases in refugees and asylum seekers—current status and going forward. Public Health Rev. 2017;38:22.
7. Masters PJ, et al. Health issues of refugees attending an infectious disease refugee health clinic in a regional Australian hospital. Aust J Gen Pract. 2018;47(5):305-310.
8. Yun K, et al. Health profiles of newly arrived refugee children in the United States, 2006–2012. Am J Public Health. 2016;106(1):128-135.
9. Baauw A, et al. Health needs of refugee children identified on arrival in reception countries: a systematic review and meta-analysis. BMJ Paediatr Open. 2019;3(1):e000516.
10. Salami B, et al. A scoping review of the health of African immigrant and refugee children. Int J Environ Res Public Health. 2021;18(7):3514.
11. Esmaili E, et al. Pediatric refugee health and patterns of health care utilization in Durham, North Carolina. N C Med J. 2021;82(3):157-163.
12. Harkensee C, Andrew R. Health needs of accompanied refugee and asylum-seeking children in a UK specialist clinic. Acta Paediatr. 2021;110(8):2396-2404.
13. Saunders NR, et al. Unintentional injuries among refugee and immigrant children and youth in Ontario, Canada: a population-based cross-sectional study. Inj Prev. 2018;24(5):337-343.
14. Nijman RG, et al. Emergency care provided to refugee children in Europe: RefuNET—a cross-sectional survey study. Emerg Med J. 2021;38(1):5-13.
15. Brandenberger J, et al. Reported challenges in health care delivery to migrants and refugees in high-income countries: a systematic review of the 3C model. BMC Public Health. 2019;19(1):755.
16. Stewart M, et al. Medical and social factors associated with the admission and discharge of acutely ill children. Arch Dis Child. 1998;79(3):219-224.
17. Sadr B. Refugee Assistance Program. Providence (RI): State of Rhode Island, Office of Health and Human Services; year unknown.
18. Watts DJ, Friedman JF, Vivier PM, Tompkins CE, Alario AJ. Health care utilization of refugee children after resettlement. J Immigr Minor Health. 2012;14(4):583-588. doi:10.1007/s10903-011-9530-1.
19. Santillanes G, Axeen S, Lam CN, Menchine M. National trends in mental health-related emergency department visits by children and adults, 2009–2015. Am J Emerg Med. 2020;38(12):2536-2544. doi:10.1016/j.ajem.2019.12.035.
20. Hoffmann JA, Stack AM, Samnaliev M, Monuteaux MC, Lee LK. Trends in visits and costs for mental health emergencies in a pediatric emergency department, 2010–2016. Acad Pediatr. 2019;19(4):386-393.
21. Abrams AH, Badolato GM, Boyle MD, McCarter R, Goyal MK. Racial and ethnic disparities in pediatric mental health–related emergency department visits. Pediatr Emerg Care. 2022;38(1):e214-e218. doi:10.1097/PEC.0000000000002221


### Authors


Giovanna Deluca, MD, MS, Brown University, Department of Emergency Medicine, Providence, Rhode Island.

Timmy Lin, MPH, Brown University, Department of Emergency Medicine, Providence, Rhode Island.

Janette Baird, PhD, Brown University, Department of Emergency Medicine, Providence, Rhode Island.

Carol Lewis, MD, Brown University, Department of Pediatrics, Providence, Rhode Island.

Kyle Martin, MD, MPH, Brown University, Department of Emergency Medicine, Providence, Rhode Island.

Sara Jlilati, MBBS, MPH, Brown University School of Public Health, Providence, Rhode Island.

Suraiya Hamidzada, MPH, Brown University School of Public Health, Providence, Rhode Island.

Seraphina Negash, MPH, Brown University School of Public Health, Providence, Rhode Island.

Alizeh Shamshad, The Warren Alpert Medical School of Brown University, Providence, RI.

Siraj Amanullah, MD, MPH, Brown University, Department of Emergency Medicine, Providence, Rhode Island.


### Disclosures


The authors have no financial disclosures.

Ethical approval to report this submission was obtained from Brown University Health Institutional Review Board.


### Correspondence


Giovanna Deluca, MD, MS
55 Claverick St., Providence, RI 02903
Giovannasdeluca@gmail.com

# Outcomes of a Novel Full-Service, Free Ophthalmology Clinic-Within-A-Clinic: A Four-Year Longitudinal Study

SOPHIA DUTTON, BA; ANAGHA LOKHANDE, MD; CHANBIN LEE, BA; VINEETHSUBBU SOMASUNDARAM, BS; JONATHAN HARRISON, BA; SAMUEL HOCHBERGER, BA; SAMUEL MICKEL-HULSE, MD; DAVID BOOY, MD; ANDREW G. YOUNG, MD; JAMIE SCHAEFER, MD; NICOLE LANZA, MD

## ABSTRACT

**PURPOSE:** We evaluate the Clínica Esperanza Ophthalmology Service, a free service for uninsured patients in southern New England.

**METHODS:** The service operates monthly under a novel clinic-within-a-clinic model, existing as a subsidiary of a local free clinic. A mixed-methods program evaluation and a retrospective chart review from December 2021 to January 2025 were analyzed using descriptive statistics.

**RESULTS:** One hundred and forty-three (143) patients were scheduled during the study period, of whom 106 (74%) were seen. Median age was 51 years and 52/106 (49%) were female. Most patients (97%) identified Spanish as their primary language. There were no significant demographic differences between those seen and no-shows. Diabetic retinopathy was the most common diagnosis (37/106, 35%), followed by dry eye (35/106, 33%), and cataracts (29/106, 27%). Half of the patients (51/106, 48%) received a referral, most commonly for refraction (23/51, 45%). Ophthalmic medication was prescribed for 53/106 (50%) patients, most commonly for artificial tears (43/53, 81%). Qualitative strengths included education and low operational overhead. Qualitative challenges included long length of encounters and consequently, low patient volumes.

**CONCLUSIONS:** Our novel ophthalmology service supplements existing operations and helps meet an unmet public health need among its region's most vulnerable patients. Opportunities for improvement include improving clinic volumes and mitigating no-show rates.

**KEYWORDS:** Program evaluation; eye diseases; health equity; health disparities; diabetic retinopathy

## INTRODUCTION

Free clinics play an increasingly important but understudied role in the United States safety-net healthcare system, emerging as access points for medically underserved populations.[1] Between 2005 and 2014, the number of free clinics in the United States has increased steadily.[2] Among these underserved populations, Latino communities face a particularly high burden of preventable and treatable eye diseases, experiencing disproportionate morbidity compared to other racial and ethnic groups.[3] Studies have shown that Latino adults are at increased risk for diabetic retinopathy, distance vision impairment, pterygium, and glaucoma, which can progress silently and lead to vision loss.[4-7] However, individuals in this population often face barriers to ophthalmologic care, including insurance gaps, language discordance, and transportation challenges; as a result, eye conditions are often undetected until advanced stages, contributing to disparities in visual outcomes.[8,9]

Ophthalmology-focused free clinic services are uniquely positioned to bridge the gap between community health and specialty care. In addition to addressing unmet needs in access, these clinics serve as important venues for both patient education and trainee development. Medical students have limited opportunities to practice ophthalmic skills during their clinical years, leading to measurable declines in proficiency.[10] Student-run free clinics have been proposed as a way to address this gap by offering supervised, extracurricular exposure to ophthalmology while simultaneously expanding access for underserved patients.[11-13] At the same time, free clinic models emphasize health literacy and counseling, which have been shown to improve patient engagement and chronic disease management in vulnerable populations.[11,14,15] In this setting, trainees gain experience caring for groups disproportionately affected by barriers to specialty care. However, prior evaluations of ophthalmology services in free clinics have been largely confined to administrative metrics or patient satisfaction surveys, with little characterization of the clinical spectrum of disease encountered.[14,15] Further, there is a dearth of prior work characterizing the epidemiology of eye conditions in free clinic settings that primarily serve Spanish-speaking patients, an especially relevant group given the growing burden of preventable vision loss among Latino patients in the United States.

In particular, Rhode Island and the broader southern New England region are home to a large and growing population of Latino residents, many of whom face persistent barriers to accessing high-quality healthcare.[16] Clínica Esperanza/Hope Clinic (CEHC) is a free, volunteer-run clinic located in Providence, Rhode Island, that provides primary care and health education to over 3,000 uninsured patients annually, over 90% of whom identify as Latino and speak Spanish

as their primary language.[17] In 2021, a monthly ophthalmology service was launched within CEHC using a novel clinic-within-a-clinic model, in which the ophthalmology services operate as a subsidiary of the existing primary care infrastructure. This program seeks to address a paucity of available ophthalmological care by operating within CHEC, a well-known and trusted local institution. The monthly ophthalmology service continues to be in full operation at the time of publication.

This study aims to understand the impact of our program, in addition to identifying opportunities for growth and outlining the structure of our clinic-within-a-clinic framework. We further aim to evaluate clinical data to better characterize the ophthalmological care needs of a primarily low-income, Spanish-speaking, patient population.

## MATERIALS AND METHODS

### Data Collection

A retrospective chart review was conducted for all patients seen by the Ophthalmology Service from its inception in December 2021 through January 2025. Data was collected on patient demographics (i.e., age, sex, preferred language) and clinical parameters (i.e., diagnoses, prescriptions, referrals). Data was also collected on clinic resources, e.g., equipment and personnel, via review of clinic documentation. This study was deemed exempt by the Brown University Institutional Review Board and adhered to the tenets of the Declaration of Helsinki and all federal and state laws, including the Health Insurance Portability and Accountability Act of 1996.[18,19] Informed consent was not required as the study involved retrospective analysis of de-identified data and did not include any intervention or collection of identifiable private information.

### Statistical Analysis

Patient data were analysed using descriptive statistics in R. To compare characteristics between patients who were seen in clinic and those who were scheduled but never seen (i.e., those who canceled, no-showed, and never rescheduled), Wilcoxon test and Fisher's exact was used. A two-tailed $p$-value of $< 0.05$ was considered statistically significant.

## RESULTS

### Patient Demographic Characteristics

A total of 143 patients were scheduled for ophthalmologic evaluation during the study period. **Table 1** summarizes the demographic characteristics of the full scheduled cohort. The median age was 51 years (interquartile range [IQR], 42–60), and the gender distribution was approximately equal, with 49% female and 51% male. Most scheduled patients identified Spanish as their primary language, with the remainder reporting English (2, 1.4%), Arabic (1, 0.7%), or Russian (1, 0.7%).

Of the 143 scheduled patients, 106 unique individuals were seen in clinic, including 16 who were evaluated at least once for follow-up care (15.1% of unique patients seen), with a median interval of 98 days between visits. Annual follow-up visits per year are shown in **Figure 4**. Thirty-seven patients were scheduled but never seen. A Wilcoxon test showed no statistically significant differences in age between patients who completed at least one visit and those who were no-shows. Fisher's exact showed no significant differences in sex or primary language between patients who completed at least one visit and those who were no-shows.

**Table 1.** Demographics of Scheduled Patients. Results are shown as median (Q1, Q3) for age; as n (%) for all other demographic characteristics.

| Characteristic | N = 143 |
|---|---|
| Age | 51 (42, 60) |
| **Gender** | |
| Female | 70 (49%) |
| Male | 73 (51%) |
| **Primary Language** | |
| Arabic | 1 (0.7%) |
| English | 2 (1.4%) |
| Russian | 1 (0.7%) |
| Spanish | 139 (97%) |

**Figure 1.** Visit attendance by year

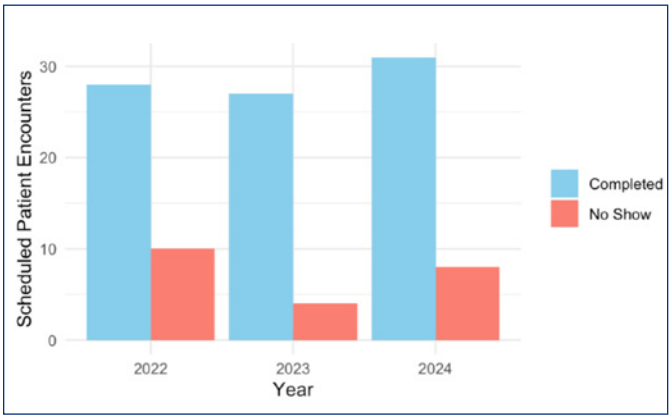
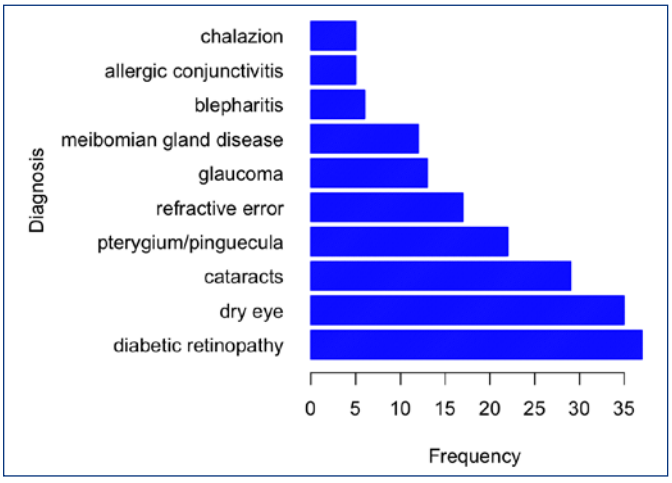



**Figure 2.** Most common clinical diagnoses



Visit attendance by year is shown in **Figure 1**. Visit attendance included only new patient visits and excludes follow-up encounters. In 2022, there were 28 completed visits and 10 no-shows; in 2023, 27 completed visits and 5 no-shows; and in 2024, 31 completed visits and 8 no-shows. No consistent upward or downward trend in no-show rates was observed over the study period. Data from 2021 and 2025 were omitted from **Figure 2** as the service was started in late 2021 and our data collection period concluded in early 2025.

## Patient Clinical Characteristics

The most common clinical diagnoses among the 106 unique patients seen in clinic are shown in **Figure 2**. Diabetic retinopathy was the most frequent reason for evaluation and ultimately the most common diagnosis (37/106, 35%), followed by dry eye (35/106, 33%), cataracts (29/106, 27%), and pterygium or pinguecula (22/106, 21%). Nearly half of the patients (49/106, 46%) were seen for a single diagnosis, while 15 patients were diagnosed with two or more conditions (15/106, 14%). Less commonly encountered conditions included: lagophthalmos (1/106, 1%), pseudoexfoliation syndrome (1/106, 1%), pyogenic granuloma (1/106, 1%), intraocular lens (IOL) subluxation (1/106, 1%), vitreous degeneration (2/106, 2%), age-related macular degeneration (AMD) (4/106, 4%), optic nerve hemorrhage (1/106, 1%), posterior capsular opacification (4/106, 4%), retinal detachment (2/106, 2%), and strabismus (1/106, 1%).

At their most recent clinic visit, 51 out of 106 patients (48%) were referred for additional evaluation or specialty care. The most common referral destination was for refraction services (23/51, 45%), followed by glaucoma (9/51, 18%), retina (6/51, 12%), and cataract surgery evaluation (3/51, 6%). Other referrals included oculoplastics evaluation (2/51, 4%), pterygium/pinguecula (2/51, 4%), IOL subluxation (1/51, 2%), dry eye management (1/51, 2%), evaluation of optic disc anomaly (1/51, 2%), strabismus (1/51, 2%), and migraine management through neurology (1/51, 2%).

At their most recent visit, 53 out of 106 patients (50%) received a prescription for ophthalmic treatment. The most prescribed or recommended agents were lubricating eye drops, namely artificial tears (AT) (43/53, 81%). Antihistamine medications included ketotifen fumarate (4/53, 8%) and combination AT and ketotifen fumarate (1/53, 2%). Antibacterial therapies included erythromycin ointment (1/53, 2%) and neomycin-polymyxin B-dexamethasone (1/53, 2%). Glaucoma medications included timolol maleate (n = 1) and dorzolamide-timolol (1/53, 2%).

## Program Review

In parallel with the chart review, we conducted a descriptive synthesis of programmatic documents and stakeholder feedback to qualitatively review clinic operations. Sources included staffing and equipment logs maintained by the service, internal clinic documentation, and discussions with medical student volunteers. Records were collated to identify information about operational strengths and challenges.

Findings from this review informed our description of the service's organizational structure, personnel, and resources. The ophthalmology service is operated in partnership with the Brown University Health Division of Ophthalmology, with staffing that includes a medical student coordinator, medical student volunteers, a faculty ophthalmologist preceptor, ophthalmology residents, and core clinic staff. Key ophthalmic equipment [**Table 2**] was obtained through departmental and private donations as well as grant funding, including university-based programs supporting medical education and community engagement. To expand patient

**Table 2.** Clinic equipment

| Equipment | Method of Obtaining |
|---|---|
| Haag Streit slit lamp | Private donation |
| 2 indirect ophthalmoscopes | Grant funding |
| 1 gonioscope | Departmental donation |
| Fluorescein strips + proparacaine, phenylephrine, tropicamide | Departmental donation |
| Welch Allyn RetinaVue 700 Imager | Clínica Esperanza |
| 2 Reichert Tono-Pen AVIA | Grant funding |
| Mobile phoropter | Private donation |
| Bawa 90D & 20D lenses | Departmental donation |
| Pinhole refractor | Departmental donation |
| Low-literacy vision chart | Grant funding |

**Figure 3.** Organizational framework of the clinic

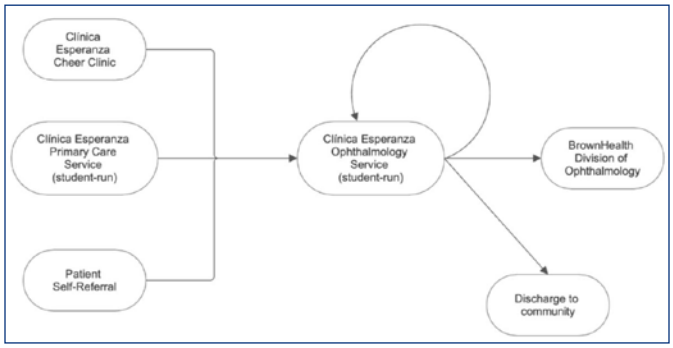
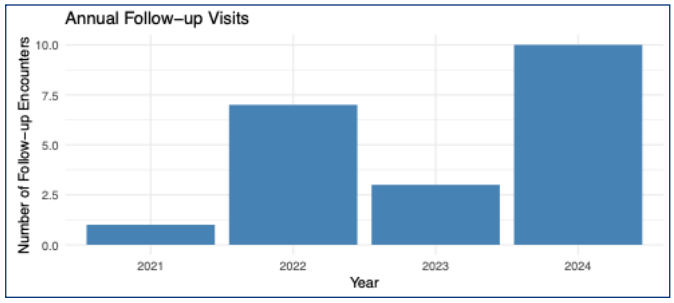



**Figure 4.** Annual follow-up visits



access, a referral pathway was established in 2025 with the Rhode Island Lion's Club, connecting uninsured and Spanish-speaking patients to low-cost optometry services.

This organizational framework is complemented by defined patient flow pathways [**Figure 3**]. Patients are referred from multiple sources, including Clínica Esperanza's Primary Care Service, the Clínica Esperanza/Hope Clinic Emergency Room Diversion Project (CHEER Clinic), and self-referral. Following ophthalmologic evaluation, patients may be managed longitudinally within the clinic, referred to the Brown University Health Division of Ophthalmology for subspecialty care, or discharged to the community with follow-up as needed. Together, these pathways support continuity of care while enabling appropriate triage to higher levels of service.

Finally, the qualitative review identified education as a central strength of the ophthalmology service, with benefits for both patients and trainees. Visits routinely incorporate counseling on disease understanding, self-management, and follow-up, with attention to linguistic concordance through educational materials provided in Spanish. For example, patients with diabetic retinopathy received counseling on the importance of glycemic and blood pressure control, while those with dry eye were provided guidance on accessible, low-cost interventions such as artificial tears and low-cost warm compress and massage methods. Bilingual counseling and the use of low-literacy vision charts (i.e., using symbols or numbers) facilitated communication for patients with limited English proficiency, a population that comprised the vast majority of those seen in our clinic. The clinic also functioned as a supervised teaching environment for medical students and residents. Trainees received structured opportunities to practice core ophthalmic skills, including slit-lamp microscopy, tonometry, and ophthalmoscopy, under direct faculty and resident supervision. Each clinic session was typically conducted monthly and lasted three hours, with approximately four to five medical student volunteers, one attending ophthalmologist, and one to two ophthalmology residents present. On average, four to five patients were scheduled per session, which allowed adequate time for instruction, patient education, and documentation. Students were trained in charting methods that respected patient privacy, while learning to connect patients with local resources that provide low-cost follow-up, such as the Lions Club referral pathways.

## CONCLUSION

This study characterizes the first four years of a free ophthalmology service operating within a local free clinic. Among the 143 patients scheduled during the study period, the majority were Spanish-speaking, middle-aged adults. Half of all seen patients were referred for further care, and half received prescription treatment. The most common presenting conditions included diabetic retinopathy, dry eye, cataracts, and pterygium, though a broad spectrum of ophthalmic disease was identified. Service volume remains modest, and the no-show rate limits the number of patients reached. Our service leverages existing free clinic operations to run with minimal overhead and has successfully employed partnerships with community organizations, private donors, and an academic ophthalmology department to secure medical equipment and referral sites for escalation of care.

The proportion of patient's seen for follow-up may reflect early phase of program implementation and well-documented rates of no-show appointments in the free clinic patient population due to a variety of social challenges.[20,21] In addition, follow-up was not clinically indicated for all patients, as many encounters served primarily as a screening entry point into specialty care, with nearly of half of individuals appropriately referred to a nearby academic ophthalmology center for ongoing subspecialty care after initial evaluation at our clinic. Others had conditions that were sufficiently managed at the initial encounter. The proportion of patients returning for follow-up within this service is comparable to rates in similar student-run ophthalmology clinics and suggests a substantial subset of patients engaged longitudinally despite these structural barriers.[14,22]

Unlike many vision screening programs, our program functions as an ophthalmology site, with access to slit-lamp examination, intraocular pressure measurements, and indirect ophthalmoscopy. Patients received on-site medications, counseling, and referrals to optometry or subspecialty ophthalmology as needed. As the in-house eye care service for our local free clinic, our Ophthalmology Service offers direct, language-concordant care to an established patient population already receiving primary care within the same setting. This integration allows for ongoing coordination with primary care and social services, reducing common access barriers such as transportation and insurance coverage.[23-25] Nonetheless, perceived and structural barriers likely remain, including inflexible work schedules, caregiving responsibilities, and immigration-related concerns, which may contribute to missed appointments.[26-28] Future directions include evidence-based approaches to mitigate no-shows, such as offering short-lead or open-access scheduling to minimize waiting times, implementing formal quality-improvement cycles to track attendance patterns, and incorporating risk-stratified outreach (such as additional reminder calls prioritized for patients with prior missed visits).[29–31]

The ophthalmology service also functions as a teaching site. Patient-facing education empowers individuals to better understand and manage their conditions, while trainee-facing education provides learners with opportunities to develop both technical ophthalmic skills and competencies in culturally and linguistically concordant care. This

dual role of the service, as a site of both patient care and clinical education, supports a sustainable model by simultaneously meeting community needs and giving trainees patient exposure and technical skills that will serve them in future clinical practice.[32,33] Future work could formally evaluate the influence of this teaching model on trainee skill development.

Compared to similar student-run or community-based eye care initiatives, our service provides an intentional focus on comprehensive care over high-volume patient screening. While many programs emphasize screening and referral only, our model emphasizes diagnosis, treatment, and longitudinal care.[34,35] The relatively low patient volume reflects an intentional prioritization of comprehensive care delivery and our status as a teaching service. Our work contributes valuable epidemiologic data on the spectrum of eye disease within an underserved, primarily Spanish-speaking population, a group underrepresented in ophthalmic research.[36-38] Our model may be scalable across other free clinic settings: by using a physical location and administrative support staff already employed by our local free clinic, the financial and logistical resources required to start and continue our ophthalmology service was minimized.

As a single-center program evaluation, our findings should be interpreted in the context of several limitations. First, we did not track patient outcomes following referral, which precludes assessment of the program's impact on more longitudinal measures such as referral completion or visual acuity improvement. Future implementation of standardized follow-up protocols will be critical to evaluate continuity of care, treatment outcomes, and patient satisfaction. Finally, the qualitative component relied on existing documentation and informal debriefs, which may not capture the full spectrum of stakeholder perspectives. Nonetheless, this pragmatic approach provided valuable insights into operational strengths and barriers that would not have been evident from chart review alone.

In summary, we describe the outcomes and longitudinal implementation of a comprehensive ophthalmology service embedded in a local free clinic. We find that diabetic retinopathy, dry eye, cataract, and pterygium/pinguecula are among the most common conditions in our patient population of primarily uninsured, Latino patients. We also find that our model demonstrates that comprehensive eye care can be delivered to high-need populations using a clinic-within-a-clinic framework. Our model is particularly well-suited for leveraging existing free clinic infrastructure and community and academic partnerships. The findings herein may serve both to better characterize common eye diseases in an underserved population and to provide a replicable model to deliver ophthalmic care to this patient cohort.

## References


1. Kumar NR, DuVernois G, Almeida-Monroe V, Siegert N, De Groot AS. Evaluating the Impact of a Student-Run Women's Clinic on Access to Gynecologic Care for Uninsured Women in Rhode Island. R I Med J (2013). 2019 Dec 2;102(10):52-56. PMID: 31795536.
2. Smith S, Thomas R, Cruz M, Griggs R, Moscato B, Ferrara A. Presence and characteristics of student-run free clinics in medical schools. *JAMA*. 2014;312(22):2407-2410. doi:10.1001/JAMA.2014.16066
3. Congdon N. Causes and Prevalence of Visual Impairment among Adults in the United States. *Archives of Ophthalmology*. 2004;122(4):477-485. doi:10.1001/ARCHOPHT.122.4.477
4. Varghese JS, Ravi Kumar V, Bartelt J, Hendrick AM, Pasquel FJ. The Role of Urban Residence, Race and Ethnicity, and Glycemic Control in Receiving Standards of Care and Progression to Vision-Threatening Diabetic Retinopathy. *Diabetes Care*. 2025;48(1):29-37. doi:10.2337/DCI24-0024
5. New York State Department of Health. Vision and Eye Health Data and Statistics; 2023. Accessed May 14, 2025. https://www.health.ny.gov/diseases/conditions/vision_and_eye_health/data_and_statistics.htm
6. Kandavel R, Kang JJ, Memarzadeh F, Chuck RS. Comparison of pterygium recurrence rates in Hispanic and White patients after primary excision and conjunctival autograft. *Cornea*. 2010;29(2):141-145. doi:10.1097/ICO.0B013E3181B11630
7. Allison K, Patel DG, Greene L. Racial and Ethnic Disparities in Primary Open-Angle Glaucoma Clinical Trials A Systematic Review and Meta-analysis. *JAMA Netw Open*. 2021;4(5):E218348. doi:10.1001/jamanetworkopen.2021.8348
8. Varma R, Mohanty SA, Deneen J, et al. Burden and Predictors of Undetected Eye Disease in Mexican-Americans: The Los Angeles Latino Eye Study. *Med Care*. 2008;46(5):497. doi:10.1097/MLR.0B013E31816080FE
9. Elam AR, Tseng VL, Rodriguez TM, et al. Disparities in Vision Health and Eye Care. *Ophthalmology*. 2022;129(10):e89-e113. doi:10.1016/j.ophtha.2022.07.010
10. Lippa LM, Boker J, Duke A, Amin A. A novel 3-year longitudinal pilot study of medical students' acquisition and retention of screening eye examination skills. *Ophthalmology*. 2006;113(1):133-139. doi:10.1016/J.OPHTHA.2005.09.003
11. Rowe LW, Scheive M, Tso HL, et al. A seven-year analysis of the role and impact of a free community eye clinic. *BMC Med Educ*. 2021;21(1). doi:10.1186/S12909-021-03026-7
12. Moxon NR, Goyal A, Giaconi JAA, et al. The State of Ophthalmology Medical Student Education in the United States: An Update. *Ophthalmology*. 2020;127(11):1451. doi:10.1016/J.OPHTHA.2020.05.001
13. Chopra N, Zhou DB, Fallar R, Chadha N. Impact of Near-Peer Education in a Student-Run Free Ophthalmology Clinic on Medical Student Teaching Skills. *J Surg Educ*. 2020;77(6):1503-1510. doi:10.1016/j.jsurg.2020.05.012
14. Okaka Y, Meah YS, Fallar R, Chadha N. Ophthalmology Services at Student-Run Free Clinics: A National Survey. *J Natl Med Assoc*. 2021;113(4):431-435. doi:10.1016/j.jnma.2021.02.004
15. Downie E, Von Hohenberg M, Harrison A, Sick B. Student-Run Free Clinic as a Source of Meaningful Ophthalmologic Care for Underserved Patients. *Journal of Student-Run Clinics*. 2017;3(1). doi:10.59586/JSRC.V3I1.46
16. Torres-Perez A, Turley E. Census data: Number of Hispanic Rhode Islanders rising | WPRI.com. September 19, 2023. Accessed June 10, 2025. https://www.wpri.com/hidden-history/hispanic-heritage-month/census-data-shows-hispanic-rhode-islanders-are-on-the-rise/
17. Wang C, Yang J, Testa J, Gill M, Leonard M, De Groot AS. Continuity of Care and Lifestyle Intervention Programs for Spanish-Speaking Immigrants Without Health Insurance at a Free Clinic in Rhode Island. *Prev Chronic Dis*. 2024;21:E92. doi:10.5888/PCD21.240136

18. WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Participants – The World Medical Association. Accessed October 20, 2025. https://www.wma.net/policies-post/wma-declaration-of-helsinki/
19. Health Insurance Portability and Accountability Act of 1996 | ASPE. Accessed October 20, 2025. https://aspe.hhs.gov/reports/health-insurance-portability-accountability-act-1996
20. Starnes JR, Slesur L, Holby N, Rehman S, Miller RF. Predicting No-shows at a Student-Run Comprehensive Primary Care Clinic. *Fam Med*. 2019;51(10):845-849. doi:10.22454/FAMMED.2019.406053
21. Boshers EB, Cooley ME, Stahnke B. Examining no-show rates in a community health centre in the United States. *Health Soc Care Community*. 2022;30(5):e2041-e2049. doi:10.1111/HSC.13638
22. Scheive M, Rowe LW, Tso HL, et al. Assessment of patient follow-up from student-run free eye clinic to county ophthalmology clinic. *Sci Rep*. 2022;12(1). doi:10.1038/S41598-022-05033-0
23. Labban M, Chen CR, Frego N, et al. Disparities in Travel-Related Barriers to Accessing Health Care From the 2017 National Household Travel Survey. *JAMA Netw Open*. 2023;6(7):e2325291-e2325291. doi:10.1001/JAMANETWORKOPEN.2023.25291
24. Dickman SL, Himmelstein DU, Woolhandler S. Inequality and the health-care system in the USA. *The Lancet*. 2017;389(10077):1431-1441. doi:10.1016/S0140-6736(17)30398-7
25. Fisher EM, Akiya K, Wells A, Li Y, Peck C, Pagán JA. Aligning social and health care services: The case of Community Care Connections. *Prev Med (Baltim)*. 2021;143. doi:10.1016/j.ypmed.2020.106350
26. Dougherty L, Lloyd J, Harris E, Caffrey P, Harris M. Access to appropriate health care for non-English speaking migrant families with a newborn/young child: A systematic scoping literature review. *BMC Health Serv Res*. 2020;20(1). doi:10.1186/S12913-020-05157-X
27. Escobedo LE, Cervantes L, Havranek E. Barriers in Healthcare for Latinx Patients with Limited English Proficiency—a Narrative Review. *J Gen Intern Med*. 2023;38(5):1264-1271. doi:10.1007/S11606-022-07995-3
28. Doshi M, Lopez WD, Mesa H, et al. Barriers & facilitators to healthcare and social services among undocumented Latino(a)/Latinx immigrant clients: Perspectives from frontline service providers in Southeast Michigan. *PLoS One*. 2020;15(6). doi:10.1371/JOURNAL.PONE.0233839
29. Mazaheri Habibi MR, Abadi FM, Tabesh H, et al. Evaluation of no-show rate in outpatient clinics with open access scheduling system: A systematic review. *Health Sci Rep*. 2024;7(7):e2160. doi:10.1002/HSR2.2160
30. Nanda T, Wang A, Ducasse LM, Chen RWS, Horowitz J. No-Show Rates and Associated Patient Factors in an Ophthalmology Resident Practice. *J Acad Ophthalmol*. 2020;12:67-73. doi:10.1055/s-0040-1712171
31. McMullen MJ, Netland PA. Lead time for appointment and the no-show rate in an ophthalmology clinic. *Clin Ophthalmol*. 2015;9:513. doi:10.2147/OPTH.S82151
32. Huang K, Maleki M, Regehr G, McEwen H. Examining the Educational Value of Student-Run Clinics for Health Care Students. *Acad Med*. 2021;96(7):1021-1025. doi:10.1097/ACM.0000000000003922
33. Rupert DD, Alvarez G V., Burdge EJ, Nahvi RJ, Schell SM, Faustino FL. Student-Run Free Clinics Stand at a Critical Junction Between Undergraduate Medical Education, Clinical Care, and Advocacy. *Acad Med*. 2022;97(6):824-831. doi:10.1097/ACM.0000000000004542
34. Friedman DS, Cassard SD, Williams SK, Baldonado K, O'Brien RW, Gower EW. Outcomes of a Vision Screening Program for Underserved Populations in the United States. *Ophthalmic Epidemiol*. 2013;20(4):201-211. doi:10.3109/09286586.2013.789533
35. Sapru S, Price SM, Hark LA, Rhodes LA, Newman-Casey PA. Recruiting Populations at Higher Risk for Glaucoma and Other Eye Diseases Experiencing Eye Health Disparities. *Ophthalmic Epidemiol*. 2024;31(3):220-228. doi:10.1080/09286586.2023.2232038/ASSET/F32F26F2-89D8-486C-83EC-20CD74E15CA3/ASSETS/GRAPHIC/IOPE_A_2232038_F0001_B.GIF
36. Berkowitz ST, Groth SL, Gangaputra S, Patel S. Racial/Ethnic Disparities in Ophthalmology Clinical Trials Resulting in US Food and Drug Administration Drug Approvals From 2000 to 2020. *JAMA Ophthalmol*. 2021;139(6):629. doi:10.1001/JAMAOPHTHALMOL.2021.0857
37. Bains A, Osathanugrah P, Sanjiv N, et al. Diverse Research Teams and Underrepresented Groups in Clinical Studies. *JAMA Ophthalmol*. 2023;141(11):1037. doi:10.1001/JAMAOPHTHALMOL.2023.4638
38. Chang SJ, Grewal KS, Selvam A, Chhablani J. Ethnoracial Representation in United States Clinical Trials for Retinal Vein Occlusion. *Am J Ophthalmol*. 2025;276:186-194. doi:10.1016/J.AJO.2025.04.011


## Authors


Sophia Dutton, BA, The Warren Alpert Medical School of Brown University, Providence, RI.

Anagha Lokhande, MD, The Warren Alpert Medical School of Brown University, Providence, RI; New York Eye and Ear Infirmary of Mount Sinai, NY, NY.

Chanbin Lee, BA, The Warren Alpert Medical School of Brown University, Providence, RI.

Vineethsubbu Somasundaram, BS, The Warren Alpert Medical School of Brown University, Providence, RI.

Jonathan Harrison, BA, The Warren Alpert Medical School of Brown University, Providence, RI.

Samuel Hochberger, BA, The Warren Alpert Medical School of Brown University, Providence, RI.

Samuel Mickel-Hulse, MD, University of North Carolina School of Medicine, Chapel Hill, NC.

David Booy, MD, Berkeley Eye Center, Houston, TX.

Andrew G. Young, MD, Department of Ophthalmology, Stein Eye Institute, David Geffen School of Medicine at UCLA, University of California, Los Angeles, CA.

Jamie Schaefer, MD, Department of Ophthalmology, University at Buffalo, Buffalo, NY.

Nicole Lanza, MD, The Warren Alpert Medical School of Brown University, Division of Ophthalmology, Providence, RI.


## Disclosures


**Funding Details:** None

**Disclaimer:** None of the authors have any proprietary interests or conflicts of interest related to this submission.

**Acknowledgments:** Authors SD and AL contributed equally. Authors JS and NL contributed equally.

This is a multi-institutional study conducted in collaboration between faculty previously affiliated with Brown University and currently at the University of California, Los Angeles; the University at Buffalo; and private practice. Portions of this work were previously presented as an abstract at the Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting in 2023 but have not been published as a full manuscript.


## Correspondence


Nicole Lanza, MD

1 Hoppin Street #200, Providence, RI 02903

401-444-6551 Fax 401-444-6587

nlanza@brownhealth.org

# Changes in Diet Among Adult Prevalent Kidney Stone Formers in the United States: The National Health and Nutrition Examination Survey, 1988–2018

EDUARDO CADORE GUZZO, MD; CHRISTINA RAKER, ScD; JIE TANG, MD, MPH


## ABSTRACT

**BACKGROUND/PURPOSE:** Dietary factors greatly influence kidney stone disease (KSD). We aimed to examine the dietary pattern changes of adult stone formers (SF) in the United States from 1988 to 2018.

**METHODS:** We used weighted, multiple linear regression analyses to examine dietary data from prevalent SF in the National Health and Nutrition Examination Survey (NHANES) III and 2007-2018.

**RESULTS:** The study was divided into four periods: 1988–1994, 2007–2010, 2011–2014, and 2015–2018. The KSD prevalence rate increased from 5.5% in 1988–1994 to 10.8% in 2015–2018. No significant changes occurred in the intake of total calories, total protein, saturated fat, or sodium. Total daily fat intake increased significantly (78.9 g in 1988–1994 to 88.7 g in 2015–2018, p=0.03). Daily potassium intake decreased significantly (2,947 mg in 1988–1994 to 2,628 mg in 2015–2018, p<0.001). Daily calcium intake (795 mg in 1988–1994 to 950 mg in 2015–2018, p<0.001) and daily fluid intake (2,120 ml in 1988–1994 to 3,124 ml in 2015–2018, p<0.001) increased significantly. No effect modification by gender or age group was detected.

**CONCLUSION:** There were significant increases in polyunsaturated fat, calcium, and fluid intakes. However, dietary potassium intake was reduced. Overall, there were no statistically significant changes in dietary intakes of calories, protein, carbohydrates, fiber, saturated fat, and sodium.


**KEYWORDS:** Kidney stone; dietary habits; NHANES; potassium; fluid intake

## INTRODUCTION

Kidney stone disease (KSD) is a prevalent and debilitating condition affecting millions globally.[1] It is caused by the complex interactions of dietary, genetic, and environmental factors that are not fully understood. However, specific nutrients and dietary patterns are implicated in stone formation and prevention.[2] For instance, high sodium intake has been linked to increased urinary calcium excretion and a consequent increase in the risk of calcium-based stone formation,[3] while high potassium intake has been associated with decreased urinary calcium excretion, reducing that risk.[4,5]

Current guidelines for the prevention of kidney stones recommend a diet rich in fruits, vegetables, and fluids, and restricted in sodium and animal proteins.[8] Nevertheless, adherence to those guidelines is variable among individuals. To better understand the rising prevalence rate of KSD, it is essential to examine the changes in dietary habits among stone formers. This study examines the data from the National Health and Nutrition Examination Survey (NHANES), a comprehensive dataset for evaluating dietary trends and their effects on health outcomes, to establish a temporal trend of dietary patterns among kidney stone formers from 1988 to 2018.

## METHODS

### Study Design and Population

This study uses NHANES data to compare the 1988–1994 cycle with the more recent 2007–2018 cycle. NHANES is a cross-sectional survey that combines self-reported data, physical examinations, and laboratory tests to provide a comprehensive picture of health and nutrition among the U.S. population.[9]

### Inclusion and Exclusion Criteria

Participants with a self-reported history of kidney stones were identified based on responses to the NHANES dietary interview and medical history questions. Only those with complete dietary data and relevant covariate information were included. Individuals with incomplete data or those reporting conditions unrelated to kidney stones were excluded. **Table 1** shows the number of patients included and excluded from this study.

### Dietary Assessment

Dietary intake was assessed using 24-hour dietary recall interviews conducted by trained interviewers. The dietary data were analyzed to evaluate adherence to kidney stone prevention guidelines, including sodium, potassium, and fluid intake. For the NHANES 2007–2018 cycles, dietary intake was based on the day-one recall.

**Table 1.** Study Population Inclusion and Exclusion Criteria

| Study population | NHANES 1988–1994 | NHANES 2007–2018 |
|---|---|---|
| Total records | 20,050 | 59,842 |
| Exclude missing KSD‡ response | 21 | 25,163 |
| Exclude age < 20 | 1,225 | 0 |
| Total remaining | 18,804 | 34,679 |
| Exclude missing dietary data | 2,835 | 3,963 |
| Total remaining | 15,969 | 30,716 |
| Exclude missing covariates | 1,861 | 3,390 |
| Total included | 14,108 | 27,326 |
| Total KSD only included | 680 | 2,636 |

Data derived from NHANES III (1988–1994) and NHANES 2007–2018 cycles. KSD: Kidney Stone Disease.

**Table 2.** Characteristics of Participants with KSD by Survey Period

| | | NHANES 1988–1994 n = 676 | NHANES 2007–2018 n = 2,636 |
|---|---|---|---|
| Age (year), mean (SE) | | 53.4 (0.8) | 53.7 (0.4) |
| Male sex, % (n) | | 58.5 (408) | 55.2 (1472) |
| Race, % (n) | Non-Hispanic White | 87.2 (457) | 76.7 (1460) |
| | Non-Hispanic Black | 3.6 (83) | 5.7 (340) |
| | Other | 9.2 (136) | 17.7 (836) |
| BMI (kg/m2), mean (SE) | | 27.8 (.30) | 30.5 (.18) |
| Diabetes, % (n) | | 8.5 (71) | 22.5 (691) |
| HbA1c (%), mean (SE) | | 5.6 (.05) | 5.9 (.03) |
| Hypertension, % (n) | | 37.7 (266) | 48.7 (1389) |
| SBP (mm Hg), mean (SE) | | 128.9 (.85) | 124.5 (.40) |
| DBP (mm Hg), mean (SE) | | 76.9 (.61) | 71.5 (.39) |
| Cardiovascular disease, % (n) | | 11.7 (115) | 12.1 (403) |
| Smoking, active, % (n) | | 23.7 (133) | 19.3 (517) |

Values are expressed as weighted means (SE) or %, unweighted n. P-values test for differences between time periods without assuming a linear association with time. SE: standard error; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; cardiovascular disease includes histories of myocardial infarction, congestive heart failure, and/or ischemic stroke.

### Covariates

Covariates included age, gender, race/ethnicity, BMI, and cardiovascular risk factors, including self-reported diabetes mellitus, hypertension, stroke, myocardial infarction, and congestive heart failure. Hemoglobin A1c (HbA1c) and blood pressure measurements were also examined as covariates.

### Statistical Analysis

Descriptive statistics were used to summarize the demographic and clinical characteristics of the two NHANES surveys. Dietary trends over time were analyzed by multivariable linear regression, adjusting for age, gender, race/ethnicity, BMI, and cardiovascular risk factors. Unadjusted and adjusted means and 95% confidence intervals (CIs) were reported for 1988–1994 and three four-year periods for 2007–2018.

Product terms were included in the models to assess the effect of measure modification by gender and age (65+ vs. <65) when the main effect of the time period was statistically significant at alpha = 0.05. All analyses were performed using survey procedures in Stata MP 18 (Stata Corp, College Station, TX), including strata, primary sampling units, and survey weights. Exam weights and day one dietary recall weights were used for NHANES 1988–1994 and 2007–2018, respectively. Weights were adjusted when combining cycles as outlined in NHANES analytic guidelines.

### Ethical Considerations

Ethical approval is not applicable to this article as it utilizes publicly available, de-identified data from NHANES. The National Center for Health Statistics Research Ethics Review Board approved the NHANES protocol. All participants provided informed consent for their data to be used in research.

## RESULTS

### Study Population

The prevalence of KSD increased from 5.6% in 1988–1994 (95% CI: 4.9–6.4) to 10.8% in 2015–2018 (95% CI: 9.9–11.9). **Table 2** outlines the characteristics of the study population. The cohort included 3,316 participants with a history of kidney stones across NHANES cycles. Non-White race, mean BMI, prevalent diabetes, mean HbA1c, and prevalent hypertension all increased between surveys. Mean SBP, mean DBP, and current smoking all decreased between surveys.

Values are expressed as weighted means (SE) or %, unweighted n. P-values test for differences between time periods without assuming a linear association with time. SE: standard error; cardiovascular disease includes histories of myocardial infarction, congestive heart failure, and/or ischemic stroke.

### Dietary Intake Trends

**Tables 3, 4, and 5** present changes in dietary intake among kidney stone formers between NHANES 1988–1994 and NHANES 2007-2018. There were no significant changes in total calorie or total protein intake [**Table 3**]. Total daily fat intake increased significantly from 78.9 g in 1988-1994 to 88.7 g in 2015-2018 (p=0.03). Specifically, the mean intake of saturated fat rose from 26.6 g to 29.3 g, though this increase was not statistically significant (p=0.089 in Model 3) [**Table 3**]. There were no significant changes in total sodium intake [**Table 4**]. Significant changes were observed in potassium and calcium intake [**Table 4**]; specifically, daily potassium intake decreased from 2,947 mg in 1988–1994 to 2,628 mg

**Table 3.** Change in Macronutrient Intake Among Participants with KSD Over Time

| Intake, day 1 recall | 1988–1994, n = 680 | 2007–2010, n = 882 | 2011–2014, n = 819 | 2015–2018, n = 935 | P |
|---|---|---|---|---|---|
| **Total calories (kcal)** | | | | | |
| Unadjusted | 2105.1 (2014.5–2196.7) | 2140.3 (2039.0–2241.7) | 2069.8 (1977.9–2161.7) | 2166.6 (2058.5–2274.7) | 0.6 |
| Model 1 | 2169.1 (2079.5–2259.8) | 2300.5 (2187.0–2414.1) | 2239.6 (2111.8–2367.3) | 2299.7 (2163.7–2435.8) | 0.5 |
| Model 2 | 2158.5 (2068.8–2248.2) | 2183.7 (2091.7–2275.7) | 2130.8 (2027.8–2233.7) | 2189.1 (2075.0–2303.1) | 0.4 |
| Model 3 | 2170.5 (2078.9–2262.1) | 2176.8 (2084.6–2269.0) | 2120.6 (2018.3–2222.8) | 2178.9 (2064.0–2293.9) | 0.5 |
| **Protein (g)** | | | | | |
| Unadjusted | 79.6 (75.2–84.0) | 80.5 (76.3–84.7) | 79 (75.9–82.1) | 83.4 (77.0–89.7) | 0.66 |
| Model 1 | 82.2 (77.7–86.7) | 87.2 (81.3–93.1) | 86.2 (80.9–91.5) | 88.9 (80.0–97.8) | 0.72 |
| Model 2 | 82.2 (77.7–86.7) | 82.5 (78.3–86.6) | 81.9 (78.0–85.7) | 84.5 (77.8–91.1) | 0.70 |
| Model 3 | 82.8 (78.2–87.4) | 82.2 (78.0–86.5) | 81.6 (77.8–85.5) | 84.1 (77.3–91.0) | 0.81 |
| **Total fat (g)** | | | | | |
| Unadjusted | 78.9 (74.8–83.1) | 82.9 (78.5–87.2) | 80.8 (76.9–84.8) | 88.7 (83.5–93.9) | 0.031 |
| Model 1 | 79.9 (75.6–84.3) | 86.4 (81.4–91.5) | 84.9 (79.3–90.6) | 91.5 (84.4–98.5) | 0.020 |
| Model 2 | 79.7 (75.4–84.0) | 83.4 (79.4–87.5) | 82.3 (77.6–86.9) | 88.7 (83.0–94.4) | 0.0098 |
| Model 3 | 80.1 (75.7–84.4) | 83.1 (79.0–87.1) | 81.8 (77.2–86.5) | 88.2 (82.4–93.9) | 0.020 |
| **Saturated fat (g)** | | | | | |
| Unadjusted | 26.6 (24.8–28.3) | 27 (25.5–28.5) | 26.4 (24.9–27.8) | 29.3 (27.3–31.2) | 0.11 |
| Model 1 | 26.9 (25.1–28.7) | 28.2 (26.4–29.9) | 27.7 (25.6–29.7) | 30.2 (27.8–32.6) | 0.099 |
| Model 2 | 26.8 (25.0–28.5) | 27.2 (25.8–28.6) | 26.8 (25.1–28.4) | 29.2 (27.2–31.3) | 0.070 |
| Model 3 | 26.9 (25.1–28.7) | 27 (25.6–28.4) | 26.6 (24.9–28.2) | 29 (27.0–31.0) | 0.089 |

Values are expressed as weighted means (95% CI). Multivariable linear regression models included the following covariates: Model 1: Age in years, gender, race/ethnicity, BMI. Model 2: Model 1 + diabetes, hypertension, cardiovascular disease, smoking. Model 3: Model 1 + HbA1c, SBP, DBP, cardiovascular disease, smoking. KSD: Kidney Stone Disease.

**Table 4.** Change in Micronutrient Intake Among Participants with KSD Over Time

| Intake, day 1 recall | 1988–1994, n = 680 | 2007–2010, n = 882 | 2011–2014, n = 819 | 2015–2018, n = 935 | P |
|---|---|---|---|---|---|
| **Sodium (mg)** | | | | | |
| Unadjusted | 3424.7 (3230.8–3618.5) | 3594.5 (3424.8–3764.2) | 3405.5 (3237.2–3573.9) | 3634.3 (3413.3–3855.3) | 0.19 |
| Model 1 | 3505.0 (3312.6–3697.3) | 3821.3 (3615.3–4027.4) | 3654.2 (3422.4–3886.0) | 3820.8 (3528.2–4113.3) | 0.18 |
| Model 2 | 3494.9 (3299.7–3690.0) | 3634.8 (3469.7–3799.9) | 3482.8 (3292.6–3673.0) | 3644.7 (3408.7–3880.7) | 0.17 |
| Model 3 | 3504.1 (3307.3–3700.9) | 3629.9 (3465.4–3794.4) | 3476.7 (3283.1–3670.2) | 3637.8 (3400.4–3875.1) | 0.18 |
| **Potassium (mg)** | | | | | |
| Unadjusted | 2946.7 (2808.4–3085.1) | 2760.1 (2604.5–2915.6) | 2567.9 (2460.2–2675.6) | 2627.8 (2477.0–2778.5) | <0.001 |
| Model 1 | 2902.2 (2759.2–3045.3) | 2768 (2589.3–2946.7) | 2606 (2465.8–2746.3) | 2620.4 (2441.7–2799.0) | 0.0058 |
| Model 2 | 2903.4 (2761.6–3045.2) | 2734.4 (2578.2–2890.5) | 2579.3 (2461.0–2697.6) | 2589 (2439.0–2739.1) | 0.0069 |
| Model 3 | 2917,8 (2776.9–3058.7) | 2726.6 (2568.7–2884.4) | 2571.6 (2454.7–2688.4) | 2577.6 (2424.9–2730.3) | 0.0022 |
| **Calcium (mg)** | | | | | |
| Unadjusted | 795.1 (745.9–844.3) | 914.1 (872.7–955.5) | 928.6 (871.4–985.8) | 950.4 (892.0–1008.9) | <0.001 |
| Model 1 | 813.2 (762.2–864.3) | 964.2 (907.7–1020.8) | 979.9 (910.1–1049.7) | 993.2 (920.5–1065.9) | <0.001 |
| Model 2 | 815.7 (764.7–866.7) | 928.9 (884.1–973.6) | 949.1 (888.0–1010.1) | 961.1 (900.7–1021.5) | <0.001 |
| Model 3 | 822.5 (770.8–874.1) | 925.9 (881.3–970.5) | 947.4 (888.1–1006.6) | 956.8 (897.0–1016.6) | <0.001 |

Values are expressed as weighted means (95% CI). Multivariable linear regression models included the following covariates: Model 1: Age in years, gender, race/ethnicity, BMI. Model 2: Model 1 + diabetes, hypertension, cardiovascular disease, smoking. Model 3: Model 1 + HbA1c, SBP, DBP, cardiovascular disease, smoking. KSD: Kidney Stone Disease.

**Table 5.** Change in Fluid Intake Among Participants with KSD Over Time

| Intake, day 1 recall | 1988–1994, n = 680 | 2007–2010, n = 882 | 2011–2014, n = 819 | 2015–2018, n = 935 | P |
|---|---|---|---|---|---|
| **Fluid (ml)** | | | | | |
| Unadjusted | 2120.4 (2006.0–2234.9) | 3035 (2875.9–3194.1) | 2863.3 (2759.2–2967.4) | 3123.6 (2995.7–3251.5) | <0.001 |
| Model 1 | 2173.3 (2045.7–2300.9) | 3166.8 (3004.4–3329.3) | 2986.7 (2851.2–3122.2) | 3241.7 (3089.4–3394.0) | <0.001 |
| Model 2 | 2160.0 (2032.1–2287.9) | 3047.5 (2903.9–3191.2) | 2862.7 (2756.7–2968.6) | 3118.3 (2996.0–3240.7) | <0.001 |
| Model 3 | 2146.8 (2016.1–2277.4) | 3041.1 (2898.7–3183.6) | 2856 (2749.8–2962.3) | 3115.2 (2990.6–3239.8) | <0.001 |

Values are expressed as weighted means (95% CI). Multivariable linear regression models included the following covariates: Model 1: Age in years, gender, race/ethnicity, BMI. Model 2: Model 1 + diabetes, hypertension, cardiovascular disease, smoking. Model 3: Model 1 + HbA1c, SBP, DBP, cardiovascular disease, smoking. KSD: Kidney Stone Disease.

in 2015–2018 (p<0.001), and daily calcium intake increased significantly from 795 mg in 1988–1994 to 950 mg in 2015–2018 (p<0.001), a decrease in potassium and an increase in calcium. Daily fluid intake increased significantly from 2,120 ml in 1988–1994 to 3,124 ml in 2015–2018 (p<0.001) [**Table 5**]. No effect modification by gender or age group was detected.

## DISCUSSION

This study examines dietary trends among kidney stone formers over 30 years of NHANES data to show how medical guidelines, specialist recommendations, and cultural shifts may have impacted their nutritional habits. The findings reveal significant changes in several critical dietary components, which may help guide future stone prevention strategies.

A concerning trend is the decreased potassium intake from 2947.6 mg to 2627.8 mg. Low potassium intake is a known risk factor for kidney stones.[4,5] Decreased potassium levels increase potassium reabsorption in the proximal tubule in part through K/H exchangers, with consequent increase in urine acidity. It, in turn, leads to decreased bicarbonate absorption and lowering of intracellular pH, which increases citrate reabsorption.[6] Decreased urinary citrate increases kidney stone risk.[7] Potassium also plays a crucial role in stone prevention by reducing urinary calcium excretion[8] and, in alkali-containing potassium salts, counterbalancing acid production from sulfur-containing amino acids in protein.[5,11] Indeed, a population study has indicated that low dietary potassium intake was associated with an increased risk of prevalent kidney stone disease.[4] In contrast, calcium intake has increased from 795.5 mg to 950.4 mg, aligning with dietary recommendations for kidney stone prevention in patients with enteric hyperoxaluria. Calcium's beneficial effects include decreasing phosphate and oxalate gastrointestinal absorption by binding these elements in the gut,[12] with low-calcium diets associated with increased hyperoxaluria.[13] It is of note, however, that certain conditions like idiopathic hypercalciuria and hyperparathyroidism can lead to increased urinary calcium excretion regardless of dietary intake.[14,15] Furthermore, a low-calcium diet is recommended for stone prevention in cases of enteric hypercalciuria. The relationship between calcium supplementation and stone risk remains a topic of debate, particularly if supplements are taken between meals, when they may be associated with increased urinary calcium excretion without affecting oxalate.[12] Due to the limitations of the NHANES data structure, we could not retrieve information regarding baseline hypercalciuria or hyperoxaluria.

Fluid intake dilutes urine, which is essential for kidney stone prevention.[16] Therefore, it is a positive highlight that it had the highest increase among dietary trends, from 2123 ml to 3123.6 ml. On the other hand, total fat intake increased from 78.9 g to 88.7 g, and saturated fat from 26.6 g to 29.3 g, mirroring the increased prevalence of obesity in the United States. Although the effect of fat in kidney stone formation is ill-defined, obesity is a well-established risk factor, partly by lowering urinary pH and reducing ammoniagenesis, increasing the risk of uric acid stones, and also due to its association with increased urinary calcium and oxalate excretion.[17,18]

In summary, the results are mixed when comparing dietary trends of prevalent KS formers with medical guidelines. While the improvement in fluid intake indicates better adherence to recommendations, the decline in potassium and increase in fat intake suggest otherwise. These changes reveal inconsistent compliance with medical guidelines and may be influenced more by broader population dietary changes and lifestyle than actual medical recommendations.

When considering this study, we acknowledge its limitations. It is based on self-reported data with potential for recall bias. The dietary assessment does not capture daily dietary variations and may not fully represent long-term habits. Finally, the study lacks data on baseline hypercalciuria and hyperoxaluria, specific liquid intake, medication and supplement use, and stone composition, which further limits our analysis.

## PRACTICAL APPLICATION

This study highlights critical dietary trends among kidney stone formers. It is encouraging to note an increase in fluid intake conforming to preventive guidelines, while the

decreased potassium intake raises concerns. The increased dietary fat intake is also concerning, particularly in increasing obesity prevalence, although its impact on KS risk has not been well defined. The findings presented here highlight the need for better strategies to educate and change populational habits.

## References


1. Hill AJ, et al. Incidence of Kidney Stones in the United States: The Continuous National Health and Nutrition Examination Survey. J Urol. 2022;207(4):851-856. doi: 10.1097/ju.0000000000002331.
2. Ferraro PM, Bargagli M, Trinchieri A, Gambaro G. Risk of Kidney Stones: Influence of Dietary Factors, Dietary Patterns, and Vegetarian–Vegan Diets. Nutrients. 2020;12(3):779. doi: 10.3390/nu12030779.
3. Ticinesi A, Nouvenne A, Borghi L, Meschi T. Salt and Nephrolithiasis. Nephrol Dial Transplant. 2016;31(1):39-45. doi: 10.1093/ndt/gfu243.
4. Tang J, Sammartino C, Chonchol M. Dietary Sodium and Potassium Intakes and Kidney Stone Prevalence: The National Health and Nutrition Examination Survey 2011–2018. Nutrients. 2024;16(14):2198. doi: 10.3390/nu16142198.
5. Ferraro PM, Mandel E, Curhan GC, Gambaro G, Taylor EN. Dietary Protein and Potassium, Diet–Dependent Net Acid Load, and Risk of Incident Kidney Stones. Clin J Am Soc Nephrol. 2016;11(10):1834-1844. doi: 10.2215/cjn.01520216.
6. Simpson DP. Citrate excretion: a window on renal metabolism. Am J Physiol. 1983;244(3):F223-F234. doi: 10.1152/ajprenal.1983.244.3.F223.
7. Moe OW. Kidney stones: pathophysiology and medical management. Lancet. 2006;367(9507):333-344. doi: 10.1016/S0140-6736(06)68071-9.
8. Pearle MS, Goldfarb DS, Assimos DG, et al. Medical management of kidney stones: AUA Guideline. J Urol. 2014;192(2):316-324. doi: 10.1016/j.juro.2014.05.006.
9. Centers for Disease Control and Prevention. National Health and Nutrition Examination Survey. https://www.cdc.gov/nchs/nhanes/index.htm.
10. Leman J, Pleuss JA, Gray RW, Hoffman RG. Potassium administration reduces and potassium deprivation increases urinary calcium excretion in healthy adults. Kidney Int. 1991;39(5):973-983. doi: 10.1038/ki.1991.123.
11. Frassetto LA, Todd KM, Morris Jr RC, Sebastian A. Estimation of net endogenous noncarbonic acid production in humans from diet potassium and protein contents. Am J Clin Nutr. 1998;68(3):576-583. doi: 10.1093/ajcn/68.3.576.
12. Bargagli M, Ferraro PM, Vittori M, et al. Calcium and Vitamin D Supplementation and Their Association with Kidney Stone Disease: A Narrative Review. Nutrients. 2021;13(12):4364. doi: 10.3390/nu13124364.
13. Hess B, Jost C, Zipperie L, Takkinen R, Jaeger P. High-calcium intake abolishes hyperoxaluria and reduces urinary crystallization during a 20-fold normal oxalate load in humans. Nephrol Dial Transplant. 1998;13(9):2241-2247. doi: 10.1093/ndt/13.9.2241.
14. Coe FL, Worcester EM, Evan PA. Idiopathic hypercalciuria and formation of calcium renal stones. Nat Rev Nephrol. 2016;12(9):519-533. doi: 10.1038/nrneph.2016.101.
15. Lila AR, Sarathi V, Jagtap V, et al. Renal manifestations of primary hyperparathyroidism. Indian J Endocrinol Metab. 2012;16(2):258-262. doi: 10.4103/2230-8210.93745.
16. Borghi L, Meschi T, Amato F, et al. Urinary volume, water and recurrences in idiopathic calcium nephrolithiasis: a 5-year randomized prospective study. J Urol. 1996;155(3):839-843.
17. Taylor EN, Curhan GC. Body size and 24-hour urine composition. Am J Kidney Dis. 2006;48(6):905-915. doi: 10.1053/j.ajkd.2006.09.004.
18. Asplin JR. Obesity and Urolithiasis. Adv Chronic Kidney Dis. 2009;16(1):11-20. doi: 10.1053/j.ackd.2008.10.003.


## Authors


Eduardo Cadore Guzzo, MD, completed a nephrology fellowship in the Division of Kidney Disease & Hypertension at Brown University Health, Providence, RI, and is currently a critical care fellow at Montefiore Medical Center, New York, NY.

Christina Raker, ScD, is with the Biostatistics, Epidemiology, Research Design, and Informatics Core at Brown University Health, Providence, RI.

Jie Tang, MD, MPH, is an Associate Professor of Medicine and Associate Director of Research in the Division of Kidney Disease & Hypertension at Brown University Health and Brown Physicians, Inc., Providence, RI.


## Disclosures

This work was supported by Brown Physicians, Inc. Foundation Category 3 Educational Funding on Kidney Stone Disease (PI: J Tang). The authors have no other relevant financial or personal conflicts of interest to disclose.

## Correspondence

Eduardo Cadore Guzzo, MD
2035 5th Ave, Unit 6R
New York, NY 10035
347-996-9105
edcguzzo@gmail.com

# Opioid, Buprenorphine, Benzodiazepine, Naloxone, and Stimulant Prescriptions Dispensed to Rhode Island Residents, 2022–2025

TAYLOR J. MELLO, MPH; STACI FISCHER, MD; KRISTEN ST. JOHN, MPH; ADAM Z. NITENSON, PhD; BENJAMIN D. HALLOWELL, PhD, MPH

## ABSTRACT

**BACKGROUND:** The Rhode Island Prescription Drug Monitoring Program (RI PDMP) captures dispensation records for controlled substance prescriptions in Schedules II–V and opioid antagonists dispensed in RI or to RI residents in other states.

**METHODS:** This report uses RI PDMP data from January 1, 2022 to December 31, 2025 to explore trends in opioid, buprenorphine, stimulant, benzodiazepine, and naloxone prescriptions dispensed to Rhode Island residents. Buprenorphine products were limited to those approved for the treatment of opioid use disorder (OUD). For the purposes of this report, buprenorphine products approved for pain management were categorized as opioids.

**RESULTS:** During this time, the number of dispensed opioids, naloxone, and buprenorphine prescriptions for OUD decreased 6%, 28%, and 11%, respectively, while the number of individuals dispensed these prescriptions decreased 5%, 28%, and 8%. Stimulant dispensations increased 16% while the number of individuals dispensed stimulants increased 19%. Benzodiazepine dispensations remained constant, but the number of individuals dispensed a benzodiazepine prescription decreased 3%. High-risk prescribing, such as individuals dispensed an opioid prescription with a ≥90 MME/day, decreased by 15%.

**CONCLUSIONS:** In a time of declining fatal overdoses, fewer RI residents are being dispensed high-risk opioid prescriptions, and buprenorphine for OUD, though the dispensing of stimulants has increased. Surveillance and analysis of dispensing of controlled substances should continue to include multiple agents in addition to opioids to understand evolving prescribing patterns and determine where provider education and regulatory changes can improve patient safety and public health.

**KEYWORDS:** Prescription Drug Monitoring Programs; Controlled Substances; Public Health Surveillance; Drug Overdose; Pharmacies

## INTRODUCTION

The Rhode Island (RI) Prescription Drug Monitoring Program (PDMP) is a centralized system managed by the RI Department of Health (RIDOH) to monitor the dispensing of Schedule II-V controlled substances and opioid antagonists to RI residents through retail pharmacies in RI and in other states.[1] The RI PDMP was founded in 2012 and has undergone many changes attributable to updating regulations aimed to prevent drug-related harms and increase PDMP effectiveness. Providers such as prescribers and pharmacies with a Controlled Substance Registration (CSR) can consult dispensing records via the electronic RI PDMP to understand 1) their own overall prescribing practices, and 2) their patients' prescriptive histories. All 50 states, 4 U.S. territories, and military health systems have installed PDMPs to track prescribing. Though each PDMP has unique data collection and regulations, all are designed to provide timely dispensing data to reduce over-prescribing, high-risk prescribing and diversion, improve patient care, and inform policy.[2] While data is mixed, a number of studies report that PDMP implementation leads to decreased opioid dispensing (or slower increase), fewer opioid prescription shipments, decreased prescription opioid diversion, and fewer opioid-involved mortalities.[3]

Several notable events happened between 2022 and 2025 that had the potential to impact dispensation trends of controlled substances. In October 2022, the U.S. Food and Drug Administration (FDA) announced a shortage of immediate-release Adderall formulations, which led to shortages of other prescription stimulant drugs that continue to persist in 2026.[4,5] In November 2022, the Centers for Disease Control and Prevention (CDC) updated the Clinical Practice Guideline for Prescribing Opioids for Pain.[6] The revisions moved away from rigid dosing and duration limits established in their earlier 2016 guidance, to flexible, patient-centered recommendations to prevent limiting access to care and undertreatment of pain.[7] In January 2023, the Consolidated Appropriations Act of 2023 was enacted by Congress, eliminating waiver requirements for buprenorphine prescribing and allowing telehealth visits for the initiation of controlled-substance prescriptions where not prohibited by state law.[8] In March 2023, the FDA approved over the counter (OTC) naloxone, when previously pharmacy naloxone was

dispensed by prescription only.[9] In June 2025, regulation changes allowed prescribers to prescribe up to a 90-day supply of non-opioid, non-narcotic Schedule II prescription drugs, when previously they were limited to 30-days.[10,11]

Though there are numerous resources to view aggregate dispensing data from the RI PDMP, the last large report published on this data is roughly four years old, before many regulatory changes occurred. The aim of this report is to provide updated data on trends in controlled substance dispensations and determine potential impacts from changing prescribing guidelines, drug availability, and the regulatory environment.

## METHODS

Records from the RI PDMP were used to identify all opioid, stimulant, benzodiazepine, and naloxone prescriptions dispensed by retail pharmacies to a RI resident between January 1, 2022 and December 31, 2025. Buprenorphine formulations used for pain management were excluded from buprenorphine counts and were instead included in the general opioid category. Buprenorphine products formulated for OUD treatment versus pain management were identified using the product's national drug code (NDC).[1] Excluded products included name brand and generic formulations of Belbuca®, Butrans®, and Buprenex®.

Methods are nearly identical to a previously published annual report.[1] In brief, demographic variables such as age and sex were reported by year for individuals dispensed opioids, stimulants, benzodiazepines, naloxone, and buprenorphine for OUD. User type (e.g., naive, non-naive, both) was reported for both opioid and stimulant patients. As described in Paiva et al (2023) and current state law,[1,12] individuals dispensed an opioid/stimulant prescription for the first time or with no opioid/stimulant prescription dispensation in the previous 30 days were classified as naive users. Individuals with opioid/stimulant prescription dispensations in the previous 30 days were classified as non-naive. Individuals who met both criteria, such as those who received a naive prescription dispensation that year and subsequently received a prescription dispensation within 30 days, were classified as both. High-risk prescribing practices were defined in two ways: 1) patients who dispensed a total daily opioid dose of at least 90 morphine milligram equivalents (MME), and 2) patients who dispensed overlapping benzodiazepine and opioid prescriptions for one or more days that year based on the prescriptions' fill date and end date. Individuals with overlapping benzodiazepine and opioid prescription dispensations over two years (e.g., December 2022 to January 2023) were counted once for each of those years. Ethnical approval was not applicable for this article.

## RESULTS

### Opioid Prescriptions

Between 2022 and 2025, there were 1,551,454 opioid prescriptions dispensed to RI residents from a retail pharmacy. Dispensations decreased 6% from 401,165 dispensations in 2022 to 375,129 in 2025. Oxycodone prescriptions made up 48% of all dispensations. Hydrocodone prescriptions made up 21% of dispensations in 2022 but decreased to 16% by 2025. Codeine prescription counts and proportion of total dispensations nearly halved by 2025 [4% in 2022 to 2% in 2025; **Table 1**].

During the study period, a total of 110,097 unique individuals were dispensed an opioid prescription, which decreased 5% from 106,112 in 2022 to 101,047 in 2025. Of the total opioid prescriptions dispensed, 57% were dispensed to females, and 43% were dispensed to males. The proportion of individuals aged 65 and older dispensed an opioid prescription made up the highest proportion among the age categories and increased 14% from 36% in 2022 to 41% in 2025 [**Table 2**]. Opioid-naïve individuals made up the highest proportion of individuals dispensed opioid prescriptions at 63% per year, while opioid non-naïve individuals made up 7%, and individuals who fit both opioid-naive and non-naive status made up 30% [**Table 2**]. Opioid non-naïve individuals showed similar demographic trends as overall opioid recipients, mostly female; however, a higher proportion of opioid non-naïve individuals were aged 55 or older compared to opioid-naive individuals (76% vs 48%).

### High-Risk Opioid Prescribing

In total, 6,206 individuals were dispensed an opioid prescription with a daily MME of 90 or higher, which decreased 15% from 5,743 individuals in 2022 to 4,889 individuals in 2025. Of these individuals, about half were female (51%), and 76% were aged 55 or older [**Table 2**]. There were 51,436 total individuals that were dispensed an overlapping benzodiazepine and opioid prescription during the study timeframe, a number which stayed consistent year by year. Females made up 63% of these individuals, and 77% of individuals were aged 55 and older [**Table 2**].

### Buprenorphine

From 2022 to 2025, there were 302,421 buprenorphine prescriptions dispensed for OUD to 10,534 unique individuals. The number of buprenorphine prescriptions dispensed for OUD decreased 11% from 81,065 prescriptions in 2022 to 72,025 prescriptions in 2025. Likewise, the number of unique individuals dispensing these prescriptions decreased 8% from 7,359 in 2022 to 6,756 in 2025 [**Table 1**, **Table 3**]. Film formulations made up 67%, tablets made up 31%, and injection formulations made up 2% of all buprenorphine prescriptions dispensed in retail pharmacies for OUD. Buprenorphine and naloxone combination products made up 88% of all buprenorphine products dispensed for OUD, and

**Table 1.** Counts of Dispensed Opioid, Buprenorphine, Stimulant, and Benzodiazepine prescriptions to Rhode Island residents, stratified by product type, 2022–2025.[a]

| | 2022 N (%) | 2023 N (%) | 2024 N (%) | 2025 N (%) | Total N (%) |
|---|---|---|---|---|---|
| **Opioids** | **401,165** | **393,073** | **382,087** | **375,129** | **1,551,454 (100)** |
| Oxycodone | 18,3160 (46) | 190061 (48) | 187588 (49) | 185887 (50) | 746,696 (48) |
| Hydrocodone | 84,702 (21) | 69412 (18) | 64008 (17) | 59311 (16) | 277,433 (18) |
| Tramadol | 62,890 (16) | 61126 (16) | 62035 (16) | 59247 (16) | 245,298 (16) |
| Morphine | 30,693 (8) | 32236 (8) | 32749 (9) | 31252 (8) | 126,930 (8) |
| Codeine | 14,541 (4) | 12936 (3) | 7659 (2) | 7683 (2) | 42,819 (3) |
| Hydromorphone | 7,544 (2) | 9214 (2) | 8131 (2) | 10153 (2) | 35,042 (2) |
| Buprenorphine* | 5,864 (2) | 7332 (2) | 10237 (3) | 12373 (3) | 35,806 (2) |
| Fentanyl | 5,460 (1) | 4616 (1) | 4299 (1) | 4199 (1) | 18,574 (1) |
| Methadone* | 4,484 (1) | 4558 (1) | 3930 (1) | 3923 (1) | 16,895 (1) |
| Tapentadol | 1,033 (<1) | 924 (<1) | 828 (<1) | 644 (<1) | 3,429 (<1) |
| Opium | 304 (<1) | 226 (<1) | 209 (<1) | 161 (<1) | 900 (<1) |
| Oxymorphone | 279 (<1) | 228 (<1) | 184 (<1) | 99 (<1) | 790 (<1) |
| Butorphanol | 138 (<1) | 145 (<1) | 169 (<1) | 158 (<1) | 610 (<1) |
| **Buprenorphine** | **81,065** | **75,621** | **73,530** | **72,025** | **302,241 (100)** |
| Bup. & Nalox. | 72,926 (90) | 66,845 (88) | 63,706 (87) | 61,722 (86) | 265,199 (88) |
| Bup. | 8,139 (10) | 8,776 (12) | 9,824 (13) | 10,303 (14) | 37,042 (12) |
| **Stimulants** | **474,342** | **466,837** | **508,389** | **548,445** | **1,998,013 (100)** |
| Amphetamine | 292,119 (62) | 253,373 (54) | 292,472 (58) | 312,341 (57) | 1,150,305 (58) |
| Methylphenidate | 77,628 (16) | 82,919 (18) | 87,483 (17) | 91,592 (17) | 339,622 (17) |
| Lisdexamfetamine | 40,835 (9) | 55,506 (12) | 50,645 (10) | 65,877 (12) | 212,863 (11) |
| Phentermine | 26,038 (6) | 31,530 (7) | 37,605 (7) | 37,745 (7) | 132,918 (7) |
| Dexmethylphenidate | 17,931 (4) | 23,307 (5) | 20,292 (4) | 21,620 (4) | 83,150 (4) |
| Dextroamphetamine | 7,537 (2) | 8,277 (2) | 8,315 (2) | 8,016 (2) | 32,145 (2) |
| Phendimetrazine | 4,865 (1) | 4,229 (1) | 3,308 (1) | 2,677 (1) | 15,079 (1) |
| Modafinil | 4,826 (<1) | 5,157 (1) | 5,600 (1) | 5,872 (1) | 21,455 (1) |
| Armodafinil | 2,091 (<1) | 2,072 (<1) | 2,124 (<1) | 0 (0) | 6,287 (<1) |
| Solriamfetol | 303 (<1) | 333 (<1) | 429 (<1) | 410 (<1) | 1,475 (<1) |
| **Benzodiazepines** | **472,624** | **46,0257** | **449,072** | **445,128** | **1,827,081 (100)** |
| Lorazepam | 142,178 (30) | 140,540 (31) | 137,071 (31) | 139,693 (31) | 559,482 (31) |
| Clonazepam | 145,383 (31) | 141,094 (31) | 137,464 (31) | 134,052 (30) | 566,993 (31) |
| Alprazolam | 127,613 (27) | 122,784 (27) | 120,875 (27) | 116,572 (26) | 487,844 (27) |
| Diazepam | 37,733 (8) | 36,651 (8) | 35,246 (8) | 34,978 (8) | 144,608 (8) |
| Temazepam | 11,563 (3) | 10,751 (2) | 10,066 (2) | 10,091 (2) | 42,471 (2) |
| Triazolam | 2,611 (1) | 2,580 (1) | 2,353 (1) | 2,206 (1) | 9,750 (1) |
| Clobazam | 2,501 (1) | 2,919 (1) | 3,249 (1) | 3,764 (1) | 12,433 (1) |
| Clorazepate | 1,203 (<1) | 1,033 (<1) | 834 (<1) | 754 (<1) | 3,824 (<1) |
| Chlordiazepoxide | 781 (<1) | 811 (<1) | 741 (<1) | 683 (<1) | 3,006 (<1) |
| Midazolam | 619 (<1) | 727 (<1) | 832 (<1) | 2,048 (1) | 4,226 (<1) |
| Oxazepam | 329 (<1) | 317 (<1) | 271 (<1) | 2,048 (1) | 2,965 (<1) |
| **Naloxone** | **14,501** | **18,115** | **15,794** | **10,470** | **58,880** |

[a] Note: Products may not add to yearly total as products with totals < 400 are excluded from tables for brevity. Among the excluded are fenfluramine, methamphetamine, benzphetamine, clinidium & combination, estazolam, flurazepam, levorphanol, dihydrocodeine, meperidine, diethylpropion, and pentazocine.
*Only includes products formulated for pain.

**Table 2.** Number of Unique Rhode Island Residents Dispensed an Opioid Analgesic Prescription, 2022–2025.

| | 2022 N (%) | 2023 N (%) | 2024 N (%) | 2025 N (%) | Total N (%) |
|---|---|---|---|---|---|
| **Dispensed an opioid** | **106,112** | **104,935** | **102,121** | **101,047** | **110,097** |
| **Sex** | | | | | |
| Female | 61,269 (58) | 60,752 (58) | 59,205 (58) | 58,639 (58) | 63,245 (57) |
| Male | 44,836 (42) | 44,179 (42) | 42,907 (42) | 42,404 (42) | 46,839 (43) |
| Unknown | 7 (<1) | <5 | 9 (<1) | <5 | 13 (<1) |
| Median Age, Years [IQR] | 58 [42,70] | 59 [43,70] | 60 [44,71] | 60 [44,71] | 57 [41,69] |
| **Age Category** | | | | | |
| <18 | 2,104 (2) | 1,872 (2) | 1,657 (2) | 1,654 (2) | 2,307 (2) |
| 18–24 | 4,886 (5) | 4,465 (4) | 4,197 (4) | 4,154 (4) | 5,449 (5) |
| 25–34 | 10,207 (10) | 9,737 (9) | 9,092 (9) | 8,790 (9) | 11,146 (10) |
| 35–44 | 12,405 (12) | 12,240 (12) | 11,773 (12) | 11,673 (12) | 13,033 (12) |
| 45–54 | 15,095 (14) | 14,666 (14) | 13,658 (13) | 13,048 (13) | 16,717 (15) |
| 55–64 | 22,902 (22) | 22,074 (21) | 21,102 (21) | 20,525 (20) | 24,029 (22) |
| 65+ | 38,513 (36) | 39,881 (38) | 40,642 (40) | 41,203 (41) | 37,416 (34) |
| **User Type** | | | | | |
| Naïve | 65,655 (62) | 65,148 (62) | 62,980 (62) | 62,345 (62) | 179,409 (63) |
| Non–naïve | 12,900 (12) | 11,935 (11) | 11,467 (11) | 11,225 (11) | 20,567 (7) |
| Both | 27,557 (26) | 27,852 (27) | 27,666 (27) | 27,477 (27) | 86,217 (30) |
| **High–Risk Opioid Prescribing** | | | | | |
| Dispensed a daily MME≥90 | 5,743 | 5,435 | 5,245 | 4,889 | 6,206 |
| **Sex** | | | | | |
| Female | 2,984 (52) | 2,844 (52) | 2,703 (52) | 2,527 (52) | 3,158 (51) |
| Male | 2,759 (48) | 2,590 (48) | 2,542 (49) | 2,362 (48) | 3,046 (49) |
| Unknown | 0 | <5 | 0 | 0 | <5 |
| **Median Age, Years [IQR]** | **65 [56,76]** | **66 [57,76]** | **67 [57,77]** | **67 [58,77]** | **64 [55,74]** |
| **Age Category** | | | | | |
| <18 | 8 (<1) | 11 (<1) | 10 (<1) | 9 (<1) | 13 (<1) |
| 18–24 | 25 (<1) | 27 (<1) | 30 (<1) | 35 (<1) | 37 (1) |
| 25–34 | 135 (2) | 111 (2) | 111 (2) | 97 (2) | 166 (3) |
| 35–44 | 327 (6) | 279 (5) | 287 (6) | 245 (5) | 401 (6) |
| 45–54 | 714 (12) | 659 (12) | 596 (11) | 524 (11) | 899 (14) |
| 55–64 | 1,488 (26) | 1,335 (25) | 1,251 (24) | 1,159 (24) | 1,745 (28) |
| 65+ | 3,046 (53) | 3,013 (55) | 2,960 (56) | 2,820 (58) | 2,945 (48) |
| **Dispensed an overlapping benzodiazepine and opioid** | **13,918** | **13,618** | **13,631** | **13,548** | **51,436** |
| **Sex** | | | | | |
| Female | 8,908 (64) | 8,558 (63) | 8,672 (64) | 8,581 (63) | 32,432 (63) |
| Male | 5,010 (36) | 5,048 (37) | 4,945 (36) | 4,962 (37) | 18,974 (37) |
| Unknown | 0 | 23 (<1) | 14 (<1) | 5 (<1) | 30 (<1) |
| Median Age, Years [IQR] | 67 [55,80] | 68 [55,80] | 68 [55,81] | 69 [56,91] | 69 [56,81] |
| **Age Category** | | | | | |
| <18 | 143 (1) | 136 (1) | 150 (1) | 144 (1) | 563 (1) |
| 18–24 | 151 (1) | 184 (1) | 169 (1) | 161 (1) | 656 (1) |
| 25–34 | 522 (4) | 484 (4) | 479 (4) | 445 (3) | 1,813 (3) |
| 35–44 | 1,048 (8) | 959 (7) | 990 (7) | 915 (7) | 3,630 (7) |
| 45–54 | 1,565 (11) | 1,523 (11) | 1,400 (10) | 1,366 (10) | 5,327 (10) |
| 55–64 | 2,742 (20) | 2,532 (19) | 2,432 (18) | 2,453 (18) | 9,253 (18) |
| 65+ | 7,747 (56) | 7,800 (57) | 8,011 (59) | 8,064 (60) | 30,194 (59) |

**Table 3.** Unique Rhode Island Residents Dispensed at least one Stimulant, Benzodiazepine, Naloxone, or Buprenorphine Prescription for Opioid Use Disorder Treatment, 2022–2025.

| | 2022 N (%) | 2023 N (%) | 2024 N (%) | 2025 N (%) | Total N (%) |
|---|---|---|---|---|---|
| **Dispensed Buprenorphine** | **7,359** | **7,347** | **7,035** | **6,756** | **10,534** |
| **Sex** | | | | | |
| Female | 2,816 (38) | 2,796 (38) | 2,716 (39) | 2,575 (38) | 4,027 (38) |
| Male | 4,543 (62) | 4,551 (62) | 4,319 (61) | 4,181 (62) | 6,507 (62) |
| **Median Age, Years [IQR]** | **45 [37,55]** | **46 [38,56]** | **47 [39,58]** | **48 [40,58]** | **44 [36,56]** |
| **Age Category** | | | | | |
| <18 | 5 (<1) | <5 | <5 | <5 | 11 (<1) |
| 18–24 | 111 (2) | 108 (2) | 75 (1) | 60 (1) | 243 (2) |
| 25–34 | 1,194 (16) | 1,034 (14) | 873 (12) | 692 (10) | 1,843 (17) |
| 35–44 | 2,267 (31) | 2,253 (31) | 2,090 (30) | 1,944 (29) | 3,181 (30) |
| 45–54 | 1,777 (24) | 1,797 (25) | 1,744 (25) | 1,735 (26) | 2,353 (22) |
| 55–64 | 1,429 (19) | 1,468 (20) | 1,476 (21) | 1,476 (22) | 1,979 (19) |
| 65+ | 576 (8) | 693 (9) | 773 (11) | 848 (13) | 924 (9) |
| **Dispensed Stimulants** | **56,429** | **60,193** | **63,928** | **67,402** | **102,395** |
| Sex | | | | | |
| Female | 32,442 (58) | 35,231 (59) | 37,952 (59) | 40,120 (60) | 61,400 (60) |
| Male | 23,985 (43) | 24,956 (42) | 25,970 (41) | 27,273 (41) | 40,983 (40) |
| Unknown | <5 | 6 (<1) | 6 (<1) | 9 (<1) | 12 (<1) |
| **Median Age, Years [IQR]** | **33 [20,46]** | **34 [21,47]** | **35 [22,47]** | **35 [22,47]** | **34 [21,47]** |
| **Age Category** | | | | | |
| <18 | 11,924 (21) | 12,073 (20) | 12,028 (19) | 12,329 (18) | 19,912 (19) |
| 18–24 | 6,473 (12) | 6,442 (11) | 6,527 (10) | 6,890 (10) | 11,635 (11) |
| 25–34 | 11,507 (20) | 12,195 (20) | 12,904 (20) | 13,341 (20) | 21,217 (21) |
| 35–44 | 10,876 (19) | 12,217 (20) | 13,606 (21) | 14,813 (22) | 20,469 (20) |
| 45–54 | 7,670 (14) | 8,466 (14) | 9,086 (14) | 9,522 (14) | 13,974 (14) |
| 55–64 | 5,375 (10) | 5,848 (10) | 6,363 (10) | 6,731 (10) | 9903 (10) |
| 65+ | 2,604 (5) | 2,952 (5) | 3,414 (5) | 3,776 (6) | 5,285 (5) |
| **User Type** | | | | | |
| Naïve | 8,199 (15) | 9,514 (16) | 10,103 (16) | 9,945 (15) | 37,761 (15) |
| Non–naïve | 21,523 (38) | 19,463 (32) | 21,779 (34) | 24,724 (37) | 87,489 (35) |
| Both | 26,707 (47) | 31,216 (52) | 32,049 (50) | 32,733 (49) | 122,705 (49) |
| **Dispensed Benzodiazepines** | **94,313** | **93,011** | **91,464** | **91,219** | **180,434** |
| **Sex** | | | | | |
| Female | 63,318 (67) | 62,293 (67) | 61,206 (67) | 60,955 (67) | 117,936 (65) |
| Male | 30,993 (33) | 30,705 (33) | 30,235 (33) | 30,256 (33) | 62,462 (35) |
| Unknown | <5 | 13 (<1) | 23 (<1) | 8 (<1) | 36 (<1) |
| **Median Age, Years [IQR]** | **58 [43,69]** | **58 [43,70]** | **59 [43,70]** | **59 [43,71]** | **57 [40,70]** |
| **Age Category** | | | | | |
| <18 | 1,798 (2) | 1,807 (2) | 1,888 (2) | 2,061 (2) | 5,234 (3) |
| 18–24 | 2,836 (3) | 2,667 (3) | 2,521 (3) | 2,689 (3) | 7,495 (4) |
| 25–34 | 8,662 (9) | 8,237 (9) | 7,845 (9) | 7,640 (8) | 18,661 (10) |
| 35–44 | 12,609 (13) | 12,393 (13) | 12,155 (12) | 12,193 (13) | 24,101 (13) |
| 45–54 | 14,981 (16) | 14,397 (16) | 13,719 (15) | 13,413 (15) | 26,065 (14) |
| 55–64 | 20,338 (22) | 19,579 (21) | 18,871 (21) | 18,570 (20) | 34,559 (19) |
| 65+ | 33,089 (35) | 33,931 (37) | 34,465 (38) | 34,653 (38) | 64,319 (37) |
| **Dispensed Naloxone** | **12,564** | **15,576** | **13,619** | **9,067** | **43,768** |
| **Sex** | | | | | |
| Female | 6,970 (56) | 8,916 (57) | 7,658 (56) | 4,766 (53) | 24,416 (56) |
| Male | 5,593 (45) | 6,658 (43) | 5,961 (44) | 4,300 (47) | 19,349 (44) |
| Unknown | <5 | <5 | 0 (0) | <5 | <5 |
| **Median Age, Years [IQR]** | **52 [37,62]** | **54 [40,65]** | **55 [40,66]** | **51 [38,62]** | **53 [38,64]** |
| **Age Category** | | | | | |
| <18 | 410 (3) | 434 (3) | 402 (3) | 345 (4) | 1,515 (3) |
| 18–24 | 577 (5) | 588 (4) | 467 (3) | 382 (4) | 1,861 (4) |
| 25–34 | 1,624 (13) | 1,689 (11) | 1,365 (10) | 1,057 (12) | 5,068 (12) |
| 35–44 | 2,136 (17) | 2,405 (15) | 2,077 (15) | 1,706 (19) | 6,912 (16) |
| 45–54 | 2,333 (19) | 2,716 (17) | 2,283 (17) | 1,674 (19) | 7,452 (17) |
| 55–64 | 2,989 (24) | 3,631 (23) | 3,253 (24) | 2,201 (24) | 10,208 (23) |
| 65+ | 2,495 (20) | 4,113 (26) | 3,772 (28) | 1,702 (19) | 10,752 (25) |

buprenorphine products without naloxone made up 12% [**Table 1**]. Of individuals dispensed buprenorphine prescriptions for OUD, 62% were male, and 52% were between the ages 35 and 54 [**Table 3**].

### Stimulant

A total of 1,999,013 stimulant prescriptions were dispensed to 102,395 unique individuals from 2022 to 2025. The number of stimulant prescriptions dispensed increased 16% from 474,342 in 2022 and 548,445 in 2025 [**Table 1**]. The number of individuals dispensed stimulant prescriptions also increased 19% from 56,429 in 2022 to 67,402 in 2025 [**Table 3**]. Amphetamine combination drugs made up 58% of all stimulants dispensed in this period, while methylphenidate made up 17% (**Table 1**]. Females made up 60% of unique individuals dispensed a stimulant prescription, individuals aged younger than 18 years accounted for 19%, and individuals aged 25 to 44 years made up 41% [**Table 3**].

There were 37,761 stimulant naïve, 87,489 stimulant non-naive, and 122,705 'combination' individuals who fit both naive and non-naive status dispensed a stimulant prescription between 2022 and 2025. Of those dispensed a naïve stimulant prescription, 62% were females and 55% of individuals were aged 34 and younger [**Table 3**]. Of non-naive stimulant users, the median age was slightly higher than that of naive users (37 years vs 32 years).

### Benzodiazepines

There were 1,827,081 total benzodiazepine prescriptions dispensed to 180,434 unique individuals between 2022 and 2025. The number of benzodiazepine prescriptions dispensed increased 6% from 472,624 in 2022 to 445,128 in 2025. Lorazepam and clonazepam each made up 31% of all benzodiazepines dispensed, and alprazolam made up 27% [**Table 1**]. The number of individuals dispensed benzodiazepines decreased 3% from 94,313 in 2022 to 91,219 in 2025. Females made up 65%, and individuals aged 55+ made up 56% of those dispensed benzodiazepines [**Table 3**].

### Naloxone

A total of 58,880 naloxone prescriptions were dispensed to 43,768 unique individuals between 2022 and 2025. The number of naloxone prescriptions dispensed decreased 28% from 14,501 in 2022 to 10,470 in 2025 [**Table 1**]. The number of unique individuals dispensed a naloxone prescription also decreased 28% from 12,564 in 2022 to 9,067 in 2025 [**Table 3**[. Females made up 56%, and individuals aged 45 and older made up 65% of those dispensed naloxone [**Table 3**].

## DISCUSSION

While many regulatory changes have been made to decrease barriers to access of non-illicit controlled substance, such as less rigid opioid prescribing guidelines, OTC naloxone, telehealth prescribing, and elimination of buprenorphine prescribing waivers, the number of opioid, benzodiazepine, buprenorphine for OUD, and naloxone prescriptions dispensed and individuals receiving those prescriptions declined from 2022 to 2025. Additionally, despite the shortage, stimulant prescription dispensations, and the number of individuals receiving them, have been steadily increasing at least since 2017.[1]

At the start of the overdose epidemic, most overdose fatalities involved prescription opioids. As such, when the opioid epidemic was first declared an official nationwide public health emergency, guidelines were put into place to reduce opioid prescribing to avoid irresponsible prescribing practices and unnecessary exposures to these highly addictive medications. These rigid guidelines and implementation of the RI PDMP likely attributed to the initial decline of opioid dispensations from 2017 to 2021.[1] Worries about these earlier guidelines causing legacy patients—individuals in long-term opioid therapy initiated under permissive prescribing practices at the start of the epidemic—to lose access to opioid medications, putting them at an unnecessary risk of physical danger and possible illicit use, began circulating.[13,14] The CDC's 2022 updated, and less-rigid, opioid prescribing guidelines advised prescribers to consider prescribing other pain-relief medications such as NSAIDs, when possible, to patients with acute pain, but to prescribe opioids to patients if the benefits outweigh potential risks.[6] While the CDC's recommendations have become more flexible, RI state regulations have not changed, and prescribers are required to follow 2016 guidelines. The continued decline in opioid prescribing is possibly due to adherence to early prescribing guidelines. However, RI has introduced legislation in 2026 to adopt the CDC's 2022 guidelines, which may result in future stabilization of opioid prescription dispensations in the state.

While non-naïve opioid patients in RI are decreasing, they are decreasing by no more than 7% per year and, in recent years, are decreasing at about 2–3% each year. This may be a result of fewer individuals initiating opioids for the first time. In addition to this, compared to RI data from 2017–2021, oxycodone use has nearly doubled while hydrocodone use has halved.[1] Studies have found that among naïve patients, while oxycodone use is associated with an increased risk of overdose, hydrocodone use is associated with an increased risk of developing chronic use.[15] While it is important to limit initiation of opioid medication to naïve individuals to avoid developing chronic use, it is equally important to consider patients on an individual basis and provide them with necessary care. This includes providing care to legacy patients and ensuring they have access to necessary medication.

The decrease in high MME opioid prescriptions is likely due to RI providers' adherence to previous CDC prescribing guidelines. Unlike the original opioid prescribing guidelines,

the 2022 guidelines do not set rigid MME restrictions. Older adults (65+ years) consistently make up more than half of the individuals dispensed overlapping opioid and benzodiazepine prescriptions. This population is especially susceptible to falls and altered mental state when on these medications.[16,17] As of 2018, it is required in RI that naloxone be co-prescribed with high-risk opioid prescriptions.[1] With the number of high-risk opioid prescriptions declining, naloxone prescriptions are also declining. This decline may also be attributed to the availability of over-the-counter options as of 2023, saturation of no-cost naloxone in the community due to increased community distribution, and the decrease in opioid overdoses resulting in the lack of urgency to carry naloxone.[9] Efforts should continue to communicate the importance of having naloxone even if an individual does not knowingly use opioids, as overdoses caused by drugs contaminated with opioids can still be reversed with naloxone.

Despite the elimination of various barriers, buprenorphine dispensations decreased slightly over the study timeframe. However, this number has only decreased by about 4% since 2017.[1] Long-acting injectable buprenorphine medications, such as Sublocade® and Brixadi®, are becoming increasingly more popular due to convenience and lower chances of diversion and are only administered in-office by clinicians.[18,19] On rare occasions, injectable buprenorphine is dispensed in retail pharmacies if a clinician lacks the product on-hand and instructs the patient to fill their prescription at a retail pharmacy and bring it to the office for administration. Though there are some injectable formulations recorded in the PDMP, we are unable to account for injectable buprenorphine formulations prescribed and dispensed in OTPs, which may have led to the number of buprenorphine prescriptions to be underestimated. It may also be that decreased buprenorphine dispensing is linked to a decrease in opioid usage or saturation of treatment among the RI population.

Previous studies show that stimulant prescribing has increased in RI since 2018 and continues to increase through 2025, much of which is dispensed to young children and adults aged 25–44.[20] Prior to 2020, the proportion of minors dispensed a stimulant prescription far outweighed the proportion of adults. However, since the COVID-19 pandemic, prescribing to adults and prescribing to stimulant naïve patients has increased, possibly due to an increase in attention-deficit/hyperactivity disorder (ADHD) diagnosed later in life, and popularization of stimulant prescriptions to facilitate weight loss.[21] Similar trends are evident in nationwide data.[22] Providers should continue to educate stimulant patients on the potential hypertensive and cardiac side effects of stimulant drugs, the risk of stimulant-use disorder, and symptoms of overamping. Future work should investigate the incidence of emergency room visits with stimulant overamping symptoms in response to the surge of stimulant prescribing.

Using RI PDMP data for this study is a great strength, as it is a comprehensive system that automatically registers prescribers and requires them to provide complete data on all controlled substances and opioid antagonists dispensed through retail pharmacies. This project is, however, subject to several limitations. First, the RI PDMP has limited demographic data for patients captured in its records and does not include race or ethnicity data. Second, the RI PDMP does not capture data on prescriptions prescribed and not dispensed. If a patient does not fill their prescription, the database does not record it. In addition to this, products not dispensed at a retail pharmacy, such as medication sold OTC, administered in OTPs, administered in the Department of Corrections, or administered in an emergency department or hospital are not captured.

While the decrease in opioid prescription dispensations is promising and could represent the many efforts taken to reduce opioid related injury, other substances such as stimulant dispensations are on the rise. Surveillance and efforts to investigate changes in the prescription landscape as it relates to the overdose epidemic should continue in efforts to further reduce the number of unintentional fatal overdoses each year.

## References


1. Paiva TJ, Nitenson AZ, Antinozzi D, Onyejekwe C, McDonald JV, Hallowell BD. Dispensed Opioid, Buprenorphine, Benzodiazepine, and Stimulant Prescriptions among Rhode Island Residents, 2017-2021. *R I Med J*. 2023;106(2):27-30.
2. The Prescription Drug Monitoring Program Training and Technical Assistance Center (PDMP TTAC). STATE PDMP PROFILES AND CONTACTS. 2026. https://www.pdmpassist.org/State
3. Finley EP, Garcia A, Rosen K, McGeary D, Pugh MJ, Potter JS. Evaluating the impact of prescription drug monitoring program implementation: a scoping review. *BMC Health Serv Res*. 2017;17(1):420. doi:10.1186/s12913-017-2354-5
4. Jensen, PharmD L. Methylphenidate Extended Release Oral Presentations. American Society of Health-System Pharmacists. December 4, 2025. https://www.ashp.org/drug-shortages/current-shortages/drug-shortage-detail.aspx?id=896&loginreturnUrl=SSOCheckOnly
5. U.S. Food & Drug Administration (FDA). FDA Announces Shortage of Adderall. U.S. Food & Drug Administration. August 1, 2023. Accessed February 3, 2026. https://www.fda.gov/drugs/drug-safety-and-availability/fda-announces-shortage-adderall
6. Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain—United States, 2022. *MMWR Recomm Rep*. 2022;71(3):1-95. doi:10.15585/mmwr.rr7103a1
7. Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pai —United States, 2016. *MMWR Recomm Rep*. 2016;65(1):1-49. doi:10.15585/mmwr.rr6501e1
8. 117th Congress. *Consolidated Appropriations Act, 2023*. Vol 2617. 2023. Accessed February 3, 2026. https://www.congress.gov/bill/117th-congress/house-bill/2617/text
9. U.S. Food & Drug Administration (FDA). FDA Approves First Over-the-Counter Naloxone Nasal Spray. U.S. Food & Drug Administration (FDA). March 29, 2023. https://www.fda.gov/news-events/press-announcements/fda-approves-first-over-counter-naloxone-nasal-spray

10. Senate Health & Human Services. *Uniform Controlled Substance Act*. Vol 0795. 2025. https://webserver.rilegislature.gov/BillText/BillText25/SenateText25/S0795.pdf
11. House Health & Human Services. *Uniform Controlled Substances Act*. Vol 5866. 2025.
12. State of Rhode Island. *Uniform Controlled Substances Act*. Vol 216. 2018. https://risos-apa-production-public.s3.amazonaws.com/DOH/REG_9702_20180806190700.pdf
13. Kertesz SG, Manhapra A, Gordon AJ. Nonconsensual Dose Reduction Mandates are Not Justified Clinically or Ethically: An Analysis. *J Law Med Ethics*. 2020;48(2):259-267. doi:10.1177/1073110520935337
14. Owens B. Opioid prescriptions down but some patients fear doctors now too strict. *Can Med Assoc J*. 2019;191(19):E546-E547. doi:10.1503/cmaj.109-5748
15. Weiner SG, Hendricks MA, El Ibrahimi S, et al. Opioid-related overdose and chronic use following an initial prescription of hydrocodone versus oxycodone. Gomes T, ed. *PLOS ONE*. 2022;17(4):e0266561. doi:10.1371/journal.pone.0266561
16. By the 2023 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. 2023;71(7):2052-2081. doi:10.1111/jgs.18372
17. Maust DT, Kales HC, Wiechers IR, Blow FC, Olfson M. No End in Sight: Benzodiazepine Use in Older Adults in the United States. *J Am Geriatr Soc*. 2016;64(12):2546-2553. doi:10.1111/jgs.14379
18. Gauffin E, Marques Franca A, Pizzaro Ferrero E, et al. Reduced need for inpatient care following introduction of long-acting injectable buprenorphine. *BMC Health Serv Res*. 2025;25(1):1397. doi:10.1186/s12913-025-13607-7
19. Socias ME, Dickhout P, Langlois J, Grant C, Nolan S. Extended-release injectable buprenorphine for the treatment of opioid use disorder among individuals at high risk of overdose: The FASTER-BUP udy. *Drug Alcohol Depend*. 2025;275:112798. doi:10.1016/j.drugalcdep.2025.112798
20. Paiva TJ, St John K, Wightman RS, Nitenson AZ, Onyejekwe C, Hallowell BD. Increased Stimulant Prescribing Following the COVID-19 Pandemic - Rhode Island, 2017-2021. *R I Med J*. 2023;106(6):52-55.
21. Staley BS, Robinson LR, Claussen AH, et al. Attention-Deficit/Hyperactivity Disorder Diagnosis, Treatment, and Telehealth Use in Adults — National Center for Health Statistics Rapid Surveys System, United States, October–November 2023. *MMWR Morb Mortal Wkly Rep*. 2024;73(40):890-895. doi:10.15585/mmwr.mm7340a1
22. Drug Enforcement Administration (DEA). *Stimulant Prescription Trends in the United States from 2012 – 2023*. IQVIA Government Solutions, Inc; 2024:1-39. Accessed February 3, 2026. https://www.deadiversion.usdoj.gov/pubs/docs/IQVIA-Report-on-Stimulant-Trends-2024.pdf

## Authors

Taylor J. Mello, MPH, Prescription Drug Monitoring Program (PDMP) Epidemiologist, Center for Health Data and Analysis (CHDA), Rhode Island Department of Health (RIDOH).

Staci Fischer, MD, Medical Director, Division of Healthcare Quality and Safety, Rhode Island Department of Health (RIDOH) .

Kristen St. John, MPH, Principal Public Health Epidemiologist, Center for Health Data and Analysis (CHDA), Rhode Island Department of Health (RIDOH).

Adam Z. Nitenson, PhD, Prescription Drug Monitoring Program (PDMP) Health Research Project Director, CHP, Rhode Island Department of Health (RIDOH).

Benjamin D. Hallowell, PhD, MPH, Team Lead, Substance Use Epidemiology Program, Center for Health Data and Analysis (CHDA), Rhode Island Department of Health (RIDOH).

## Correspondence

Taylor Mello, MPH
Taylor.Mello@health.ri.gov

# FREE TO FOCUS ON KARLY.

With healthcare's constant complexities and distractions, it can be difficult to focus on patients. We can help, with proven medical professional liability insurance and so much more. So you are free to focus on delivering superior patient care.

- Medical Professional Liability Insurance
- Claims Analytics
- Risk Mitigation
- Medicare Contractual Risk Protection
- And more

coverys.com 800.225.6168

COVERYS FREE TO FOCUS℠

# Accidental Drug Overdose Deaths—Rhode Island, January 1, 2023–December 31, 2025

HEIDI R. WEIDELE, MPH; BENJAMIN D. HALLOWELL, PhD

## INTRODUCTION

In Rhode Island (RI), fatal overdose is a leading cause of preventable death and has been a priority area for public health initiatives for the state.[1] In 2022, RI experienced the highest number of overdose deaths ever recorded, with 436 individuals lost to accidental drug overdose in a single year.[2] Encouragingly, in 2023 and 2024 overdose fatalities sharply declined in RI, following regional and national trends.[3] To inform new and ongoing public health initiatives to prevent or reduce substance use and related harms, this analysis aims to describe the current state of the overdose epidemic in RI and how overdose trends have changed over time.

## METHODS

We obtained data from the Office of State Medical Examiners (OSME) for accidental fatal overdoses that occurred in RI from January 1, 2023 to December 31, 2025. Manner of death (accident vs. suicide) and substances contributing to death are determined by the medical examiners based on their clinical judgement and consideration of autopsy results, toxicology testing, scene investigation, and medical history. Demographic categories were combined to comply with the RI Department of Health (RIDOH) Small Numbers Policy. Decedent age was categorized as Less than 25, 25–34, 35–44, 45–54, 55–64, and 65+. Decedents were grouped by ethnicity and race, with all Hispanic individuals captured as Hispanic or Latino and non-Hispanic individuals captured as Non-Hispanic Black, Non-Hispanic White, or Non-Hispanic, other race/unknown. Individuals who were non-Hispanic American Indian or Alaska native, Asian, or unknown race were classified as other race/unknown. Due to small numbers, rates were restricted to RI residents who were non-Hispanic Black, non-Hispanic White, or Hispanic or Latino. Population estimates were obtained from CDC WONDER by year, with 2024 estimates used to calculate 2025 rates.[4]

Overdoses were classified by drug type, including involving illicit drugs alone, prescription drugs alone, a combination of illicit and prescription drugs, or having unknown or missing drug type. More than one substance can contribute to cause of death, so substance categories are not mutually exclusive. Overdoses involving 'Any Opioid' is inclusive of overdoses caused by fentanyl, buprenorphine, methadone, and other opioids, while overdoses categorized as involving 'Any Stimulant' is inclusive of overdoses involving cocaine, MDMA, and amphetamines. In addition to showing trends by year, substances contributing to cause of death were analyzed by age and race and ethnicity groups to help inform tailored prevention initiatives.

Overdose location captures where the overdose took place, and not necessarily where the death occurred. Location was categorized as Private, Semi-Private, Public, and Unknown/Missing.

To assess statistical significance, we utilized chi square and Fishers exact tests. P-values <0.05 were considered statistically significant. Analyses were performed in SAS [Version 9.4].

## RESULTS

From 2023 to 2025, a total of 952 fatal overdoses occurred in RI [**Table 1**]. In 2025, there were 219 individuals who experienced a fatal overdose, which is a 33.4% decrease compared to 2024 (n=329), and 46% decrease compared to 2023 (n=404).

Similar to previous years, in 2025 most overdoses occurred among males (70%), non-Hispanic White individuals (72%), and people ages 35 to 64 (74%; **Table 1**). Compared to 2023, in 2024 the number of fatal overdoses declined across every age group except individuals aged 55–64, which saw a 15% increase. From 2024 to 2025, fatal overdoses declined or stayed the same across all age groups. While the rate of fatal overdoses declined among all race and ethnicity groups from 2023 to 2025, in 2025 the rate of overdose was highest among non-Hispanic Black residents (31.6 per 100,000) compared to non-Hispanic White (16.5 per 100,000) and Hispanic or Latino (13.4 per 100,000) residents [**Figure 1**].

Overall, 87% of overdoses involved illicit drugs, either alone or in combination with prescription drugs [**Table 2**]. While the number of overdoses involving illicit drugs alone or a combination of illicit and prescription drugs decreased 54% and 46% respectively from 2023 to 2025, fatal overdoses involving prescription drugs alone increased 24%. In 2025, opioids (73%) and stimulants (65%) were the leading substances contributing to death, with fentanyl contributing to 57% and cocaine contributing to 56%. When stratified by age, 100% of overdoses among individuals 25–34 years

old were opioid-involved, which gradually decreased as age groups increased, from 81% opioid-involved among individuals 35–44, 74% among individuals 45–54, to 56% among individuals 55–64 (data not shown). When stratified by race/ethnicity, 91% of Hispanic or Latino deaths involved opioids, compared to 60% and 70% of non-Hispanic Black and non-Hispanic White individuals respectively. Of note, 88% of deaths among non-Hispanic Black individuals involved stimulants, compared to 59% among Hispanic or Latino individuals, and 64% among non-Hispanic White individuals [**Figure 2**].

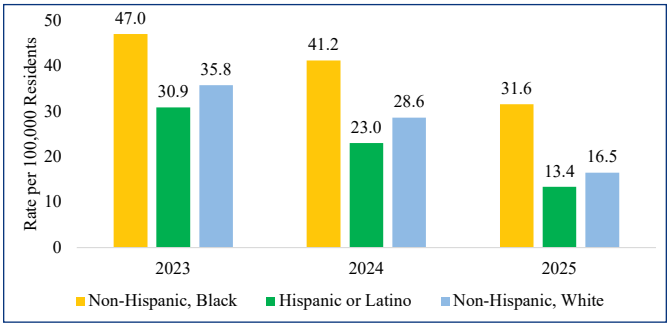
Overall, most overdoses took place in a private setting (69%), followed by public (11%) and semi-private (5%) locations [**Table 2**].

**Table 1.** Demographic characteristics of individuals who died of an accidental overdose in Rhode Island: January 1, 2023–December 31, 2025

| Decedent Demographic | Overall N=952 n (%) | 2023 N=404 n (%) | 2024 N=329 n (%) | 2025 N=219 n (%) | p-value[1] |
|---|---|---|---|---|---|
| **Sex** | | | | | |
| Male | 670 (70) | 280 (69) | 231 (70) | 159 (73) | 0.6885 |
| Female | 282 (30) | 124 (31) | 98 (30) | 60 (27) | |
| **Age Category** | | | | | |
| Less than 25 | 30 (3) | 16 (4) | 7 (2) | 7 (3) | 0.3555 |
| 25–34 | 143 (15) | 68 (17) | 45 (14) | 30 (14) | |
| 35–44 | 246 (26) | 113 (28) | 79 (24) | 54 (25) | |
| 45–54 | 231 (24) | 96 (24) | 82 (25) | 53 (24) | |
| 55–64 | 227 (24) | 78 (19) | 90 (27) | 59 (27) | |
| 65+ | 75 (8) | 33 (8) | 26 (8) | 16 (7) | |
| **Race/Ethnicity** | | | | | |
| Non-Hispanic, Black | 94 (10) | 36 (9) | 33 (10) | 25 (11) | 0.3249 |
| Hispanic or Latino | 151 (16) | 66 (16) | 53 (16) | 32 (15) | |
| Non-Hispanic, White | 690 (72) | 297 (74) | 239 (73) | 154 (70) | |
| Non-Hispanic, Other/ Unknown Race | 17 (2) | 5 (1) | <5 | 8 (4) | |

Source: Office of State Medical Examiners. [1]Chi-square test. Counts less than five are suppressed to comply with the Rhode Island Small Numbers Policy.

**Figure 1.** Rate of accidental overdose deaths among Rhode Island residents, stratified by decedent race and ethnicity: January 1, 2023–December 31, 2025



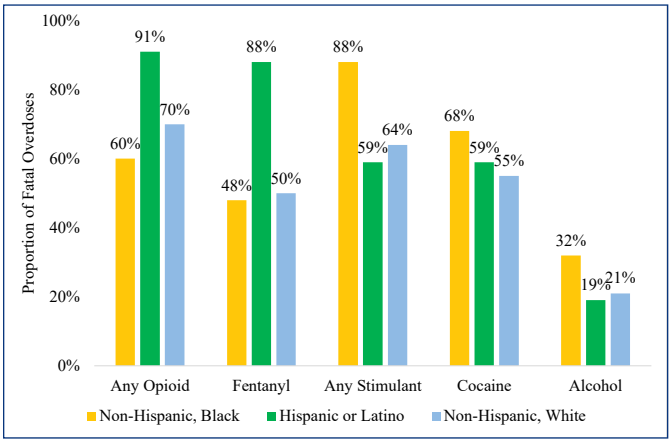

Source: Office of State Medical Examiners. Note: Population denominator based on CDC WONDER single-race population estimates for each year accessed May 28, 2026; 2024 estimate applied for 2025 rates.

**Table 2.** Substances that contributed to cause of death for individuals who died of an accidental overdose in Rhode Island: January 1, 2023–December 31, 2025

| Overdose Circumstances | Overall N=952 n (%) | 2023 N=404 n (%) | 2024 N=329 n (%) | 2025 N=219 n (%) | p-value[1] |
|---|---|---|---|---|---|
| **Drug Type** | | | | | |
| Illicit Only | 540 (57) | 257 (64) | 165 (51) | 118 (54) | <0.0001± |
| Prescription Only | 123 (13) | 33 (8) | 49 (15) | 41 (19) | |
| Combination | 284 (30) | 112 (28) | 112 (34) | 60 (27) | |
| Unknown/ Missing | 5 (<1) | <5 | <5 | 0 | |
| **Substances Contributing to Death** | | | | | |
| Any Opioid | 732 (77) | 345 (85) | 228 (69) | 159 (73) | <0.0001 |
| Fentanyl | 627 (66) | 314 (78) | 189 (57) | 124 (57) | <0.0001 |
| Methadone | 111 (12) | 37 (9) | 39 (12) | 35 (16) | 0.0400 |
| Buprenorphine | 33 (3) | 10 (2) | 10 (3) | 13 (6) | 0.0687 |
| Any Stimulant | 612 (64) | 252 (62) | 217 (66) | 143 (65) | 0.5656 |
| Cocaine | 556 (58) | 234 (58) | 199 (61) | 123 (56) | 0.5833 |
| Amphetamines | 112 (12) | 47 (12) | 39 (12) | 26 (12) | 0.9942 |
| Alcohol | 214 (22) | 77 (19) | 89 (27) | 48 (22) | 0.0351 |
| Antidepressants | 141 (15) | 49 (12) | 56 (17) | 36 (16) | 0.1328 |
| Benzodiazepines | 129 (14) | 49 (12) | 48 (15) | 32 (15) | 0.5458 |
| Antipsychotics | 51 (5) | 15 (4) | 25 (8) | 11 (5) | 0.0651 |
| Over the Counter | 39 (4) | 13 (3) | 17 (5) | 9 (4) | 0.4160 |
| Kratom | 6 (<1) | <5 | <5 | <5 | 0.2305 |
| **Overdose Location[2]** | | | | | |
| Private | 656 (69) | 284 (70) | 227 (69) | 145 (66) | 0.0190 |
| Semi-Private | 52 (5) | 23 (6) | 15 (5) | 14 (6) | |
| Public | 106 (11) | 30 (7) | 40 (12) | 36 (16) | |
| Unknown/ Missing | 138 (15) | 67 (17) | 47 (14) | 24 (11) | |

Source: Office of State Medical Examiners. [1]Chi-square test. [2]Private included apartment or residence, semi-public included hotel, motel, shelter, nursing home, hospital, prison, group home, assisted living, or treatment facility, while public included theater, concert, show, office, park, school, bar/restaurant, roadway, or cemetery. ±Fishers exact test. Counts less than five are suppressed to comply with the Rhode Island Small Numbers Policy.

**Figure 2.** Substances contributing to accidental overdose deaths in Rhode Island, stratified by decedent race and ethnicity: January 1, 2025–December 31, 2025




Source: Office of State Medical Examiners. Note: Substance categories are not mutually exclusive; more than one substance can contribute to cause of death.

## DISCUSSION

From 2023 to 2025, accidental overdose deaths in RI declined by 46%. Encouragingly, these declines were observed among all population groups. The declines observed in RI align with neighboring states who reported similar decreases in overdose deaths during this period, including Massachusetts, Maine, Connecticut, and Vermont.[5-8]

In response to the rising overdose deaths in RI and the highest number of overdose deaths ever recorded in 2022, the State of Rhode Island set a goal to reduce overdose deaths by 30% from 2022 to 2030 as a part of the RI 2030 Action Plan.[9] In 2025, RI experienced its third consecutive decrease in annual overdose deaths since its peak in 2022, with a 50% decrease in overdose deaths from 2022 to 2025, surpassing the State's goal to reduce fatal overdoses by 30% by 2030. This is the lowest number of fatal overdoses that the state has experienced since 2012, when 183 individuals experienced an accidental overdose death.

Though there was an observed decrease in both the counts and proportion of overdoses caused by opioids, stimulants, fentanyl, and cocaine between 2023 and 2025, these substances remain a main concern and the driver of most fatal overdoses in the state. Of note, while declines were seen across most substances of concern and drug types, the proportion and number of deaths involving prescription only drugs increased from 2023 to 2025. Additional surveillance work should be performed to inform future prevention efforts focused on reducing prescription involved fatal overdoses.

In April 2026, the RI Kratom Act was passed, which allowed for the manufacture and sale of kratom products to individuals age 21 and older.[10] Kratom is a product that can be ingested or injected to produce stimulant- or opioid-like effects.[11] Kratom, as well as its alkaloids, mitragynine and 7-hydroxymitragynine (also known as 7-OH), do not have any approved therapeutic use by the Federal Drug Administration (FDA). Kratom products themselves pose health risks, including the potential for withdrawal, dependence, and death. Currently, the RI State Health Laboratories (SHL) only test for kratom and mitragynine, but do not test for the more potent 7-OH, which means that the potential impact of kratom on fatal overdose is likely underestimated. To determine the impact of legalization on overdose deaths, the health department will continue to monitor this substance over time, and the RISHL will be adding 7-OH testing in 2026.

While it is not possible to attribute the decline in overdose deaths to a single contributing factor, it is likely due to several initiatives undertaken by RI's community-based organizations and their dedicated staff with lived experience, healthcare professionals, municipalities, and government organizations to meet individuals where they are and provide free treatment/recovery options, naloxone, education, and basic needs services to individuals at risk of an overdose.

### References


1. Chan PA. Determining Public Health Priorities in Rhode Island. *Rhode Island Medical Journal.* 2026;109(4):62-63.
2. Weidele HR, Hallowell BD. Accidental Drug Overdose Deaths in Rhode Island: January 1, 2022–December 31, 2024. *Rhode Island Medical Journal.* 2025;108(8):57-59.
3. Ahmad FB, Cisewski JA, Rossen LM, Sutton P. Provisional drug overdose death counts. National Center for Health Statistics. 2026. doi: https://dx.doi.org/10.15620/cdc/20250305008
4. Single-race Population Estimates, United States, 2020-2024. July 1st resident population by state, age, sex, single-race, and Hispanic origin, on CDC WONDER Online Database. http://wonder.cdc.gov/single-race-single-year-v2024.html
5. Massachusetts Department of Public Health. (2026, June 5). *Massachusetts opioid-related overdose deaths fall under 1,000 for the first time in over a decade* [Press release]. https://www.mass.gov/news/massachusetts-opioid-related-overdose-deaths-fall-under-1000-for-the-first-time-in-over-a-decade.
6. University of Maine. (2026). Maine Monthly Overdose Report. https://mainedrugdata.org/wp-content/uploads/2026/06/2026-04-ME_OD_Report-Final.pdf
7. Connecticut State Department of Public Health. (2026). Fatal Unintentional and Undetermined Intent Drug Overdose Report, Connecticut. https://portal.ct.gov/dph/-/media/dph/injury-and-violence-prevention/opioid-overdose-data/monthly-death-reports/2019-january-2026_drug-overdose-deaths-monthly-report_connecticut_2-24-2026_final.pdf
8. Vermont Department of Health. (2026). 2025 Fatal Overdose Report. https://www.healthvermont.gov/sites/default/files/document/dsu-fatal-overdose-report-2025.pdf.
9. People, Place & Health Collective. (2024). The Action Plan. Prevent Overdose RI. https://preventoverdoseri.org/the-action-plan
10. RI General Law § 21-28.12
11. Rhode Island Department of Health. (2026). Kratom Licensing. https://health.ri.gov/licensing/kratom-licensing


### Authors


Heidi R. Weidele, MPH, Fatal Overdose Epidemiologist, Substance Use Epidemiology Program (SUEP), Center for Health Data and Analysis (CHDA), RIDOH.

Benjamin D. Hallowell, PhD, Team Lead, SUEP, CHDA, RIDOH.


### Correspondence


Heidi R. Weidele, MPH
heidi.weidele@health.ri.gov

# Rhode Island Monthly Vital Statistics Report
# Provisional Occurrence Data from the Division of Vital Records

| VITAL EVENTS | REPORTING PERIOD | | |
|---|---|---|---|
| | SEPTEMBER 2024 | 12 MONTHS ENDING WITH SEPTEMBER 2024 | |
| | Number | Number | Rates |
| Live Births | 873 | 10,814 | 10.2* |
| Deaths | 984 | 10,655 | 10.1* |
| Infant Deaths | 1 | 44 | 4.1# |
| Neonatal Deaths | 0 | 30 | 2.8# |
| Marriages | 378 | 6,699 | 6.3* |
| Divorces | 237 | 2,533 | 2.4* |

* Rates per 1,000 estimated population
# Rates per 1,000 live births

| Underlying Cause of Death Category | REPORTING PERIOD | | | |
|---|---|---|---|---|
| | MARCH 2024 | 12 MONTHS ENDING WITH MARCH 2024 | | |
| | Number (a) | Number (a) | Rates (b) | YPLL (c) |
| Diseases of the Heart | 203 | 2,337 | 213.0 | 2,630.0 |
| Malignant Neoplasms | 185 | 2,182 | 198.8 | 4,275.0 |
| Cerebrovascular Disease | 33 | 473 | 43.1 | 490.0 |
| Injuries (Accident/Suicide/Homicide) | 63 | 831 | 75.7 | 9,853.0 |
| COPD | 34 | 479 | 43.6 | 482.0 |

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.
(b) Rates per 100,000 estimated population of 1,097,379 for 2020 (www.census.gov)
(c) Years of Potential Life Lost (YPLL).

NOTE: Totals represent vital events, which occurred in Rhode Island for the reporting periods listed above.
Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

## Why join RIMS?

The Rhode Island Medical Society is your voice at the State House and in the community. In 2025, we secured wins on prior authorization, clinician wellness, and primary care funding—but this work depends on physician support. Without membership, RIMS cannot continue to advocate, educate, and protect the profession. Join or renew today—and consider getting involved in one of our committees. Together, we are stronger. The Rhode Island Medical Society is the only organization dedicated solely to advocating for physicians and their patients in our state.

### In 2025, RIMS members helped

- Eliminate prior auth for PCP-ordered services (3-year Medicaid pilot)
- Secure fair Medicaid rates—up to 100% of Medicare starting Oct. 2025
- Protect physician wellness with the Clinician Wellness & Support Act

### We're not stopping here

RIMS is fighting for the future of telemedicine, tackling workforce shortages, and reducing administrative burdens.

**Click to join**

https://rhodeislandmedicalsociety.wildapricot.org/Join-us/

## Wins for providers

RIMS worked to secure and support key budget investments.

### Medicaid primary care rate increase

Up to 100% of medicare rates
Starting October 2025

### Medicaid prior authorization pilot

Eliminates prior authorization for Medicaid for three years
Starting October 2025

### Physician loan repayment funding

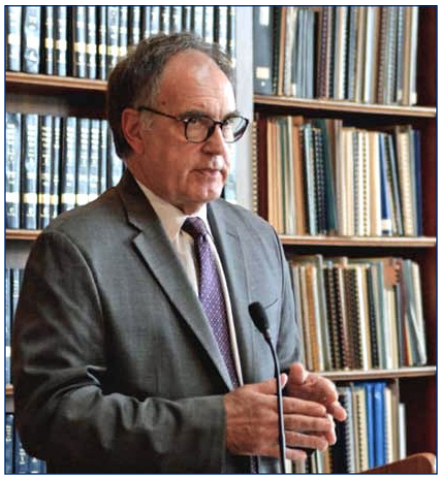
Includes $200,000 in funding to recruit and retain clinicians

### Health center funding

Sustained investments in FQHCs and community health

### Health services funding assessment

$30Mannually for primary care and other critical programs



## Our priorities

RIMS focused on strengthening Rhode Island's healthcare system, protecting physicians' well-being, reducing administrative burdens, and improving access to care. Together with members, specialty societies, and partner organizations, we made significant progress on our top priorities.

### The Rhode Island Prior Authorization Reform Act (SB 168/HB 5120)

Eliminates prior authorization for admissions, services, and procedures ordered by in-network primary care physicians in a three-year pilot.
**Effective:** October 1, 2025.
**Status:** Passed and signed
**Sponsored by**: Rep. Brandon Potter; Sen. Melissa Murray

### The Rhode Island Clinician Wellness and Support Act (SB 695/HB 6036)

Recognizes RIMS' Physician Health Program in statute, strengthens confidentiality protections, and updates licensing language to encourage clinicians to seek care without fear.
**Status:** Passed and signed
**Sponsored by:** Rep. John "Jay" Edwards; Sen. Bridget Valverde

### "I'm Sorry" Bill (H6210/S66)

Although not yet enacted, RIMS made significant progress this session on legislation to allow physicians to express sympathy or apologize after an adverse outcome without it being used as evidence of liability. We met twice with the Rhode Island Association for Justice (trial lawyers) and reviewed their suggested language—which we ultimately could not support—laying important groundwork for next session.
**Sponsored by:** Rep. Teresa Tanzi; Sen. Pamela Lauria

YOU'RE INVITED

# RHODE ISLAND MEDICAL SOCIETY
# CONVIVIUM
## 214TH ANNUAL MEETING & AWARDS DINNER

Join us as we present awards to recognize colleagues, inaugurate new leadership, and celebrate 214 years of organized medicine in Rhode Island.

Convivium celebrates the achievements of individual physicians as well as the collective strength of Rhode Island's medical community.

SEPTEMBER 24, 2026

**THE SQUANTUM ASSOCIATION**

TICKETS

**$125 / MEMBERS**
**$150 / NON-MEMBERS**

REGISTER TODAY

PREFER TO PAY BY CHECK?
MAIL BY AUGUST 20, 2026 TO:

**RHODE ISLAND MEDICAL SOCIETY**
C/O 2026 CONVIVIUM
225 DYER STREET
SECOND FLOOR
PROVIDENCE, RI 02903

**YOUR VOICE.**
**YOUR PATIENTS.**
**YOUR PROFESSION.**

## RIMS gratefully acknowledges the practices who participate in our discounted Group Membership Program

BROWN Health UNIVERSITY

Emergency Medicine
Medicine
Miriam Hospital Hospitalists
Primary Care
Surgery

CCAP
COMPREHENSIVE COMMUNITY ACTION PROGRAM
YOUR COMMUNITY'S HELPING HAND

Thundermist HEALTH CENTER

east bay community action program
THE BRIDGE to SELF-RELIANCE

UNIVERSITY ORTHOPEDICS
Healers. Innovators. Teachers.

WellOne
Primary Medical and Dental Care

Wood River
Health Services
The Heart of South County since 1976

# Bridging the Gap: Supporting Primary Care Pediatricians in the Management of Common Gastrointestinal Conditions

PRERANA BARANWAL, MD

Although the field of medicine is ultimately based in science, the practice of medicine involves consideration of complex disease processes and sometimes even disagreement amongst providers about the optimal management of a condition for a particular patient. However, when it comes to the subspecialty referral process, everyone is seemingly in agreement: it can be a frustrating and lengthy process for all parties involved, whether it be the patient, the primary care provider (PCP), or the subspecialty provider, regardless of subspecialty.

As a pediatric gastroenterologist, I see this issue firsthand on a near-daily basis. Unfortunately, the demand for pediatric gastroenterologists far exceeds the supply, which can lead to long wait times, uncertainty about next steps, and frustration. Most pediatric patients with gastrointestinal (GI) signs/symptoms are initially evaluated by their pediatrician or PCP. While many patients with GI complaints are (and should be) ultimately referred to pediatric gastroenterology, some referrals are for conditions that can be partially or fully managed in the primary care setting with appropriate support. It is thus essential to strengthen the collaboration between pediatric gastroenterologists and PCPs to improve access to care for children with GI signs/symptoms.

## Challenges for the General Pediatrician/Primary Care Provider (PCP)

General pediatricians are usually the first point of contact for patients with GI signs/symptoms. As a result, they possess a unique opportunity to triage and initially manage, as appropriate, a patient's signs/symptoms. However, general pediatricians face a plethora of challenges in their daily work.[1] Visit times are short, with 15 minute visits being exceedingly common—this too with the expectation of managing the full, comprehensive care of a patient! Patients have varying levels of medical complexity and a diverse range of conditions that must be addressed by the PCP, often requiring longer than the allotted visit time. Moreover, PCPs may have uncertainty about the diagnostic tests that would be appropriate to perform initial screening,[2,3] and may feel they have limited access to subspecialty consultation. PCPs may feel pressured by caregivers of patients for an "immediate" answer, often leading to premature referral. All of these aspects of care compound and make it difficult for general pediatricians to manage common GI conditions in the primary care setting. Pediatric gastroenterologists hold an important role in helping support our generalist colleagues in managing common GI conditions, with the ultimate goal of improving access to care for patients with GI signs/symptoms.

## Opportunities for Subspecialist Support

There are a variety of ways to strengthen the collaboration between pediatric gastroenterologists and PCPs. First, disseminating knowledge about common GI conditions in easily digestible ways, including case-based discussions, can help provide clear, actionable guidance for PCPs.[4] As a subspecialty we can provide simple algorithms for common GI problems, such as initial constipation management and initial workup of abdominal pain, as well as guidance for when a referral may be more urgently needed.[4] Ideally, these algorithms can be provided in the form of CME lectures with virtual capabilities to allow for greater attendance, or brief lunch-time lectures with discussions between subspecialists and generalists (again, with virtual capabilities to allow for greater attendance). Additionally, promoting increased awareness about where to find easily accessible guidelines for common GI conditions, such as those created by the national pediatric GI organization, the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN), can further help to disseminate knowledge about common GI conditions.

Second, facilitating more collaborative communication between the pediatric GI provider and the generalist can help both parties to better understand how best to approach a specific patient's individual needs.[5] One practical example of this is using electronic consults ("e-consults"), which may allow for an initial chart-based consultation by the subspecialist with follow-up recommendations given to the PCP (or alternatively, a recommendation that the patient be seen in-person by the GI team). Additionally, providing clear referral guidelines, and alarm signs/symptoms to look for, can help provide generalists with a guide as to the urgency of a referral. Ensuring ample communication from both PCPs and pediatric gastroenterologists to each other can help facilitate an open dialogue (especially in cases of uncertainty) and help get the patient the care they need sooner.[5]

Third, building educational partnerships early on in training (residency, fellowship) can help create a more collaborative workforce. By providing trainees with a care model that allows for open communication between specialists and generalists, and which provides trainees with role models approaching care in this way, we can help educate the

next generation of physicians to accept open communication between providers as simply another aspect of their daily work.[6,7]

## Benefits for the Patient, Providers, and Healthcare System

More efficient access to appropriate care is beneficial for patients, providers (generalists and subspecialists), and the healthcare system. Patients receive faster management of common GI conditions. More collaborative communication between providers leads to not only more efficient use of subspecialty care, decreased wait times, and improved access to GI subspecialists, but also better continuity of care for each patient. Ultimately this leads to more efficient use of resources in the healthcare system. When generalists feel supported in managing common GI conditions, patients receive appropriate and timely care, while subspecialists remain available for more complex or uncertain cases.

## Looking Ahead

Strengthening the collaboration between pediatric gastroenterologists and general pediatricians is an opportunity for subspecialists and generalists alike to improve access to care for children with GI signs/symptoms. By increasing ongoing educational efforts, promoting collaborative communication, and building educational partnerships early on in training, general pediatricians can feel empowered to manage common GI conditions, while ensuring that patients are able to obtain more timely access to specialized GI care when needed.

## References


1. Sharma S, Stewart MJ, Mathias H, et al. Primary healthcare provider-perceived barriers to implementing an evidence-based pathway for undifferentiated lower gastrointestinal tract symptoms: A qualitative inquiry. *PLoS One*. 2024;19(12):e0313201. Published 2024 Dec 31. doi:10.1371/journal.pone.0313201
2. Heinsch ML, Nightingale S. Functional gastrointestinal disorders in children and adolescents: Knowledge, practice and attitudes of Australian paediatricians. *J Paediatr Child Health*. 2019;55(9):1063-1069. doi:10.1111/jpc.14342
3. Gordon M, Groen J, Sinopoulou V, et al. European and North American guidelines for treating irritable bowel syndrome and functional abdominal pain in childhood: a guide for health-care professionals. *Lancet Child Adolesc Health*. 2025;9(11):808-816. doi:10.1016/S2352-4642(25)00209-34.
4. Mallon D, Vernacchio L, Trudell E, et al. Shared care: a quality improvement initiative to optimize primary care management ofconstipation.*Pediatrics*.2015;135(5):e1300-e1307.doi:10.1542/peds.2014-1962
5. Stille CJ, McLaughlin TJ, Primack WA, Mazor KM, Wasserman RC. Determinants and impact of generalist-specialist communication about pediatric outpatient referrals. *Pediatrics*. 2006;118(4):1341-1349. doi:10.1542/peds.2005-3010
6. Meijer LJ, de Groot E, Blaauw-Westerlaken M, Damoiseaux RA. Intraprofessional collaboration and learning between specialists and general practitioners during postgraduate training: a qualitative study. *BMC Health Serv Res*. 2016;16(a):376. Published 2016 Aug 11. doi:10.1186/s12913-016-1619-8
7. Pany MJ, McWilliams JM. Physician-Peer Relationships and Patient Experiences With Specialist Care. *JAMA Intern Med*. 2023;183(2):124-132. doi:10.1001/jamainternmed.2022.6007



## Author

Prerana Baranwal, MD, Assistant Professor of Pediatrics, The Warren Alpert Medical School of Brown University; Pediatric Gastroenterologist, Hasbro Children's/Brown University Health, Providence, RI.


## Disclosures


**Acknowledgments:** None

**Ethical Approval Statement:** Ethical approval is not applicable to this article.

**Disclosures/Conflicts of Interest:** None



## Correspondence

Prerana Baranwal, MD
Division of Pediatric Gastroenterology, Nutrition, & Liver Diseases
Hasbro Children's Hospital
593 Eddy Street, Providence, RI 02903
401-444-8306
prerana_baranwal@brown.edu

# Accessibility of Over-the-Counter Naloxone in Providence, RI, Retail Pharmacies

RUBY J. GROVES; SONIYA G. K. CHAWLA; JOCELYN ANTONIO, MPH; TIA E. SANDERS; CAROLINE J. KISTIN, MD, MSc

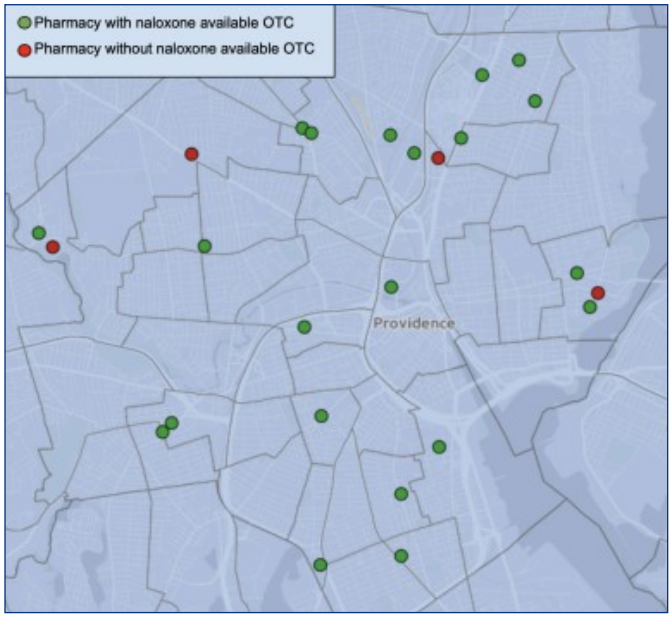
Annually, over 100,000 Americans die from drug overdoses —most involving opioids.[1]

Naloxone, a life-saving opioid overdose-reversal medication, was approved by the United States Food and Drug Administration (FDA) for sale without a prescription in 2023.[2] To evaluate the impact of this ruling, we assessed the availability of over-the-counter (OTC) naloxone in all retail pharmacies in Providence, Rhode Island. Providence is the state's largest city and has an overdose death rate significantly higher than the state average.[3] Given that Providence has been ranked among cities with the highest income inequality in the U.S., an analysis of naloxone availability at pharmacies in different neighborhoods is particularly relevant.[4]

During the summer of 2024, our study team visited all 25 retail pharmacies in Providence and attempted to buy naloxone without a prescription. We recorded availability, price, naloxone location within the store, and what kind of help employees offered. Naloxone was available OTC at 21 of 25 pharmacies (84%), suggesting that the FDA's approval has meaningfully expanded access [**Figure 1**]. CVS and Walgreens were more reliable in price and availability, while independent pharmacies were inconsistent. The average cost of naloxone was $49.19 pre-tax, ranging from $34.99 to $104.87, which is a substantial cost barrier. Chain pharmacies ranged from $34.99 to $44.99.

While expensive, naloxone was widely available OTC, which is helpful for people wishing to purchase anonymously (as there is no pharmacy record or bill). Pharmacists were knowledgeable and supportive, often providing instructions for use of naloxone, emphasizing its life-saving importance, and mentioning local community-based free naloxone resources. However, barriers remain. In over half of the pharmacies, naloxone was kept behind the front counter, requiring customers to ask for it. In practice, this may discourage purchase due to stigma or confusion. At 35% of chain pharmacies, front-of-store staff did not know what naloxone was or where it was located. Some provided inaccurate information or questioned the buyer's motivation—one asked if the buyer was "overdosing right now." Stigma may remain a barrier to harm reduction and presents an opportunity for ongoing staff training to ensure a stigma-free environment. In many stores, the first employees who customers interact with are not pharmacists. If those employees do not know naloxone is available—or treat its purchase suspiciously—true customer access may be low.

**Figure 1. Availability of OTC naloxone in Providence, RI, pharmacies**
Green dots represent retail pharmacies where the study team member was able to purchase naloxone without a prescription. Red dots represent retail pharmacies where the study team member was unable to purchase naloxone without a prescription. Census tracts, according to 2020 census data, are overlaid in grey lines.




In Providence, OTC naloxone is widely available across the city. In addition to pharmacies, community organizations provide free naloxone and training on its use. Prevent Overdose RI is a state initiative to increase both education about and access to naloxone—a resource that can be shared with customers by pharmacy staff.[5] In our study, we found that retail pharmacists are often already making these recommendations. Finally, naloxone saves lives, but it is not a cure for the opioid epidemic. True progress requires a harm-reduction network that includes integrated treatment, recovery, and educational services, in addition to overdose prevention. Future work may focus more on how retail pharmacies can be further integrated with other state and city-wide overdose prevention services.

## References


1. Ahmad F, Cisewski J, Rossen L, Sutton P. Provisional Drug Overdose Death Counts. Published online January 14, 2026. https://dx.doi.org/10.15620/cdc/202503050
2. FDA Approves First Over-the-Counter Naloxone Nasal Spray. US Food & Drug Administration. March 29, 2023. Accessed January 15, 2026. https://www.fda.gov/news-events/press-announcements/fda-approves-first-over-counter naloxone-nasal-spray
3. Rhode Island Sees Decrease in Drug Overdose Deaths, Continues a Two-Year Decline. The Executive Office of Health and Human Services, State of Rhode Island. June 11, 2025. Accessed September 26, 2025. https://eohhs.ri.gov/press-releases/rhode-island-sees-decrease-drug-overdose-deaths-continues-two-year-decline
4. Berube A. City and metropolitan income inequality data reveal ups and downs through 2016. Brookings. Published online February 5, 2018. Accessed January 20, 2026. https://www.brookings.edu/articles/city-and-metropolitan-income-inequality-data-reveal ups-and-downs-through-2016/
5. Rhode Island Governor's Overdose Task Force. Prevent Overdose RI – End the epidemic. Accessed December 10, 2025. https://preventoverdoseri.org/


## Authors


Ruby J. Groves, Williams College, Williamstown, MA.

Soniya G. K. Chawla, Brown University, Providence, RI.

Jocelyn Antonio, MPH, Hassenfeld Child Health Innovation Institute, Brown University School of Public Health, Providence, RI.

Tia E. Sanders, Hassenfeld Child Health Innovation Institute, Brown University School of Public Health, Providence, RI.

Caroline J. Kistin, MD, MSc, Department of Health Services, Policy, and Practice, Brown University School of Public Health, Providence, RI.


## Disclosures

There are no conflicts of interest to declare.

**Acknowledgment:** This research was funded by an internal grant from the Hassenfeld Child Health Innovation Institute.

## Correspondence


Ruby J. Groves
401-743-1066
rjg2@williams.edu

# Lucius F. C. Garvin, MD: 1876 Centennial Perspective on Life, Liberty, Longevity

MARY KORR
RIMJ MANAGING EDITOR

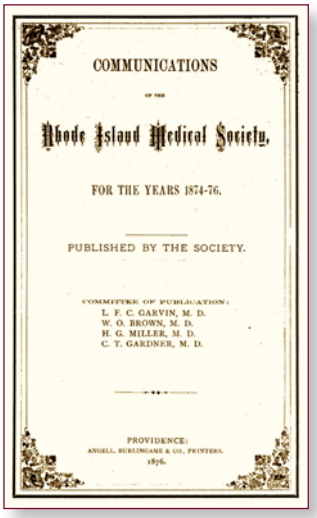

COMMUNICATIONS
OF THE
Rhode Island Medical Society.
FOR THE YEARS 1874-76.
PUBLISHED BY THE SOCIETY.
COMMITTEE OF PUBLICATION:
L. F. C. GARVIN, M. D.
W. O. BROWN, M. D.
H. G. MILLER, M. D.
C. T. GARDNER, M. D.
PROVIDENCE:
ANGELL, BURLINGAME & CO., PRINTERS.
1876.

**Image 1.** Cover image of the *Communications of the Rhode Island Medical Society* [HAITHI TRUST1]

In March 1876, **LUCIUS F. C. GARVIN, MD**, presented a Centennial discourse at a meeting of the Rhode Island Medical Society, which was published in the Society's *Communications*,[1] [**Image 1**]. Dr. Garvin was 35-years-old and a member of the publications committee at the time he gave this address, in which he reflected on the lifespans and lifestyles of the signers of the Declaration of Independence and other notables of the era, comparing them to those of his own time 100 years later.

He began with a somber note. "The return of the historic and venerated date '76 has led to a comparison of ourselves with our ancestors, not always, it must be confessed, to our advantage. The signers of the Declaration of Independence [**Image 2**], almost without exception, lived to a hale old age. Of the signers from Rhode Island, **Stephen Hopkins** reached seventy-eight; the other, **William Ellery**, expired in his arm-chair, without sickness

**Image 2.** Portraits & autographs of the signers of the Declaration of Independence
[LIBRARY OF CONGRESS, OLE EREKSON, LITHOGRAPHER, CIRCA 1876. HTTPS://LCCN.LOC.GOV/2003666901]

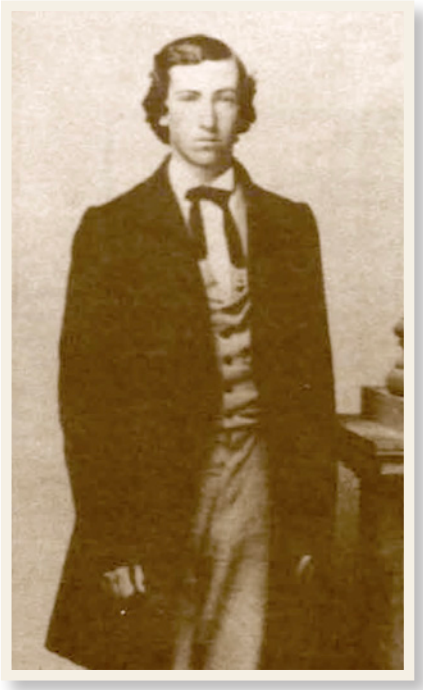


**Image 3.** Amherst College archival photo of **Lucius Garvin** as a student, class of 1862 [RHODE ISLAND HISTORY, MAY 1980[3]]

or pain, while engaged in reading *Cicero De Officüs*, at the age of ninety-two."

Dr. Garvin also noted that **Benjamin Franklin** was made ambassador to France at 70, governor of Pennsylvania at 79, member of the Constitutional Convention at 81, and "died in full possession of his faculties at 84." **Samuel Adams** lived to be 82, **John Adams**, 90, and **Thomas Jefferson**, 83.

In contrast, he recounted some of the recent deaths of notable persons in his day: **Andrew Johnson**, at the age of 67, **Charles Sumner** and **Henry Wilson** at 63, **Horace Greeley** at 62, **Thomas A. Jenckes** at 57, **Orris S. Ferry** at 53. "Most of these men during their later years were seriously disabled and frequently tortured by wearing chronic disease…Is such waste of the country's best material a necessity? If it can be shown that the great men of America attained a more advanced age one hundred years ago than now, will it not go far to prove the present death rate excessive and needless?"

He posited that "the disparity springs from a cause which is not beyond our discernment. We have learned to live shut up within doors more constantly and more completely than our fathers. Now a journey to Washington occupies twenty-four hours in a crowded car, by day and night alike close and abominable. When John Adams went from his farm at Braintree to Philadelphia in 1775, by open conveyance, the trip with its stops at Hartford, New York, and Trenton, was a month's vacation… Modern statesmen seem to have actually less hygienic wisdom than is contained in the old nursery rhyme:

*After breakfast, work awhile,*
*After dinner sit and smile,*
*After supper walk a mile…*


**Image 4.** Exterior view of Lonsdale Company's Bleachery in West Lonsdale [RHODE ISLAND COLLECTION, PROVIDENCE PUBLIC LIBRARY. HTTPS://PROVLIBDIGITAL.ORG/ISLANDORA/OBJECT/PC7061]

## Medical journey

Lucius Garvin, born in Tennessee to parents originally from New England, entered Amherst College in 1859 and graduated in 1862 [**Image 3**]. When the Civil War broke out, he enlisted in the Massachusetts Volunteer Infantry. The regiment was transported to North Carolina, where disease was rampant in the marshlands where they were quartered. Pvt. Garvin contracted malaria and spent months in the hospital, where he was given large doses of quinine, which impaired his hearing for the rest of his life, according to his induction bio at the RI Heritage Hall of Fame.[2]

During this time, he decided to pursue a career in medicine, and entered Harvard Medical School, graduating in 1867. Following an internship in Boston, he set up a private practice in Pawtucket, where he had earlier apprenticed under **SYLVANUS CLAPP, MD**.[3]

In 1876, the young Dr. Garvin accepted a position from the Lonsdale Company to set up a medical practice. Mills, machine shops, and blocks of workers' homes engulfed the three towns of Lincoln, Cumberland, and Pawtucket along the Blackstone River [**Images 4,5,6**]. As company physician, he was on call 24/7. He saw patients at his home at 577 Broad Street in Lonsdale every day for two hours, where he also performed surgery. He made house calls on foot or by horse and buggy.

In 1869, he married **LUCY WATERMAN SOUTHMAYD, MD**, who was a graduate of the New England Female Medical College, and a physician and physiology teacher at Mount Holyoke for a time. They were the parents of three daughters, one of whom, Florence, became a well-known suffragette. Lucy Garvin died in 1898. Nine years later, he married **SARAH TOMLINSON**, who had been blind since the age of six, and attended the Perkins School for the Blind. The couple had two sons.

In the essay, he eschewed that "corruption and incompetence in public life, which appears to be greater now than at any period within the history of the government, is attributable in no insignificant degree to eating and drinking, breathing and sleeping, working and playing improperly, and its remedy partially consists in a complete revolution of our every-day habits of living."

**Image 5.** Group portrait of child laborers at Lonsdale Company Bleachery
[RHODE ISLAND COLLECTION, PROVIDENCE PUBLIC LIBRARY. HTTPS://PROVLIBDIGITAL.ORG/ISLANDORA/OBJECT/VM013WC0541]

It was the plight of the mill children which led him into the political arena, and eventually to the State House, where he served as governor from 1903–1905 [**Image 7**]. The annals of Rhode Island history and the RI Heritage Hall of Fame capture his accomplishments, as well as an article in the November 2014 Heritage section of the *Rhode Island Medical Journal*.[4]

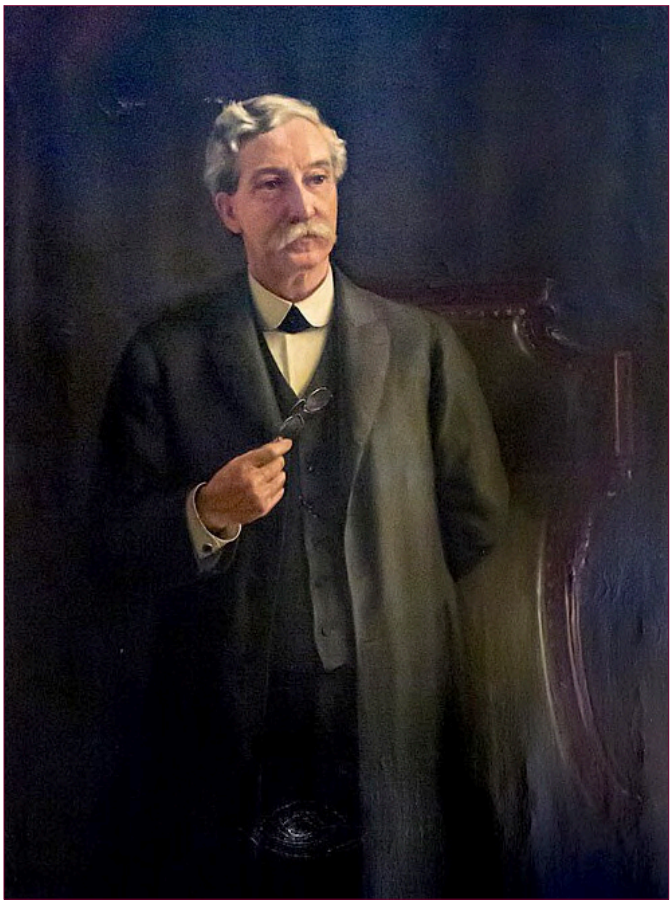


**Image 7.** Formal portrait of R.I. Gov. **Lucius F. C. Garvin, MD**, at the RI State House.

Dr. Garvin practiced medicine for more than half a century. He died suddenly at home on Oct. 2, 1922, at the age of 81, ascribed to heart disease. According to an article in the *New York Times* on his passing, he never owned an automobile and, "up to a few days ago he did his traveling by bicycle."[5]

He, like the aforementioned signers of the Declaration, lived a long and productive life, and one could surmise, that despite his workload and political and civic endeavors, took his own advice from the rhyme he mentioned in his Centennial essay:

*After breakfast, work awhile,*
*After dinner sit and smile,*
*After supper walk a mile…* ❖

**Image 6.** Photo of Ann & Hope mill with railroad tracks and train station in the foreground. The mill's tower features a clock and a sign that reads "Ann & Hope 1886".
[RHODE ISLAND COLLECTION, PROVIDENCE PUBLIC LIBRARY. HTTPS://PROVLIBDIGITAL.ORG/ISLANDORA/OBJECT/VM0053D18]

## References


1. Garvin LCF. The Premature Death of Great Men. *Communications* of the Rhode Island Medical Society. March 1876. https://babel.hathitrust.org/cgi/pt?id=mdp.39015073450622&seq=1
2. RI Heritage Hall of Fame. https://riheritagehalloffame.com/governor-lucius-garvin/
3. Gersuny C. Uphill Battle: Lucius F. C. Garvin's Crusade for Political Reform. Rhode Island Historical Society. *Rhode Island History*, May 1980.
4. Korr M. November 1902: Lucius F. C. Garvin, MD, elected governor. *Rhode Island Medical Journal*, Nov. 2014: pps. 69-70. http://www.rimed.org/rimedicaljournal/2014/11/2014-11-67-lexicon-heritage.pdf
5. *New York Times*, Oct. 3, 1922.


## Correspondence

mkorr@rimed.org

## URI Trustees authorize next phase of public medical school development at the University of Rhode Island

KINGSTON–JUNE 26, 2026 — The University of Rhode Island Board of Trustees formally authorized the next phase of developing a public medical school at the University, following the State of Rhode Island's historic investment of $5 million in startup funding approved by Governor **DAN MCKEE** and the Rhode Island General Assembly.

The Board's action authorizes University leadership to begin implementing key elements of the medical school development process, including conducting a national search for a founding dean, hiring a project manager and development officer, and initiating curriculum planning.

The vote marks a significant milestone in a multi-year effort to address Rhode Island's healthcare workforce challenges and strengthen access to care across the state. It follows the work of a Rhode Island Senate Special Legislative Commission that examined the state's healthcare workforce needs, physician shortages, and the growing primary care crisis. After reviewing extensive data and hearing testimony from healthcare leaders and stakeholders, the commission recommended advancing the creation of a public medical school at URI.

That recommendation was further supported by an independent feasibility study, which concluded that establishing a medical school at the University of Rhode Island is "both viable and necessary to meet the state's pressing healthcare needs." The study found that a public medical school would strengthen Rhode Island's physician workforce, improve healthcare access, and help retain more medical talent within the state.

The study also projected substantial long-term economic benefits. At full maturity, the program is projected to generate $8.70 in economic return for every $1 invested—building on URI's existing return of $17.39 for every $1 invested by the state—reflecting the University's role as a major driver of Rhode Island's economy and workforce development.

URI President **MARC PARLANGE** said the board's action launches an important new phase in the University's efforts to address both Rhode Island's healthcare needs and its long-term economic future. "The need for more physicians—particularly in primary care—has been well documented, and the healthcare challenges facing Rhode Island demand long-term solutions," said Parlange. "Today's action allows us to begin building a stronger in-state pathway for future physicians while leveraging URI's existing strengths in health education, research, and clinical partnerships. A public medical school has the potential to expand access to care, strengthen our healthcare workforce, attract talent and investment, and create lasting economic and societal benefits for Rhode Island."

With the initial state investment now secured, URI will begin the next phase of planning and development, including recruiting leadership, establishing operational structures, and beginning the curriculum and facilities design process. The University will continue working closely with healthcare providers, state officials, and community stakeholders to advance the successful development of a public medical school that serves the needs of Rhode Island residents and helps secure the state's healthcare future. ❖

## Blue Cross & Blue Shield of Rhode Island seeks applications for its BlueAngel Community Health Grants

PROVIDENCE — Blue Cross & Blue Shield of Rhode Island (BCBSRI) will soon begin accepting applications from nonprofit organizations for its BlueAngel Community Health Grants. The grant funding for 2027 will support projects related to housing, food, maternal health, and youth mental health.

For more than 25 years, BCBSRI has invested in programs that help Rhode Islanders live healthier lives. The BlueAngel Community Health Grant program is a key part of BCBSRI's commitment to improving health and well-being across Rhode Island by addressing the social and environmental factors that influence health. Through these investments, BCBSRI seeks to support community-driven solutions, address disparities, and help ensure all Rhode Islanders have the opportunity to live healthy lives.

Details are available at http://www.bcbsri.com/about/blueangel. Applications will become available on August 3 and must be submitted by 5pm on September 4.

"At BCBSRI, we know that health is shaped by much more than access to medical care," said **CAROLYN BELISLE**, Vice President, Corporate Social Responsibility. "The BlueAngel Community Health Grant program allows us to partner with organizations addressing the issues Rhode Islanders tell us matter most—from housing and food security to maternal health and youth mental health. We are excited to connect with organizations doing this important work and look forward to partnering with them to build healthier communities across Rhode Island."

Guided by insights from the RI Life Index—BCBSRI's partnership with the Brown University School of Public Health—the 2027 grants will invest in these four priority areas:

- Healthy Housing – Safe and affordable homes
- Healthy Food – Access to nutritious food
- Healthy Moms – Maternal health and well-being
- Healthy Mind – Youth mental health and wellness

The 2027 BlueAngel Community Health Grant program will provide:

- Two years of funding (January 2027–December 2028)
- $100,000 annually
- Additional opportunities for organizational support and capacity-building resources

BlueAngel Community Health Grants are the cornerstone of BCBSRI's community-investment activities and have contributed more than $8 million in funding to Rhode Island-based nonprofits since their inception. ❖

## CharterCARE Health first in Rhode Island to introduce multi-site breast tumor localization technology

PROVIDENCE — The CharterCARE Health of Rhode Island Breast Health Program is the first in Rhode Island, and one of the first in New England, to offer surgeons the advantage of wireless localization technologies to identify and distinguish up to four separate tumors using different imaging reflector types.

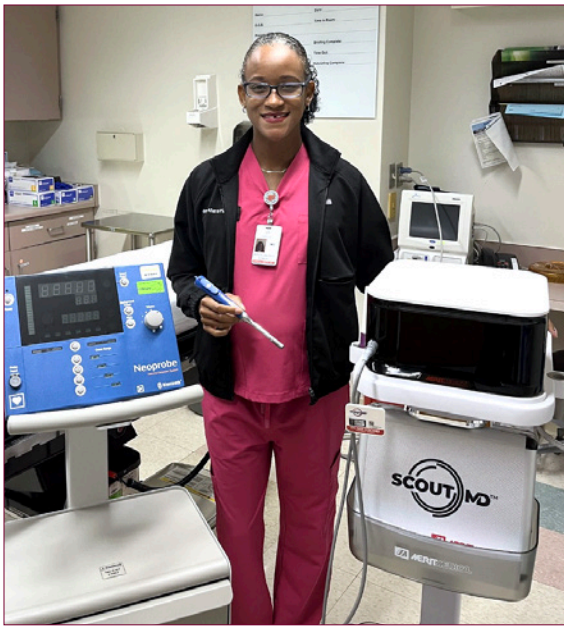
**AYANA ALLARD-PICOU, MD, FACS**, Director of the CharterCARE Breast Health Program at Roger Williams Medical Center, successfully completed several procedures recently.

Scout MD allows surgeons to identify and distinguish up to four separate breast tumors, allowing for more minimal, breast preservation surgery. This imaging technology uses unique reflector shapes and radar signals to allow for precise navigational planning and surgery. Scout MD eliminates the need for traditional wire localization which, in turn, gives surgeons greater flexibility in breast conserving procedures.

Dr. Allard-Picou commented, "We are excited to bring the new Scout MD technology to Roger Williams Medical Center and to offer our breast cancer patients access to the latest advances in breast localization technology. This system allows us to accurately identify and remove breast tumors while providing greater flexibility for complex breast cancer operations. Most importantly, it reflects our ongoing commitment to providing our patients with high-quality, state-of-the-art cancer care close to home."

CharterCARE CEO **JEFF LIEBMAN** stated, "Acquisition of this advanced imaging technology is one of the first capital investments we have made under our new not-for-profit ownership structure. This initiative is also representative of our continued commitment to offering the latest cancer care to patients in the Rhode Island".

Dr. Allard-Picou also credited the collaborative effort in implementing this new technology, specifically team members from the breast center, breast radiology, surgical oncology, surgical services, supply chain, and hospital leadership. ❖




Dr. Ayana Allard-Picou with the Scout MD technology. (CharterCARE Health)

## Morton Hospital completes 100th Inspire® sleep apnea treatment

TAUNTON, MA — Morton Hospital has successfully completed its 100th Inspire® sleep apnea treatment, a significant milestone that highlights the hospital's commitment to bringing innovative, cutting-edge treatments to patients throughout Southeastern Massachusetts.

Inspire is an FDA-approved, implantable device for patients with moderate to severe obstructive sleep apnea who are unable to tolerate or benefit from CPAP therapy. Morton Hospital launched its program in 2023 under the leadership of **AMEER SHAH, MD**, otolaryngology specialist and director of the Inspire program, and **IMAD BAHHADY, MD**, pulmonary critical care and sleep medicine specialist and medical director of the hospital's Center for Sleep Medicine. Since introducing the program, the hospital has helped dozens of patients achieve better sleep and improved quality of life.

"Reaching our 100th Inspire implant is a remarkable milestone and a testament to the trust our patients place in our team," said Dr. Shah. "What makes this achievement especially meaningful is the collaboration behind every case. From patient evaluation and education to surgery and follow-up care, our success is made possible by an exceptional multidisciplinary team, including Dr. Bahhady and our Center for Sleep Medicine team, as well as our outstanding perioperative services staff. Their expertise, dedication, and commitment to patient care have helped us build a program that is truly changing lives."

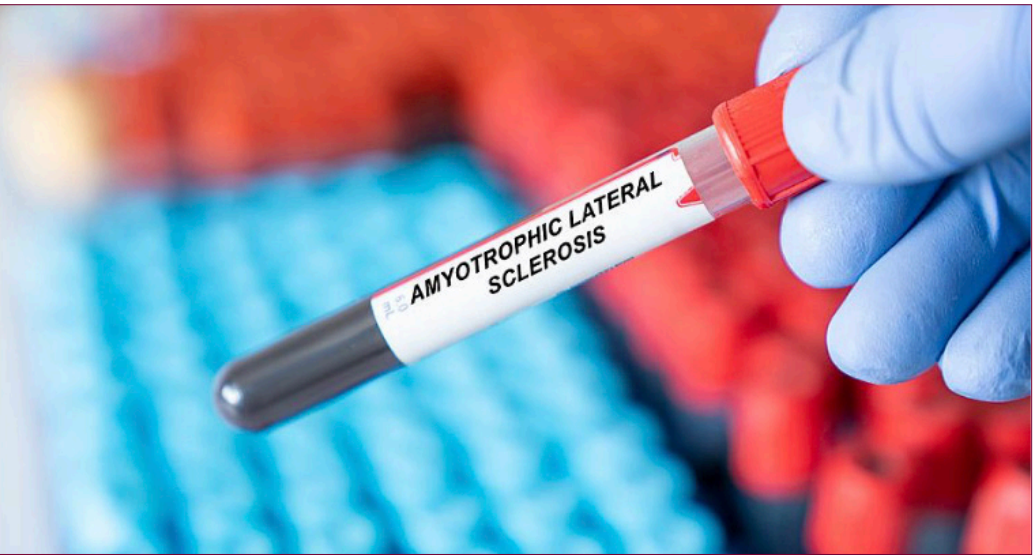
As the first and only hospital in the Southeastern Massachusetts region to offer Inspire therapy, Morton Hospital has become a destination for patients seeking advanced treatment for sleep disorders. According to Inspire's clinical data, Morton Hospital's program currently ranks #1 in the northeast and #4 in the country for patient outcomes, including patient satisfaction rates and reduction in sleep events per hour post procedure.

"This milestone represents much more than a number," said **JILL O'BRIEN, MD**, Morton Hospital's chief medical officer. "It reflects our commitment to bringing advanced, highly specialized care to the communities we serve. Morton Hospital continues to invest in innovative programs that improve access to cutting-edge treatments close to home. Completing our 100th procedure demonstrates both the growth of our clinical capabilities and our dedication to meeting the evolving healthcare needs of our community." ❖

## New blood-based biomarkers predict when ALS symptoms will emerge

BETHESDA, MD — Months to several years before amyotrophic lateral sclerosis (ALS) symptoms arise, levels of certain blood proteins may dramatically shift. Researchers analyzed data from the long-running, National Institutes of Health (NIH)-funded Pre-symptomatic Familial ALS (Pre-fALS) study, to identify a line-up of key proteins that may predict the emergence of clinically manifest ALS. By anticipating the arrival of symptoms, investigators could intervene with preventative therapies before the irreversible motor neuron damage that is characteristic of ALS sets in.

"If someone carrying an ALS-associated genetic variant had asked me in the past when they would become symptomatic, I would have struggled to provide a reasonable estimate," said senior author **MICHAEL BENATAR, MD, PhD**, a professor of neurology and public health sciences at the University of Miami. "These biomarkers give us a far better idea of the timing, allowing us to estimate the time to symptom onset with an average error of about 18 months. That's something we can work with."




For nearly 20 years, the Pre-fALS study, led by Dr. Benatar and **JOANNE WUU, ScM**, research associate professor of neurology and public health sciences at the University of Miami, has collected data and biological samples from people who are at significantly elevated genetic risk for ALS but have not yet progressed, or phenoconverted, to the disease. While this cohort is unique, permitting the examination of presymptomatic ALS, recent studies suggest that findings from Pre-fALS are likely relevant to the broader population.

In 2017, an analysis of 10 Pre-fALS participants who had developed symptoms showed that neurofilament light chain (NfL), a structural protein in neurons, spiked in their blood in the months preceding ALS phenoconversion.

As more study participants have begun showing symptoms or signs of disease, new opportunities to search for other pre-symptomatic ALS biomarkers have emerged.

Now, the investigators applied a high-throughput protein, or proteomic, analysis method called Olink to plasma samples from 137 study participants, 33 of whom had demonstrated clinical manifestations of ALS or frontotemporal dementia. Having collected data on the levels of more than 5,000 proteins, the team identified 92 whose levels differed in people before they eventually showed symptoms.

Using machine-learning techniques, the authors tested how various combinations of proteins could predict future risk of phenoconversion. They settled on a select panel of 19, including NfL, that maximized predictive accuracy across time horizons ranging from six months to five years. The researchers demonstrated that, with data on these 19 proteins, their predictive models could estimate a patient's onset within less than two years of the actual time that they showed signs of disease.

They also produced similar results using data from the UK Biobank, which, despite some limitations, is more representative of the general population than the genetically predisposed cohort of Pre-fALS.

"With preventative gene-targeting treatments now becoming available, there is a particularly urgent need for reliable biofluid-based signatures that indicate near-term onset in individuals that carry ALS risk genes," said **AMY BANY ADAMS, PhD**, acting director of NIH's National Institute of Neurological Disorders and Stroke (NINDS).

Tofersen, a drug approved for symptomatic ALS, is currently being evaluated as a preventative therapeutic in pre-symptmoatic ALS through ATLAS, a clinical trial designed by Benatar in partnership with the company Biogen. ATLAS will test whether starting treatment shortly before symptoms appear could avert or delay the onset of ALS.

"This is all possible because of the members of the carrier community who believe in our mission of preventing ALS and have supported and participated in our research. It has been one of my life's greatest privileges to give something back," Dr. Benatar said.

This research was supported by NIH through NINDS grants R01NS105479 and U54NS092091. ❖

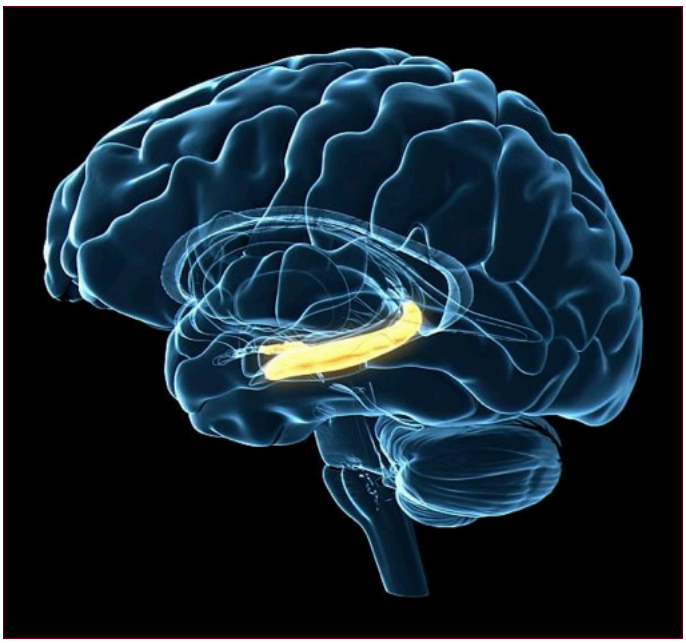
### Reference

Ximing Ran, Joanne Wuu (co-first authors), Zhaohui S. Qin, et al. Longitudinal plasma proteomics predict phenoconversion to clinically manifest ALS. Nature Medicine. July 27, 2026. DOI: 10.1038/s41591-026-04528-

## Brain immunity may undergo a major midlife overhaul

BETHESDA, MD — A National Institutes of Health (NIH)-funded study indicates that the immune cell landscape of the hippocampus, a brain region critical for learning and memory, rapidly undergoes substantial remodeling beginning in midlife. This previously unrecognized shift suggests a potential mechanism by which aging may contribute to chronic neuroinflammation commonly observed in neurodegenerative disease.

"Aging is the single largest risk factor for dementia, but our understanding of how it drives disease is still incomplete," said **RICHARD HODES, MD**, director of NIH's National Institute on Aging (NIA). "This previously hidden microglial shift, now uncovered by innovations in technology and thinking, may be an important clue to help us complete the puzzle."



Using advanced single-cell analysis techniques, a collaborative team of researchers from the University of California, San Diego, the New York Genome Center and the University of California, Irvine, analyzed postmortem hippocampal tissue from 40 neurologically healthy adults ranging in age from 20 to 95 years. The findings suggest that the brain's primary immune cells, called microglia, progressively decline between approximately 50 and 75 years of age, becoming replaced by cells with elevated inflammatory signatures and other features resembling characteristics of peripheral blood-derived immune cells.

These results call into question the longevity of microglia which emerge during embryonic development, which scientists have long thought renew throughout the human lifespan.

To investigate how aging affects the human brain at an unprecedented resolution, the researchers applied traditional measures of gene expression alongside more advanced techniques to analyze the genome's 3D architecture and array of chemical modifications, called the epigenome.

"Gene expression tells us what a cell is doing today, but epigenetic signatures preserve information about where a cell came from," said first author **NATHAN ZEMKE, PhD**, director of single-cell genomics at the UC San Diego Center for Epigenomics. "By combining these approaches, we uncovered a major shift in the identity and lineage of immune cells in the aging human brain's immune cells that gene expression data alone would not have revealed."

Their findings also indicated that cells known to maintain the protective blood-brain barrier deteriorated with age. And across many brain cell types, aging accompanied a widespread and coordinated disruption of genome architecture.

"The progressive structural disruptions were closely linked to shifts in gene regulation and cell identity, potentially revealing a fundamental feature of aging in the human brain," said **BING REN, PhD**, a corresponding author of the study, scientific director and CEO of the New York Genome Center, and professor of genetics and development at Columbia University.

Future studies will investigate the mechanisms driving the loss of resident microglia and determine whether the newly identified immune-cell transition contributes directly to Alzheimer's disease and other age-related neurological disorders.

"Understanding these cellular transitions may provide new opportunities to develop interventions that preserve brain function and reduce vulnerability to neurodegenerative disease," said **XIANGMIN XU, PhD**, professor and director of Center for Neural Circuit Mapping at UC Irvine, and a corresponding author of the study.

NIH supported this research through NIA grants R01AG067153 and R01AG082127 and the NIH Common Fund 4D Nucleome (4DN) program grant 1U01DA052769. This study is part of a collection of 4DN-supported papers published in Science and Science Advances that offer unprecedented insight into how the human genome's 3D organization influences development, aging, and a host of diseases. ❖

### Reference

Nathan Zemke, et al. Epigenetic and 3D genome reprogramming during the aging of human hippocampus. Science. 2026. DOI: 10.1126/science.adt8307

# Appointments

## Julie Abilheira, RN, MS, appointed President of Brown University Health's Massachusetts hospitals

PROVIDENCE — Brown University Health has appointed **JULIE ABILHEIRA, RN, MS**, as president of its Massachusetts hospitals, Morton Hospital in Taunton and Saint Anne's Hospital in Fall River. In her new role, Abilheira will lead strategic, clinical, and operational priorities for both hospitals, with a focus on advancing Brown Health's integrated care model, enhancing service excellence, and expanding access to care.

Abilheira brings more than 25 years of healthcare leadership experience to the position. Most recently, she served as senior vice president of clinical services, overseeing medicine, cancer, radiation oncology, and dermatology services at Brown University Health.

"I am deeply honored to have the opportunity to serve as president of two vibrant and vital community hospitals," said Abilheira. "I have been incredibly impressed by the talent, compassion, and dedication of the physicians and staff at both hospitals. Their commitment to the patients and families they serve is truly unmatched, and I look forward to supporting them as we continue to build on the strong foundations already in place throughout our communities."

Working alongside Abilheira will be **HEIDI TAYLOR**, who has expanded her leadership responsibilities and now serves as chief operations officer and chief financial officer for Brown University Health's Massachusetts hospitals. Taylor, who previously served as president and vice president of finance at Morton Hospital, brings more than 30 years of healthcare leadership experience in finance and operations. ❖

## Julia A. Katarincic, MD, named President of University Orthopedics, Chief of Orthopedics for Brown University Health, and Chair of the Department of Orthopaedics at Brown

EAST PROVIDENCE — University Orthopedics recently announced that **JULIA A. KATARINCIC, MD**, has been named President of University Orthopedics. In addition, Dr. Katarincic has been appointed Chief of Orthopedics for Brown University Health and Chair of the Department of Orthopaedics at The Warren Alpert Medical School of Brown University.

A nationally recognized hand surgeon and respected physician leader, Dr. Katarincic has been an integral part of University Orthopedics for many years. She previously served as chief of the practice's Hand and Wrist Center, chaired the organization's Operations Committee, and has been a member of the Executive Committee. A dedicated educator, she has also received multiple Teacher of the Year awards for her commitment to mentoring the next generation of orthopedic surgeons.

"Dr. Katarincic has earned the respect of her colleagues through her collaborative leadership style, thoughtful decision-making, and unwavering commitment to excellence in patient care, education, and research," said University Orthopedics Chief Operating Officer **MICHELLE R. DEROCHE**. "Her deep understanding of our organization and our mission makes her exceptionally well positioned to lead University Orthopedics into its next chapter."

The leadership transition also marks an opportunity to recognize the extraordinary contributions of **EDWARD AKELMAN, MD**, who, over the past decade, has served as President of University Orthopedics, Chair of the Department of Orthopaedics at The Warren Alpert Medical School of Brown University, and Chief of Orthopedics for Brown University Health.

During Dr. Akelman's tenure, University Orthopedics expanded into Massachusetts, recruited outstanding physicians and advanced practice providers, broadened its specialty orthopedic services, and continued its commitment to exceptional patient care, innovation, education, and research. He'll remain with University Orthopedics as a physician, focused on the patient care he's always loved.

"It is truly an honor to follow in Dr. Akelman's footsteps," said Dr. Katarincic. "Over the years, Ed has been a mentor, colleague, and friend whose vision and leadership have helped shape University Orthopedics into one of the region's premier orthopedic practices. I am deeply grateful for his guidance and look forward to building on the strong foundation he has created while continuing our unwavering commitment to exceptional patient care, education, and research."

Dr. Katarincic earned her Bachelor of Arts in mathematics from Dartmouth College and her Doctor of Medicine degree from the University of Pittsburgh School of Medicine. She completed her internship and orthopedic surgery residency at Rhode Island Hospital and a fellowship in Hand and Microvascular Surgery at Mayo Clinic. She is board-certified by the American Board of Orthopaedic Surgery, with a Certificate of Added Qualification in Surgery of the Hand. ❖

# Appointments

## Bethany Gentilesco, MD, named senior associate dean for inclusive community at Brown

PROVIDENCE — **BETHANY GENTILESCO, MD**, associate professor of medical science and of medicine, clinician educator, at the Warren Alpert Medical School of Brown University, has been appointed the senior associate dean for inclusive community, effective August 1.

A native of New York, Dr. Gentilesco earned her undergraduate degree at Amherst College and medical degree at Joan and Sanford I. Weill Medical College of Cornell University in 2001. After residency training at Stanford University, she began her career as an academic hospitalist and joined the Brown faculty in 2007.

In addition to serving as an associate residency program director for the Department of Medicine, Dr. Gentilesco chairs the department's Diversity, Equity, and Inclusion Committee. Her ongoing scholarly projects focus on the teaching of race and racism in medical training and she completed the Brown Advocates for Social Change and Equity (BASCE) fellowship. In 2024, she received the Mentorship Award in Diversity and Equity at The Warren Alpert Medical School.

As senior associate dean for inclusive community, Dr. Gentilesco will serve as the primary leader of the Office of Belonging, Equity, Diversity, and Inclusion within the Division. ❖

# Recognition

## Gerontological Society of America names URI professor Nekehia Quashie, PhD, among its newest fellows

KINGSTON — **NEKEHIA QUASHIE, PhD**, assistant professor of public health in the University of Rhode Island's College of Health Sciences, has been named a fellow by the Gerontological Society of America for her outstanding contributions to the field of gerontology.

Fellow status is the highest category of the organization's membership. Only about 50 professionals nationwide are selected for the distinction annually. Quashie was chosen in the category of Behavior and Social Sciences.

"This is the ultimate recognition of my scholarly contributions to research on aging and more broadly, my professional service to the field of gerontology," said Quashie.

The new fellows will be recognized at the Gerontological Society of America's annual meeting in National Harbor, Maryland from Nov. 4-7. Quashie has been a member of the Society since 2015, after completing her PhD in sociology from the University of Utah in 2014.

"In addition to presenting at the annual conference, I have gladly served the organization in multiple ways, from reviewing abstracts submitted for the conference to organizing and leading writing groups that support early scholars—from doctoral students to junior faculty—to advance our research agendas," said Quashie.

Quashie is currently an associate editor for the Journal of Gerontology: Social Sciences, one of the flagship journals of the organization. ❖

## South County Hospital designated with a Silver Plus Achievement Award

WAKEFIELD — South County Hospital has been recognized by The American Heart Association and American Stroke Association for continued success in using the Get With The Guidelines® program. This award reflects a commitment to using the most up-to-date evidence-based treatment guidelines to improve patient care and outcomes in our community.

South County Hospital was named a Silver Plus Achievement Award Hospital with Target: Type Two Diabetes, Honor Roll.

"South County Hospital is committed to improving patient care by adhering to the latest treatment guidelines," said **PETER F. GRAVES, MD, MBA**. "Get With The Guidelines helps our teams put proven science into practice every day. Research shows this approach can support better recovery, with the ultimate goal of helping people live longer, healthier lives."

Get With The Guidelines brings the expertise of the American Heart Association and American Stroke Association into hospitals nationwide, helping ensure patient care is aligned with the latest research- and evidence-based guidelines. Get With The Guidelines - Stroke is an in-hospital program designed to improve stroke care through consistent adherence to these guidelines, which can minimize long-term effects of stroke and help prevent death. ❖

# Recognition

## Brown University Health hospitals recognized for exceptional stroke treatment

PROVIDENCE — Four Brown University Health hospitals have been nationally recognized for providing exceptional patient care and outcomes by The American Heart Association (AHA).

Rhode Island Hospital, The Miriam Hospital, Newport Hospital and Saint Anne's Hospital have all received the prestigious Get With The Guidelines®-Stroke GOLD PLUS Quality Achievement Award. The award recognizes programs that demonstrate commitment to ensuring stroke patients receive the most appropriate treatment according to nationally recognized, research-based guidelines, ultimately leading to more lives saved and reduced disability.

All four hospitals also received AHA's Target: Type 2 Diabetes Honor Roll designation for demonstrating they met quality measures with over 90% compliance for the prior year.

"As Rhode Island's only Joint Commission-certified Comprehensive Stroke Center, we know that every second counts when it comes to stroke care," said **MELISSA HARMON, MSN, RN, ASC-BC**, manager of the Comprehensive Stroke Program at Rhode Island Hospital. "Our teams are committed to delivering rapid, high-quality care that gives patients the best possible chance for recovery."

"We strive to provide exceptional care to our patients each day, and we are grateful to be recognized by the AHA again this year for the high-quality care that we provide to our stroke patients," said **KAREN SCHAEFER, MSN, APRN, AGCNS-BC, ASC-BC, FCNS** stroke program manager for The Miriam Hospital and Newport Hospital. "Early stroke detection and treatment are key to improving survival, minimizing disability and accelerating recovery times. Get With The Guidelines helps us ensure patient care is aligned with the latest research- and evidence-based guidelines."

Additionally, the hospitals were honored for:

- **Rhode Island Hospital** received the AHA's Target: Stroke Honor Roll Advanced Therapy and Target: Stroke Honor Roll Elite Plus designations, in addition to Advanced Therapy and AHA's Target: Type 2 Diabetes Honor Roll.
- **The Miriam Hospital** received AHA's Target: Stroke Honor Roll Elite Plus as well as the AHA's Target: Type 2 Diabetes Honor Roll designations.
- **Newport Hospital** received AHA's Target: Stroke Honor Roll designation and AHA's Target: Type 2 Diabetes Honor Roll.
- **Saint Anne's Hospital** received AHA's Target: Type 2 Diabetes Honor Roll. V

## Kent Hospital earns American Heart Association Stroke Gold Plus recognition

WARWICK — Kent Hospital has received the American Heart Association's Get With The Guidelines®-Stroke Gold Plus quality improvement award with Target: Type 2 Diabetes Honor Roll. This award is for Kent's commitment to ensuring people experiencing stroke receive timely, appropriate treatment based on nationally recognized, research-based guidelines, ultimately helping to save lives and reduce disability.

"Earning the Get With The Guidelines®-Stroke Gold Plus recognition is a testament to our Kent Hospital team's unwavering dedication to life-saving care," said **CAROLYN JACKSON**, President and COO, Kent Hospital. "This achievement starts the very moment a patient enters our doors, driven by the rapid, expert responses of our Emergency Department staff who work seamlessly with our stroke specialists to deliver critical treatments when every second counts. By consistently meeting these high national benchmarks, we are ensuring that our community members receive the most advanced, evidence-based care precisely when they need it most."

Kent Hospital also received the American Heart Association's Target: Type 2 Diabetes™ Honor Roll award. Target: Type 2 Diabetes aims to ensure patients with Type 2 diabetes, who might be at higher risk for complications, receive the most up-to-date, evidence-based care when hospitalized due to stroke. ❖

## Roger Williams Medical Center receives Get With The Guidelines®-Stroke Gold Plus

NORTH PROVIDENCE — Roger Williams Medical Center has received the American Heart Association's Get With The Guidelines®-Stroke Gold Plus quality achievement award, the highest recognition, for its commitment to ensuring people experiencing stroke receive timely, appropriate treatment based on nationally recognized, research-based guidelines, ultimately helping to save lives and reduce disability.

"Roger Williams and CharterCARE Health of RI are committed to improving patient care by adhering to the latest treatment guidelines," said **JEFF LIEBMAN**, CharterCARE CEO. "Get With The Guidelines helps our teams put proven science into practice every day. Research shows this approach can support better recovery, with the ultimate goal of helping people in Providence and surrounding communities live longer, healthier lives."

He credited the work of the hospital's stroke committee under the leadership of **GAYLE REBOVICH, MD**, Director of the Division of Neurology; **CANDY WRAY, RN**, Nurse Manager of the ED, and **RACHEL BERNIER**, Clinical Quality Coordinator. The committee included **SHELLI HARDING**, **SARAH KONECNIK**, **TRACEY CASALA**, **MICHELLE SOLITRO-FITZGERALD**, **ANATOLY KAZAKIN, MD**, **MEGAN LEVIGNE**, **RUSSELL DAVIS**, **KARA LEFEBVRE**, **ELIZABETH GREENE**. ❖

# Recognition

## Blue Cross & Blue Shield of Rhode Island recognized as 2026 World's Top Disability Inclusive business

PROVIDENCE — Blue Cross & Blue Shield of Rhode Island (BCBSRI) has been recognized as a World's Top Disability Inclusive Business for its performance on the 2026 Disability Index®. The designation marks the fifth consecutive year BCBSRI has achieved a top score.

This recognition reflects BCBSRI's progress towards building a workplace where all employees can contribute and drive long-term success. Companies scoring at the highest proficiency levels earn recognition as World's Top Disability Inclusive Businesses.

Disability Index is the world's leading independent benchmarking tool for evaluating corporate disability inclusion and is used by hundreds of leading companies across the globe.

"Our leadership and associates are dedicated to building a workplace where everyone feels supported and valued," said **CAROLYN BELISLE**, Vice President of Corporate Social Responsibility. "This honor recognizes that commitment and motivates us to use insights from our Disability Index scores to continue advancing our inclusion efforts."

BCBSRI's top score reflects its comprehensive array of programs and policies that support a culture of accessibility and belonging, including:

The Disability Inclusion Network, an employee business resource group that promotes and provides guidance on accessibility and inclusion for people with disabilities and impairments.

Project SEARCH, an internship program based at BCBSRI that prepares high school students with intellectual or developmental disabilities for post-graduation employment.

Grants and in-kind support for community organizations that serve people with disabilities

Inclusive workplace policies and practices, including hiring, recruitment, and retention efforts, and initiatives that promote physical, digital, and systemic accessibility.

A highly active supplier engagement program that encourages engagement with disability-owned businesses. ❖

# Obituaries

**EDWARD R. FELLER, MD**, 80, of Providence, passed away unexpectedly on July 21, 2026, at his residence. He was the devoted husband of the late Wendy (Levins) Feller, a beloved actress and member of the Rhode Island theater community. Their remarkable and vibrant relationship could light up a room.

Born in Brooklyn, New York, a son of the late Abraham and Emma "Ginny" (Tannenbaum) Feller, Dr. Feller had been a resident of Providence since 1978.

He earned a bachelor's degree from the University of Pennsylvania in 1967 and his medical degree from New Jersey Medical School in 1973. He completed a residency in internal medicine in 1975 at McGill University Royal Victoria Hospital, Montreal, and his fellowship in gastroenterology in 1977 at the Massachusetts General Hospital.

Dr. Feller was Clinical Professor of Medical Science at the Warren Alpert Medical School of Brown University for over 40 years. He previously served as Co-Director of the Community Health clerkship and as Director of the Division of Gastroenterology at The Miriam Hospital. He was Co-Editor-in-Chief of the Rhode Island Medical Journal from 2018 to 2021.

Throughout his career, Dr. Feller was passionate in his commitment to medical students and their education. He mentored generations of medical students who were devoted to him. He received the Faculty Award for Teaching on 14 occasions, and he was awarded the Senior Citation, Alpert Medical School of Brown University's highest honor seven times. Dr. Feller also authored or co-authored well over 100 journal articles, book chapters, and op-eds, the majority of which involved collaborations with medical students.

In his personal life, Dr. Feller was an avid ultramarathon runner, completing 50-mile and 100-mile races in the wilderness. He was also a connoisseur of the arts, with a deep appreciation for theater, music, and literature. Finally, he loved his family and his friends.

Dr. Feller is survived by his two children, Dr. Alexander Arthur Feller of Manhattan and Dr. Sophie Claire Feller of Los Angeles; his brother, Dr. Joseph Feller; his nephews, Dr. Ross Feller, Dr. Reid Feller, and Jonathan Shecter; and his niece, Jane Saul (Shecter). He also leaves behind his treasured companion, his Goldendoodle Oliver.

Funeral services for Dr. Feller were held on July 27, 2026, at Temple Beth El, 70 Orchard Ave., Providence, with burial in Swan Point Cemetery. Memorial contributions in Dr. Feller's honor may be made to: the Warren Alpert Medical School of Brown University, Division of Advancement: https://bbis.advancement.brown.edu/bbphenix/giving/biomed

To share a memory, visit: https://www.dignitymemorial.com/obituaries/providence-ri/edward-feller-12976546 ❖

**CHARLES "BUD" BERNARD KAHN, MD**, 87, passed away on June 29, 2026. He was the beloved husband of the late Susan (Segal) Kahn; they were married for almost 54 years before her passing in 2020.

He graduated from the University of Colorado for both undergraduate and medical school, where he was first in his medical school class. He completed his residency at the Brigham & Women's Hospital and fellowship at the Deaconess Hospital in Boston.

Dr. Kahn served as a major in the Army and worked at the Joslin Clinic in Boston, before founding the state's largest diabetes and endocrinology practice. Over his 50-plus years of medical practice, he was a clinical professor at Brown University Medical School, the first physician elected chairman of The Miriam Hospital Board of Trustees, a member of the Lifespan Board of Trustees, President of the Rhode Island Medical Society, and volunteer and Physician of the Year at the Rhode Island Free Clinic. He also volunteered at the Moi University School of Medicine in Eldoret, Kenya, four times and served on the Board of Trustees at the Wheeler School.

He was an avid photographer, golfer, skier, runner and loved to travel. Most importantly, he was a beloved member of the community and an amazing husband, friend, father, and grandfather.

He is survived by his son, Maxwell Kahn, and his wife Deborah Weinswig of New York, NY; his daughter, Sheri Kahn of Wellesley, MA; his sister, Susan Gersten; and his grandchildren, Ezra, Zahava, and Madeleine "Maddy" Kahn. He was predeceased by his sister, Vicki Ross.

Contributions in his memory may be made to Rhode Island Free Clinic, Development Office, 655 Broad Street, Providence, RI 02907 or to Temple Emanu-El.

Arrangements are in the care of Sugarman-Sinai Memorial Chapel, Providence. For condolences, visit: www.sugarman-sinai.com ❖

**JAMES F. PADBURY, MD**, 78, passed away suddenly in June. He graduated from UCLA Medical School and completed an internship and chief residency at UCSF/Zuckerberg San Francisco General, and a pediatric residency at Boston Children's Hospital. He then joined Harbor-UCLA Medical Center where he rose to Professor of Pediatrics and Chief of the Neonatal Division. He joined Brown University's Warren Alpert Medical School in 1995. Over the next 25 years, he served as pediatrician-in-chief at Women & Infants. Under his leadership, Women & Infants became a premier neonatal program and opened the nation's

largest single family room NICU in 2009—a model he championed as expanding neonatology mission from quality of life, with care tailored to each infant.

He held continuous National Institutes of Health funding for over 40 years and led major advances in our understanding of adrenergic receptor biology in the newborn, placental epigenetics, and the genomics of preterm birth. He chaired the Human Embryology and Developmental Study Section at the National Institutes of Health (NIH), and as Principal Investigator of the NIH Center of Biomedical Research Excellence (COBRE) in Perinatal Biology at Brown, where he helped many early career investigators launch independent research.

After leaving Brown and returning to California, he joined the Pediatric Faculty at UCSF.

He is survived by his wife Mary, and their four children: Morgan, wife Katie; Timothy, wife Marissa; Kate, husband Andrew, and Colin, wife Tabor, and five grandchildren, as well as many friends, colleagues and the families whose lives he touched.

His family will spread his ashes sailing to Catalina were he ran many marathons and raced his sailboat. ❖