

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

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ABSTRACT

BACKGROUND: The rise in xylazine-adulterated fentanyl and heroin has been designated as an emerging public health threat due to a devastating 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 α -2 agonist, can cause acute central nervous system depression.^{6,7} Alarming, 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 health-care 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.

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.

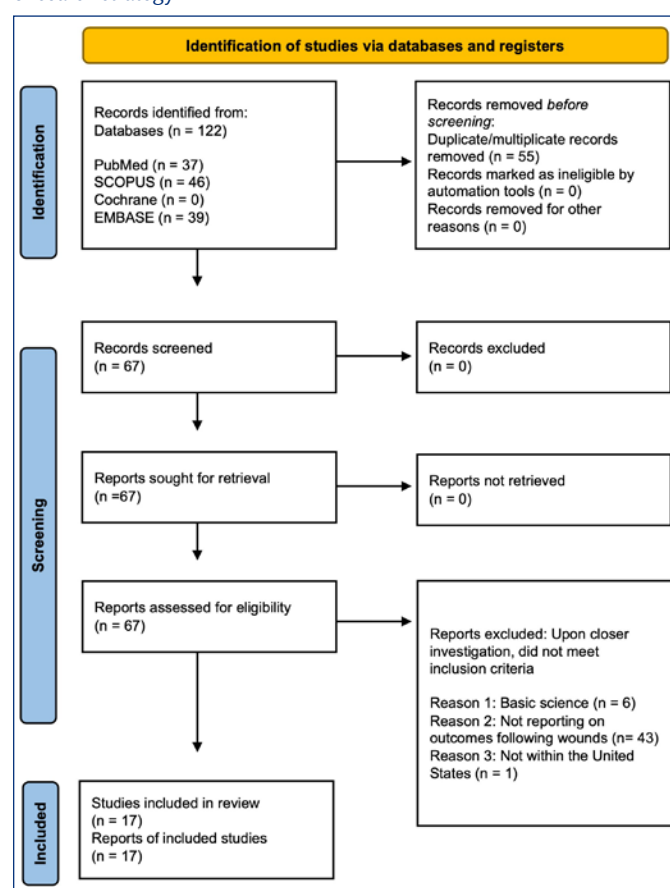
Data Collection and Analysis

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 criteria¹⁴⁻³⁰; 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

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



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
Downton, 2023 ¹⁶	Good	69M; 37M; 54F	Yes	UE	3 yrs; 16 mos; 13 mos	1; 1; 2	Wound care; Wound care; 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; 40sM	Yes	LE	5 d; 1 wk	1; 1	Wound care
Soderquist, 2023 ²⁹	Mod	3 M and 5 F, avg. age 34	—	UE	—	4	Amputation
Naidu, 2024 ¹⁸	Mod	43F; 33F; 43F; 37F; 32M	Yes	UE	4 mos; 5 mos; — Multiple yrs; —	4; 4; 2; 4; 4	Graft and flap to amputation; Fasciotomies and allograft to amputation; Wound care with outpatient fingertip amps; Graft and flaps; 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; 38M; 35M; 31F; 33M; 20sF; 48M	—	UE	2 yrs; 2 yrs; —; 2 mos; —; 5 d	3; 4; 4; —; 2; 2; 2	Bone reconstruction; Amputation; Amputation; No care; Graft; Graft; I&D
Sun, 2024 ¹⁹	Mod	30F; 40F; 34M	Yes	UE	1.5 yrs; Several mos; —	2; 2; 2	Graft; I&D (left before graft); Graft
Warp, 2024 ¹⁷	Good	43F	Yes	LE, UE	—	1	Wound care
Yeung, 2024 ²⁰	Good	28F; 32F; 40F; 33F	Yes; —; Yes; —	LE; LE, UE; UE; LE, UE	—	3; 2; 3; 2	I&D; Fasciotomy, I&D; Wound care; Grafts
Arango, 2025 ²¹	Good	47 M and 35 F, avg. age 40.3	—	43 LE, 82 UE, 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, avg. age —	—	19 LE, 55 UE	—	—	33 wound care, 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, avg. age 40.8	—	50 LE, 35 UE	—	—	—
Lutz, 2025 ²⁵	Good	15 M and 14 F, avg. age —	—	26 LE, 27 UE, 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%)

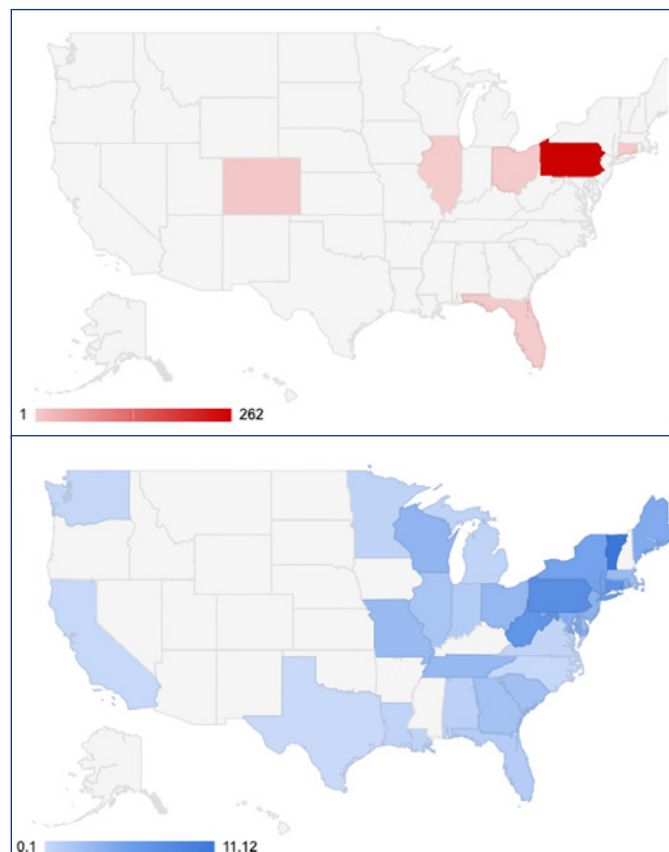
patient-reported wound duration; the average reported wound duration was 10.7 months (± 10.9), and ranged from five days to three years. Wound stage was determinable for 36 of 277 patients, utilizing either the case's reported stage or evaluated by the authors using description and/or clinical imaging 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 non-punitive 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 devastating 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, Worrlow WM. Treatment of Xylazine-Associated Injection Skin Injuries. *Case Reports in Dermatological Medicine.* 2024;1(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, Steinhauer 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. *JAMANetwork 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

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