



RECOMMENDATIONS FOR CARING FOR INDIVIDUALS WITH XYLAZINE-ASSOCIATED WOUNDS

January 8th, 2023



HEALTH FEDERATION
OF PHILADELPHIA

The keystone of community health since 1983

Acknowledgements

This report would not be possible without the trust and engagement of people who have xylazine-associated wounds in wound care. Thank you for allowing your lived experiences to be shared with the review committee to develop recommendations described in this report.

The review committee consisted of physicians, surgeons, nurses, therapists, and public administrators who committed their time to reviewing patient cases and identifying best-practices for caring for people with xylazine-associated wounds. Thank you for your time and dedication to improving the care for people with xylazine-associated wounds.

Efforts to develop this report were informed by the City of Philadelphia Overdose Fatality Review (OD STAT) recommendation: “The Division of Substance Use Prevention and Harm Reduction at the Philadelphia Department of Public Health should facilitate a wound care learning collaborative to ensure current best practices and trainings are shared among providers. The learning collaborative should address both treatment and the stigma associated with wounds.” OD STAT is a program administered by the Division of Substance Use Prevention and Harm Reduction at the Philadelphia Department of Public Health with support from a Centers for Disease Control and Prevention Overdose Data to Action Grant (NU17CE924977).

Suggested Citation: Philadelphia Department of Public Health, Division of Substance Use Prevention and Harm Reduction. Recommendations for caring for individuals with xylazine-associated wounds. January, 8th, 2024.

NOTE: Brand names included in this report are used to facilitate implementation of recommendations and do not represent endorsement or disapproval of any specific product.

Table of Contents

EXECUTIVE SUMMARY	1
INTRODUCTION	2
OVERVIEW OF XYLAZINE	2
RECOGNIZING XYLAZINE-ASSOCIATED WOUNDS	2
RECOMMENDATIONS	4
DEFINING BASIC WOUND CARE AND KNOWING WHEN ADVANCED WOUND CARE IS NEEDED	4
DEBRIDEMENT	6
MEDICATION MANAGEMENT: ANTIBIOTICS.....	7
Medication Management: Pain and Opioid Dependency.....	9
Surgical Interventions: Skin Grafting and Amputation	10
Wound Care Supplies.....	11
Training and Resources for Providing Wound Care	14
Communication Between Providers	15
Misinformation and Stigma	15
Billing and Coding for Wound Care.....	16
Housing and Nutrition.....	17
Patient Education.....	18
Appendix: Contributing Authors	19
References:	20

EXECUTIVE SUMMARY

Everyone deserves to receive the standard of care, however, there is a currently a lack of standard of care for xylazine-associated wounds. Xylazine-associated wounds are a distinct and new presentation of complications associated with substance use.^{1,2} In the absence of evidence-based practices for treating xylazine-associated wounds, clinicians and non-clinicians with experience caring for individuals with xylazine-associated wounds are well positioned to identify best-practices. This report summarizes recommendations for best-practices in providing care for individuals with xylazine-associated wounds.

These recommendations were developed through a case series hosted by the Division of Substance Use Prevention and Harm Reduction (SUPHR) at the Philadelphia Department of Public Health (PDPH) and the Substance Use Response, Guidance and Education (SURGE) program at the Health Federation of Philadelphia. The case series reviewed the care of four individuals with xylazine-associated wounds and were presented by clinicians working in outpatient, street-based, hospital, and methadone treatment settings in Philadelphia. Attendees included clinicians and non-clinicians working in hospitals, community-based organization, and public administration in Philadelphia. Each case and case discussion were summarized and reviewed by staff at SUPHR and SURGE who developed initial draft recommendations. A select committee of clinicians (See Appendix) with experience providing care to individuals with xylazine-associated wounds was convened to review recommendations, which were revised through an iterative process.

This report identifies 35 recommendations for best-practices across 12 topic areas in the care for individuals with xylazine-associated wounds. In addition, 9 areas of further investigation, where issues were recognized but recommendations were not developed, are included in this report.

The 12 topic areas in the care of individuals with xylazine-associated wounds included in this report, include:

- 1) Defining Basic Wound Care and Knowing when Advanced Wound Care is Needed
- 2) Debridement
- 3) Medication Management: Antibiotics
- 4) Medication Management: Pain and Opioid Dependency
- 5) Surgical Interventions: Skin Grafting and Amputation
- 6) Wound Care Supplies
- 7) Training and Resources for Providing Wound Care
- 8) Communication Between Providers
- 9) Misinformation and Stigma
- 10) Billing and Coding for Wound Care
- 11) Housing and Nutrition
- 12) Patient Education

INTRODUCTION

OVERVIEW OF XYLAZINE

Xylazine, is a non-opioid alpha-2 receptor agonist approved by the Food and Drug Administration (FDA) for sedation and analgesia in veterinary medicine.³ Xylazine is not approved for use in humans as it causes excessive central nervous system depressant effects, such as low blood pressure and sedation.³⁻⁵ Xylazine first emerged as an illicit substance in the early 2000s in Puerto Rico and 2006 in Philadelphia, PA under the street names “anestesia de caballo” and “tranq”.⁶ In Philadelphia, xylazine is primarily found with illicitly manufactured fentanyl, but, nationally, xylazine has also been found alongside other synthetic opioids, cocaine, methamphetamines, heroin, and benzodiazapines.^{7,8} Although some people who use substances report seeking out xylazine, many people consume xylazine unknowingly.^{8,9} Xylazine is thought to have synergistic effects when used with opioids; in combination, xylazine and opioids produce increased sedation, muscle relaxation, vasodilation, bradycardia, decreased perception of painful stimuli, and respiratory depression.^{4,8}

While xylazine-associated wounds have been recognized as a distinct clinical entity, their etiology is not well understood.^{1,10-13} Biopsies of xylazine-associated wounds have revealed epidermal necrosis with focal fibrin thrombi, nonspecific inflammation, and subcutaneous necrosis as well as bacterial colonization.¹⁴⁻¹⁶ Suggested mechanisms of xylazine-associated wounds include peripheral vasoconstriction leading to poor perfusion and necrosis, and small vessel disease.^{1,10,12,13} Xylazine-associated wounds increase the risk of bacteremia, endocarditis, sepsis, limb amputation, and death.^{10,17-19}

RECOGNIZING XYLAZINE-ASSOCIATED WOUNDS

In 2009, Rodríguez et al. first recorded a higher prevalence of skin ulcers among people who injected xylazine-containing substances than people who injected substances without xylazine.²⁰ In 2012, Reyes et al. published images of xylazine-associated abscesses, ulcerations, and lesions, including the presentation of xylazine-associated wounds.¹⁷ Later case reports from Philadelphia, PA, New Haven, CT, Camden, NJ, and Columbus, OH further document and characterize xylazine-associated wounds and soft tissue injuries.^{10,11,13,16,21-25} Skin wounds associated with xylazine use (i.e., xylazine-associated wounds) are consistently described as partial to full thickness skin lesions with progressive necrosis of the skin, muscle, tendon, and bone.^{2,10,11,13,16,21} Although xylazine-associated wounds commonly develop at sites of injection, they can appear anywhere on the body (i.e. away from sites of injection) and irrespective of the method of xylazine administration.^{1,10,14,17,19} Xylazine-associated wounds may initially appear as areas of blistered skin, often over reddish-purple discolored tissue, which evolve into a thick layer of eschar overlying a partial or full thickness ulcer that progressively increases in size and depth.^{2,17,23} (Figure 1) Indeed, xylazine-associated wounds are often typified by the presence of necrotic tissue (eschar and slough) and wound diameters greater than 10cm.^{10,11,13,16,17,21-23,25}

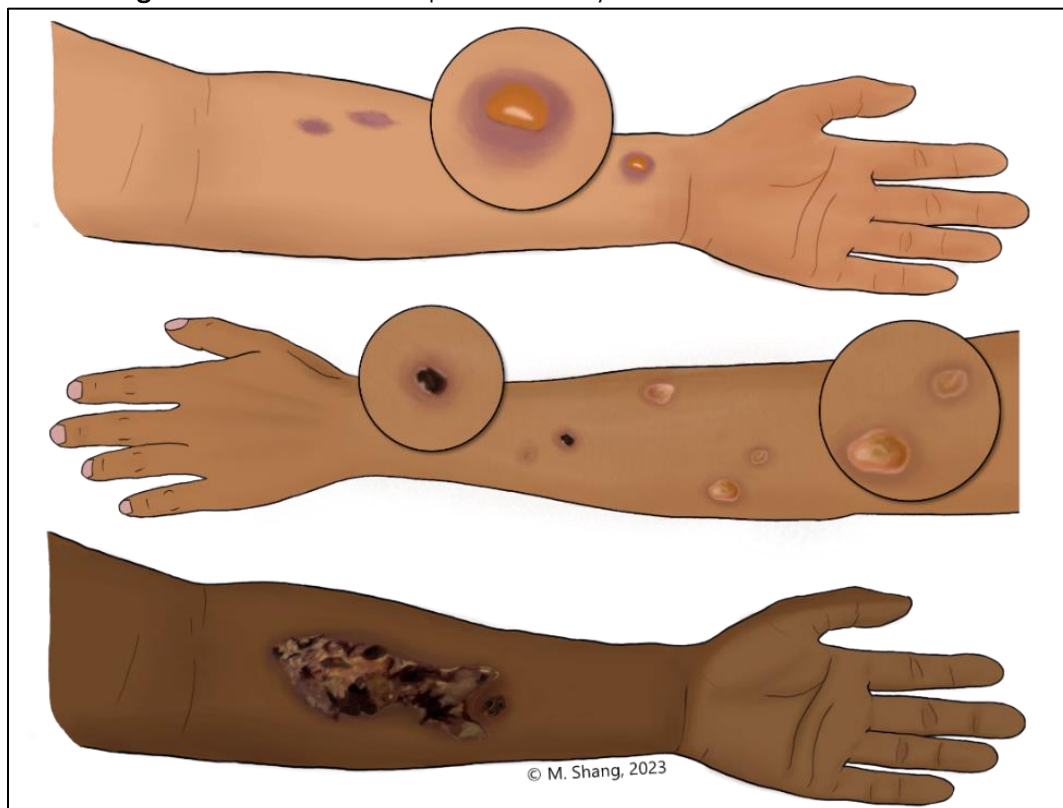
Individuals with xylazine-associated wounds often have a history of substance use or actively use substances. Thus, clinicians should have a high clinical suspicion for xylazine-associated wounds

among their patients who regularly use fentanyl or other substances. Clinicians can also be aware of the following characteristics of xylazine-associated wounds:

- Rapid progression
 - Usually starts as a blister and progresses to an open lesion then expands to a size often greater than 10cm with areas of necrosis.
- Necrotic
 - Dead tissue that is also clinically referred to as “eschar” or “slough”.
 - Eschar – typically dry, dark, firm, and adherent
 - Slough – typically wet, yellow or white, soft, and stringy
- Heterogenous
 - Wounds may have areas of exposed underlying structures, such as tendon or bone, alongside necrotic tissue and healing granulation tissue.
- Typically occur on limbs
- Associated with illicit substance use
- Not always associated with a site of injection

Figure 1 illustrates the spectrum of presentations of xylazine-associated wounds on different skin tones.²⁶ The topmost arm shows reddish-purple bordered blisters, as often appears in the initial stage a xylazine-associated wound. The middle arm shows simultaneous xylazine-associated wounds at different stages of progression, appearing as circular, discrete lesions. The bottom arm shows a further progressed xylazine-associated wound with eschar, slough, and open wound bed.

Figure 1: Illustration of Spectrum of Xylazine-Associated Wounds²⁶



RECOMMENDATIONS

DEFINING BASIC WOUND CARE AND KNOWING WHEN ADVANCED WOUND CARE IS NEEDED

Individuals with xylazine-associated wounds may receive wound care in a variety of settings including community-based organizations, mobile health units, emergency departments, and substance use treatment settings; but not all settings are equipped to provide advanced wound care, such as debridement or evaluation by a clinician to determine if antibiotics are needed. Discerning between basic and advanced wound care offers guidance to the extent of wound care a provider without clinical training should provide, such when an individual with xylazine-associated wounds has an indication for urgent or emergent care but decides not to go. In addition, defining a scope of basic and advanced wound care offers guidance for clinicians to empower individuals with xylazine-associated wounds to provide self-care. Lastly, defining indications for referrals to advanced wound care can support settings where wound care has not historically been available, such as community-based organizations and substance use treatment programs, to provide basic wound care. Supporting low-barrier access to wound care for xylazine-associated wounds can reduce stigma by encouraging individuals to disclose their wounds to providers and offer a strategy for early identification of complications of xylazine-associated wounds.²

When an individual with a xylazine-associated wound has signs or symptoms that indicate possible complications, such as exposed bone or tendon or signs of local or systemic infection, they should be referred to a provider with appropriate clinical training. When an individual has an indication for advanced wound care that wound care should be provided by a licensed clinician. In community settings, service providers may not have clinical training or access to resources – such as pulse oximeters or blood pressure cuffs – to complete assessments. Thus, providers in community settings may need to rely on observable and reported signs and symptoms of xylazine-associated wound complications, such as infection.

Importantly, many individuals with xylazine-associated wounds may also experience housing instability and lack access to clean water. Without clean water, individuals with xylazine-associated wounds are not able to independently complete self-care, which increases their risk for infection. Further investigation is needed to establish access to clean water for unhoused individuals with xylazine-associated wounds.

Recommendations:

- 1) Basic wound care that can be provided by providers without clinical training includes cleaning wounds with saline or soap and water, applying petroleum-based ointments, and covering with two-layer dressing as illustrated in Figure 2.
- 2) People providing wound care should avoid using any agents that are toxic to human cells, such as alcohol or peroxide, which can dry a wound.

- 3) The presence of at least one indicates a referral to clinical provider who is licensed to provide advanced wound care is needed:
- Exposed bone and/or tendon
 - Inability to move a joint or decreased range of motion at site of a wound
 - Signs symptoms of systemic infection, including:
 - Fever
 - Unexplained nausea and vomiting (e.g., not explained by opioid withdrawal)
 - Change in mental status unrelated to substance use
 - Signs and symptoms of local infection, including:
 - Purulent drainage (e.g., pus)
 - Swelling
 - Malodor (after cleansing)
 - Fluctuance (e.g., boggy or change in firmness indicating a collection of pus under the wound or skin)
 - Increased pain
 - Erythema (e.g., redness or darkening) of the skin surrounding the wound
 - Warmth over the skin or joint
 - Crepitus (e.g., cracking or crunching sound under the wound or skin, indicating a soft tissue infection by a gas producing bacteria)
- 4) Individuals with an indication for advanced wound care should receive wound care from a clinically trained professional with the appropriate license.

Area for further investigation:

1. Establishing access to clean water for individuals with xylazine-associated wounds who are unhoused.

Figure 2: Basic wound care

<p>1. Clean</p> <ol style="list-style-type: none"> 1. Wash or sanitize your hands and use gloves if you have some. 2. Clean wound with soap and water or saline. Do not use alcohol or peroxide on a wound because they are too harsh. 3. With a wet piece of gauze gently wipe the wound and surrounding skin to remove any dried drainage and dead tissue that's able to be removed easily and painlessly. 	<p>2. Moist</p> <ol style="list-style-type: none"> 1. Spread a barrier ointment like A&D™ or Vaseline™ around the edges of the wound. This will help protect the wound and keep it from getting bigger. 2. Apply the same ointment (A&D™ or Vaseline™) to a non-adherent dressing. A non-adherent dressing can look like gauze that's shiny on one side, or greasy mesh like Adaptic™ or Xeroform™. 3. Place the non-adherent dressing with the ointment on the wound. This is your "inner dressing." 
<p>3. Covered</p> <ol style="list-style-type: none"> 1. Place an ABD Pad, an extra layer of dry gauze, or cloth on top of the inner dressing. This is your "outer dressing" that will help soak up drainage. 2. Wrap the wound with a gauze roll, athletic wrap, or ACE™ bandage. The wrap should be tight enough to keep the dressings in place, but not so tight that it cuts off blood flow. 3. Change the inner and outer dressing every 1-3 days or when it is soaked. 	<p>Things to watch for:</p> <p>The wound: is getting more painful, draining more pus than usual, or has an odor even after cleaning it.</p> <p>The surrounding skin: feels hot, and looks swollen, red, or darkened.</p> <p>You are: able to see bone or tendon, having fevers, chills, nausea or vomiting, or are unable to feel or move that part of your body normally.</p> <p>If you see black material in your wound you may need debridement which is best done by a medical professional.</p> <p>Takeaways:</p> <p>Keep your wound CLEAN, MOIST, AND COVERED. A dry wound won't heal!</p> <p>You know your body best – go to a clinic or hospital if you are experiencing any of the things to watch out for.</p> <p>See substanceusephilly.com/services to learn where you can get wound care.</p>

DEBRIDEMENT

A typical characteristic of xylazine-associated wounds is devitalized or necrotic tissue, such as eschar and slough. Necrotic tissue in a wound increases bacterial burden and risk of infection, as well as inhibits healing.²⁷ Debridement is used to decrease the amount of necrotic tissue in a wound to promote healing and is a cornerstone of caring for people with xylazine-associated wounds.

There is a spectrum of debridement, including autolytic, enzymatic, conservative sharp, and surgical debridement. Autolytic debridement leverages the body's natural immune processes for removing dead tissue.²⁷ Autolytic debridement is promoted by keeping wound beds moist. Non-clinicians and individuals self-managing their xylazine-associated wounds can safely facilitate autolytic debridement by completing basic wound care discussed above and illustrated in Figure 2. In addition, silver sulfadiazine which is topical antibiotic that requires a prescription, promotes autolytic debridement and can be cool and comforting when applied. Enzymatic debridement is a method of removing necrotic tissue using collagenase, an enzyme that breaks down the collagen in necrotic tissue. Enzymatic debriding agents are topical therapies that require a prescription from a provider with the appropriate clinical training.²⁸ Enzymatic debridement may be used as the primary approach for debridement. However, collagenase does not penetrate dry eschar, and the Wound, Ostomy, and Continence Nurses Society recommends cross-hatching eschar prior to applying enzymatic debridement.^{28,29} Thus, enzymatic debridement may have limited efficacy for the treatment of xylazine-associated wounds with high eschar burden, and clinicians may combine enzymatic debridement with other approaches, such as conservative sharp debridement, to increase the efficacy of eschar removal.²⁸ Severe xylazine-associated wounds, such as those with heavy eschar burden, may take months or years to debride using only autolytic or enzymatic debridement. Lastly, it should be noted that enzymatic debridement can cause stinging that may be uncomfortable to some individuals with xylazine-associated wounds.

Sharp debridement encompasses approaches to removing necrotic wound tissue in outpatient, inpatient, and surgical settings. Conservative sharp debridement can be provided in the outpatient setting and is limited to using sharp instruments to remove loose necrotic tissue.^{30,31} Surgical debridement is the most intensive sharp debridement approach that is completed in an operating room or at the bedside in an inpatient setting and requires sedation and general anesthesia to remove adherent necrotic tissue and layers of the wound bed that have stalled in the healing process.^{21,27} Surgical debridement is typically pursued as a last resort, and primary indications include deep infection or abscess causing systemic illness. Exposed bone or tendon in a xylazine-associated wound is an indication to refer an individual for a surgical debridement consultation. However, individuals with xylazine-associated wounds who have exposed tendon or bone may maintain good healing potential with or without surgical intervention. Goals of surgical debridement should include augmenting wound care to assist in tissue regrowth, decreasing infection, and promoting coverage of bone and tendon with a dermal substitute to delay or avoid the need for amputation. Aggressive surgical debridement of necrotic tissue that is not the cause of systemic illness may lead to faster exposure of tendon and bone and progression to amputation, and therefore should be avoided. Conservative sharp debridement combined with enzymatic or

autolytic debridement can be an effective alternative to surgical debridement for patients who are unable to access or tolerate surgical debridement. Importantly, conservative sharp debridement should only be attempted in settings that can provide appropriate analgesia given people with xylazine-associated wounds may have hyperalgesia and opioid tolerance due to chronic use of illicit fentanyl.³²

Xylazine-associated wounds are complex and difficult to heal. Many factors, including unstable housing, inadequate nutrition, and active substance use often complicate and delay wound healing for many individuals with xylazine-associated wounds. For these reasons, many clinicians advocate for conservative sharp debridement over surgical debridement to limit the area of open wound while still increasing the percentage of viable tissue, improving the periwound skin (*skin surrounding the wound bed*), and decreasing the amount of wound exudate, malodor, and risk of infection. Despite barriers, in the experience of the contributing experts, wound healing and closure can be achieved among individuals with active substance use. Thus, it is important to emphasize that active substance use is not a contraindication for debridement.²

Recommendations:

- 1) Active substance use is not a contraindication to receiving surgical and non-surgical wound care.
- 2) Keeping xylazine-associated wound beds moist can promote autolytic debridement and can be achieved by non-clinical professionals using basic wound care.
- 3) Enzymatic debridement with collagenase is effective in removing necrotic tissue from xylazine-associated wounds and should be provided by clinically trained providers.
- 4) Conservative sharp debridement can be provided in the outpatient setting by clinically trained providers and may prevent infection and improve wound healing. Such procedures should only be performed in settings that can provide proper analgesia to patients who are likely to experience significant hyperalgesia and opioid tolerance.
- 5) Surgical debridement may be indicated if there is deep infection or abscess. Exposed tendon or bone may benefit from operative intervention with placement of a dermal substitute to maintain or enhance tissue growth and delay or avoid amputation.

MEDICATION MANAGEMENT: ANTIBIOTICS

Xylazine-associated wounds may be complicated by local or systemic infection requiring treatment with oral or intravenous antibiotic therapy.^{14,19} Not unlike the general public, individuals with xylazine-associated wounds often have difficulty completing oral antibiotic regimens in the outpatient setting. Factors like unstable housing, limited space to store medication, theft of medication, and active substance use further complicate individuals' ability to complete prescribed antibiotic regimens. To ensure that individuals with xylazine-associated wounds complete their antibiotic regimens, prescribers can work with their patients to develop strategies for adherence such as directly dispensing antibiotics, including a lanyard pill pouch when dispensing oral medication, and presenting for observed dosing.

The guidance for swabbing and culturing xylazine-associated wounds is the same as for all other wounds. The Infectious Disease Society of America does not recommend culturing wound beds

because they are more likely to pick up non-pathologic skin colonizers.^{33,34} Chronic wounds are likely to be colonized with microbes, so positive cultures of chronic wounds are not always an indication of an acute infection or an indication for antibiotic treatment.^{33,35,36} However, when xylazine-associated wounds display signs of infection, culturing deep tissue, muscle, or bone in an operative setting may help guide antibiotic therapy.

Intravenous antibiotic therapy should be provided to individuals with xylazine-associated wounds and signs of systemic infection. However, many people with xylazine-associated wounds have active substance use that is associated with patient-directed discharges against medical advice that can result in incomplete intravenous antibiotic regimens.^{11,21,37} Long-acting injectable antibiotic therapy, such as dalbavancin, may improve completion of intravenous antibiotic regimens among individuals with xylazine-associated wounds who require long-term antibiotics. Dalbavancin has been associated with improved clinical outcomes including clinical cure and lower readmission rates among people who inject substances and may facilitate early hospital discharges.^{38–40}

Topical antibiotics are commonly used in combination with petrolatum-based ointments to decrease bacterial burden of xylazine-associated wounds and promote autolytic debridement. Table 1 describes topical antibiotics commonly used in the care of people with xylazine-associated wounds. Caution should be used when applying topical antibiotics as some, such as neomycin, have been associated with contact dermatitis.⁴¹

1% silver sulfadiazine (e.g., Silvadene™) has been a preferred topical therapy in caring for individuals with xylazine-associated wounds. Silver sulfadiazine is a prescription topical antibiotic that is often used in the treatment of burn wounds in outpatient and inpatient settings. It has broad spectrum antimicrobial effects and a low chance of generating antibiotic resistance.^{42,43} The antimicrobial effect of silver sulfadiazine stays active for over 72 hours after application, which provides ongoing treatment for patients who have less access to dressing changes.⁴³ In addition, silver sulfadiazine maintains moisture that can promote autolytic debridement and reduce tissue trauma during dressing changes.⁴⁴ It should be noted that some people experience allergic reactions to the sulfadiazine moiety and that silver sulfadiazine and collagenase should not be used in combination as silver ions deactivate the essential enzymes of collagenase.^{44,45}

Recommendations:

- 1) Most wounds only require topical antibiotics that should be administered with the guidance of a clinically trained providers licensed to prescribe medications.
- 2) Silver sulfadiazine is a preferred topical antibiotic therapy for xylazine-associated wounds and should be administered by clinically trained providers.
- 3) Oral antibiotics should be used only when there are signs and symptoms of a localized infection and should be provided by a clinically trained providers licensed to prescribe medications who should work with their patients to develop strategies for completing antibiotic regimens.
- 4) Intravenous antibiotics should be used when there is evidence of systemic infection.

Area for further investigation:

- 1) Developing strategies for long-acting injectable antibiotic therapy in the treatment of individuals with xylazine-associated wounds and signs of systemic infection.

Medication Management: Pain and Opioid Dependency

Xylazine-associated wounds are often associated with pain that requires pharmacologic management.^{11,13,16,22,23} Individuals with chronic xylazine exposure via the illicit fentanyl supply will often have opioid dependency and opioid use disorder with associated hyperalgesia and high opioid tolerance.^{7,32,46} Providers caring for individuals with xylazine-associated wounds should consider and integrate the individual's need for medical management of pain and opioid dependency.

This report does not provide comprehensive guidance on the management of opioid or xylazine dependency or withdrawal. Xylazine dependency and withdrawal is not yet a defined syndrome, and understanding of its clinical presentation and management is evolving.^{1,10,47,48} In 2022, the Philadelphia Department of Public Health released a health alert and health update to provide guidance for the management of xylazine dependency and withdrawal, which can be found [here](#) and [here](#). The American Society of Addiction Medicine provides national practice guidelines for the treatment of opioid use disorder including opioid withdrawal, which can be found [here](#). D'Orazio, et al. recently published a narrative review that includes guidance for the treating individuals experiencing withdrawal from xylazine and fentanyl.¹ The Centers for Disease Control and Prevention provides guidance for prescribing opioids to treat pain among patients with opioid use disorder, which can be found [here](#).

Individuals with xylazine-associated wounds often present to emergency departments with wounds at advanced stages, requiring hospital admission. Early involvement of hospital-based Addiction Medicine or Addiction Psychiatry consult services can lead to improved management of pain and opioid withdrawal. In the inpatient setting, a successful strategy has been using a low-dose buprenorphine induction approach to treat opioid dependency, while concurrently treating pain using short-acting opioids.^{13,49} In the methadone treatment setting, a successful strategy has been using split dosing of methadone to improve pain control.⁵⁰ Patients with opioid use disorder admitted to the hospital who receive management of their pain and withdrawal with opioid agonists are less likely to leave against medical advice.⁵¹ In all settings, proper pain management for bedside procedures, dressing changes, and wound-associated pain is essential. This is especially pertinent to patients with illicit fentanyl dependence who are at risk for severe withdrawal and opioid-induced hyperalgesia.^{32,46}

For individuals with xylazine-associated wounds who are ready for substance use disorder treatment, clinicians should provide low-barrier referrals for assessment and placement at the appropriate level of care. Increasing the capacity of substance use disorder treatment programs to provide care for xylazine-associated wounds is an area of active investigation. Patients with wounds that require intravenous antibiotics or inpatient level of care may be eligible for admission to level 4 substance use disorder treatment programs.⁵² One case reviewed for this report included care provided in a methadone clinic setting. However, not all levels of substances use

treatment may have the appropriate licensing and accreditation for providing wound care. However, this is an evolving area of work. When referring an individual with xylazine-associated wounds to substance use treatment, wound care providers should communicate a wound care assessment and plan to the receiving provider.

Recommendations:

- 1) Individuals with a xylazine-associated wound receiving care in a hospital should have Addiction Medicine or Addiction Psychiatry consulted for management of opioid dependency and pain management.
- 2) Individuals with xylazine-associated wounds who are on methadone may benefit from split dosing to improve pain control.
- 3) Individuals with xylazine-associated wounds who are admitted to the hospital may receive buprenorphine using a low-dose induction protocol and opioid-short acting opioids for concurrent treatment of opioid dependency and pain.
- 4) Individuals with xylazine-associated wounds who are ready for substance treatment should receive low-barrier referrals for assessment and placement in the appropriate level of care.

Areas for further investigation:

- 1) Characterizing signs and symptoms of xylazine dependency and withdrawal.
- 2) Defining effective treatment for xylazine dependency and withdrawal.
- 3) Developing strategies to communicate wound care assessment and plans to substance use treatment programs to facilitate referrals.
- 4) Determine accreditation and licensure requirements for wound care to be provided across substance use disorder levels of care.

Surgical Interventions: Skin Grafting and Amputation

Individuals with xylazine-associated wounds are often recommended to undergo amputation, however it is not clear if existing clinical indications for amputation can be readily applied to individuals with xylazine-associated wounds. Protocols for the treatment of burn wounds offer strategies, such as dermal substitutes, for treating xylazine-associated wounds in the hospital setting which may improve clinical outcomes. One such guidance is avoiding amputation and providing limb-sparing care.^{1,21} Early Burn Surgery consultation may help initiate treatments that avoid amputation. In the experience of the contributing experts, one strategy that is applied to burn wounds that has been helpful in healing xylazine-associated wounds is the application of biodegradable temporizing matrix – a synthetic dermal substitute which promotes tissue growth and tissue coverage over tendon and bone. However, caution is required when applying burn-indicated therapies to xylazine-associated wounds. For example, a biological dermal substitute that has a poor infection profile and should not be placed on xylazine-associated wounds.⁵³ In addition, closing a xylazine-associated wound with a skin graft may put individuals at greater risk of systemic infection if they are actively using substances. Some clinicians restrict skin grafting xylazine-associated wounds to individuals who have not used illicit substances for a period of time (e.g., six weeks). However, this goal is difficult to achieve for many individuals with concurrent fentanyl-xylazine dependence. As in other xylazine-associated wound treatment decisions,

treatment plans should be guided by a harm reduction perspective of ongoing substance use and individual and provider goals, in order to optimize health outcomes.

Recommendations:

- 1) Biological dermal substitutes have a poor infection profile and should not be placed on xylazine associated wounds.
- 2) Synthetic dermal substitutes, such as biodegradable temporizing matrix may be helpful in maintaining healthy tissue and decrease amputation rates.
- 3) Closing a wound with a skin graft may put patients at greater risk of systemic infection, some providers may restrict skin grafting to patients who have not been actively using illicit substances for a period of time (e.g., six weeks).

Areas for further investigation:

- 1) Understanding the role of amputation in the care of individuals with xylazine-associated wounds.
- 2) Developing clinical protocols for applying burn wound treatment strategies to xylazine-associated wounds.

Wound Care Supplies

Wound care providers use several supplies to promote healing by cleaning, treating, and protecting wounds. Wound care supplies range from over-the-counter dressings and ointments to prescription topical therapies for cleaning, decreasing bacterial burden, and supporting debridement. The selection of wound care supplies can depend on available resources, training, and individualized clinical decision making.² Table 1 below describes wound care supplies that are commonly used in the care of individuals with xylazine-associated wounds.

Table 1: Supplies for xylazine-associated wounds

Supply	Description/Note	Pro/Con	Prescription Required?
CLEANSING (supplies used to clean wound bed, periwound, and surrounding skin)			
Woven gauze	4x4 cotton surgical sponge	Textured gauze that cleans more effectively / Should not be used as a contact dressing because can stick to wound bed and cause trauma with removal	No
Potable tap water	Well tolerated cleanser	Readily available to housed patients / Not always available to unhoused patients	No
Normal saline	Fluid solution that is 0.9% sodium chloride	Readily available and well tolerated	No
Wound cleanser (e.g., Skintegrit [™])	Rinsing solutions	Somewhat reduces bioburden, nontoxic to human cells / May sting	No

Vashe™	Nontoxic to human cells	Reduces bioburden and odor / Expensive	No
Quarter strength Dakins Solution™ (0.125%)	Diluted sodium hypochlorite (e.g., bleach)	Reduces bioburden and odor/ May sting, limited toxicity to human cells, do not mix with ammonia	No
DRESSING			
Contact Dressings (primary dressings placed directly on the wound bed)			
Oil emulsion (e.g., Adaptic™)	Nonocclusive (allows drainage to pass through to an absorbent dressing), nonadherent fabric mesh in oil	Limited sticking to wound bed and allows drainage to pass through to absorbent layer	No
Nonadherent pads (e.g., Telfa™)	Nonwoven cotton/polyester with nonstick layer (contact and/or absorbent)	Limited sticking to wound bed, absorbs light drainage, and is inexpensive	No
Occlusive Petrolatum (e.g., Xeroform™)	Occlusive (not permeable by air and liquid) fine-woven fabric in petrolatum and bismuth	Limited sticking to wound bed, some antimicrobial properties, and promotes autolytic debridement / Caution with maceration, and don't use with iodine allergy	No
Alginate, carboxymethylcellulose (CMC) absorptive dressing	Turn from dry to gel—use only with heavy drainage	Absorbs heavy drainage, promotes autolytic debridement, and has antimicrobial properties when imbued with silver / Expensive	No
Absorbent Dressings (secondary dressings placed on top of the contact layer to soak up wound exudate and provide protection to the wound)			
Foam	Bordered or non-bordered (contact and/or absorbent)	Gentle, limited sticking to wound bed; absorbs light to heavy drainage; cushions from pressure or shear force (e.g. feet)	No
Abd pad	Gauze pads with an absorbent layer Recommend to use with contact layer dressing	Absorbs moderate to heavy drainage, provides cushioning and is inexpensive	No
Super absorb pad	Gauze pads with a layer of superabsorbent polymer	Locks in heavy drainage away from the wound / Can be bulky and is expensive	No
Supportive Dressings			

(keep the contact and supportive dressings in place, augment durability, and protect the wound from the external environment and prevent wound drainage from reaching clothing)			
Rolled gauze	Elastic or Kerlix	Breathable	No
Self-adhesive wrap (e.g., COBAN™)	Self-adhering	Protects bandage from environment, and clothes from drainage and can seal in moisture / use with caution as can cause a tourniquet effect with tight wrapping	No
Elastic bandage	Ace wrap	Protective, somewhat breathable and can be easily adjusted and reused	No
Retention netting (e.g., Tubigrip™)	Cloth sleeve	Most breathable and can unwrap then rewrap	No
PERIWOUND BARRIERS			
(ointment and film agents used to protect the periwound area from drainage that can cause maceration)			
<i>Maceration = skin softened by persistent exposure to fluids (e.g., wound drainage)</i>			
A&D	Petrolatum + vitamins A&D	Donates some moisture as it protects, vitamins for tissue repair, and is inexpensive	No
Dimethicone	Primarily dimethicone often with other ingredients	Donates less moisture	No
Zinc (e.g., Triad™)	Primarily zinc often with other ingredients	Zinc improves tissue repair and is somewhat antimicrobial / Donates minimal moisture	No
No sting skin prep (e.g., Cavilon™)	Film barrier (some skin prep does not protect against drainage)	Good drainage protection, and increases adhesion for border dressings and band-aids / Donates minimal moisture	No
TOPICALS			
(agents, such as ointments and gels, used directly on the wound bed and surrounding skin to promote healing and prevent infection)			
Petrolatum based ointment (e.g., A&D, Vaseline™, Aquaphor™)	Not antimicrobial but helps prevent bacterial colonization	Keeps wound moist, somewhat promotes autolytic debridement and is inexpensive	No
Medihoney™	leptospermum Manuka medical-grade honey, antimicrobial	Promotes moisture, generally antimicrobial (acidic – low pH), anti-inflammatory, nontoxic to human cells, promotes debridement / expensive, caution when applying in hotter months as many unsheltered patients are often bothered by flies and maggots.	No
Polyhexamethylene biguanide (PHMB)	Antimicrobial, in petrolatum or hydrogel base, or	Broad spectrum antimicrobial (incl. against <i>Methicillin-resistant Staphylococcus aureus</i> [MRSA],	No

	imbued into dressings	<i>Vancomycin-resistant Enterococcus</i> , <i>E. coli</i> , <i>Pseudomonas</i>); nontoxic to human cells, base determines if helps with debridement (hydrogel > petrolatum), and stays active for several days / expensive	
Silver hydrogel (e.g., Silvasorb™)	Antimicrobial	Broad spectrum antimicrobial (incl. against MRSA, <i>E. coli</i> , <i>Pseudomonas</i>), gel base aids debridement, stays active and noncytotoxic for several days / expensive, don't use with collagenase	No
Silver sulfadiazine (Silvadene™)	Antimicrobial used in burn wounds to prevent infection	Broad spectrum antimicrobial (incl. against MRSA, <i>E. coli</i> , <i>Pseudomonas</i>), nontoxic to human cells, petrolatum base can aid debridement, stays active for several days / Should not be used with collagenase or on patients who have a sulfa allergy	Yes
Mupirocin	Antibiotic in petrolatum	Antimicrobial (including against MRSA, <i>Streptococcus</i>)	Yes
Collagenase (Santyl™)	Enzymatic debriding agent	Breaks down dead tissue, doesn't harm healthy tissue / Requires daily dressing changes, has short duration of activity, very expensive, and inactive at low pH (e.g., acidic) that can be caused by other products (e.g., medihoney)	Yes

Training and Resources for Providing Wound Care

Clinicians and non-clinicians who provide care to individuals with xylazine-associated wounds have various backgrounds in wound care. Xylazine-associated wound care needs have been reported to be barriers to admission to substance use treatment programs, which may be due to limitations in the scope of practice and lack of capacity and training for providing wound care in behavioral health settings. Training clinicians across physical and behavioral health settings on best practices for the care of individuals with xylazine-associated wounds may decrease barriers to receiving healthcare, including substance use disorder treatment. In addition, providing training on basic wound care to non-clinicians working in community-based settings that regularly engage with individuals with xylazine-associated wounds, such as harm reduction organizations, can increase access to wound care and establish pathways to substance use treatment. Lastly, increasing the availability of community-based wound care can expand access to site for individuals with xylazine-associated wounds to follow-up after receiving hospital-based or specialty care.

Recommendations:

- 1) Increase access to training on best practices for the care of xylazine-associated wounds for clinicians in substance use treatment programs, hospital and emergency room settings, and community-based clinics.

- 2) Increase access to training on providing basic care of xylazine-associated wounds for non-clinically trained professionals.
- 3) Patients receiving wound care in a hospital-based or specialty clinic setting may receive follow-up care at other community sites.

Communication Between Providers

Individuals with xylazine-associated wounds receive care in a variety of settings including street-based, mobile unit, outpatient, emergency department, substance use treatment and inpatient settings. As individuals with xylazine-associated wounds transition between care settings, limited communication between providers contributes to poor continuity of care. Many individuals with xylazine-associated wounds avoid medical settings due to experiences of stigma, withheld care, discrimination, and concerns that their opioid dependency and pain will be undertreated.^{15,54–57} As a result, community providers caring for individuals with xylazine-associated wounds have developed informal approaches to communicate with hospital-based clinicians and peers recovery specialists to provide a clinical hand-off when referring individuals to the emergency department.

Community-based organizations meet the needs of individuals with xylazine-associated wounds who intentionally avoid medical settings by providing basic wound care and wound care supplies. However, community-based organizations may not have clinically trained staff. Lack of communication between community-based organizations without clinically trained staff and clinically trained providers can lead to delays in referring to higher levels of care. Another informal strategy that has been developed to address this need is for providers with the appropriate clinical training to provide telehealth consults to non-clinicians and non-prescribers. Formalizing and strengthening communication between providers requires developing a general wound care consent, compliant with the Health Insurance Portability and Accountability Act, that allows for information sharing. Overall, implementing a formalized infrastructure for referral and communication between community organizations and higher levels of care would improve patient outcomes.

Recommendations:

- 1) Strengthen Health Insurance Portability and Accountability Act (HIPAA) compliant communication between hospitals and community-based wound care providers, as well as between different community-based providers, to improve continuity of care.
- 2) Professionals without clinical training should have a strong functional referral relationship with clinical providers who can provide a higher level of care.
- 3) Establish processes for clinically trained prescribing providers to offer guidance and/or telehealth consults for non-clinicians and/or non-prescribing clinicians providing wound care.

Misinformation and Stigma

Stigma towards individuals with substance use disorder, whether actively using or in recovery, leads to discriminatory treatment. Discriminatory treatment causes people to delay or eschew care, which can lead to loss of life and limb.^{15,54,56} Individuals with xylazine-associated wounds may experience increased stigma due to the severe appearance or associated malodor of their

wounds.² Stigma is a fundamental cause of health inequity that must be eliminated to provide effective care for individuals with xylazine-associated wounds.⁵⁸ Thoughtful, concrete strategies to educate staff and providers in stigma elimination and trauma-informed care provision is a critical component of improving wound care for people with xylazine-associated wounds.

Stigma reduction education might include the importance of recognizing stigma and trauma experienced by patients in healthcare settings, the prevalence of xylazine in the local illicit opioid supply, the signs and symptoms of xylazine intoxication, as well as facts about xylazine-associated wounds such as: (1) xylazine-associated wounds are not communicable, (2) xylazine-associated wounds can appear anywhere on people who have ingested xylazine irrespective of method of administration or site of injection, (3) not everyone with a xylazine-associated wound will lose a limb, and (4) not all xylazine-associated wounds require antibiotic or surgical intervention; some wounds are best treated with basic wound care. Decreasing stigma in and around medical encounters can increase access to care and promote engagement in care.^{54,59} Positive, non-stigmatizing health care encounters are evidence-based interventions for improving care engagement among for people who use substances who have wounds or skin and soft tissue infections.¹⁵ Encounters for wound care and dressing changes are excellent opportunities to provide such an intervention. Strategies may include emphasizing a patient's autonomy and comfort during any wound care.² These strategies include:

- Asking what dressings have worked for them in the past
- Having a patient remove their dressings themselves
- Offering time-outs or breathers during dressing changes
- Administering pain medication for dressing changes (See pain management section above)
- Minimizing pain and tissue trauma during dressing changes by soaking dry, stuck dressings with water or normal saline solution.

Recommendations:

- 1) Providers should use a non-judgmental, trauma-informed approach to providing wound care.
- 2) Wound care providers should receive stigma reduction training.
- 3) Providers without clinical training should refer to public health and clinical guidance to provide patients with information about how to care for wounds.

Billing and Coding for Wound Care

The public health, community, and clinical response to providing wound care for individuals with xylazine-associated wounds has not been consistently reimbursed by health insurance. The Centers for Medicare & Medicare Services (CMS) recently created a place of service code for services delivered in a non-permanent location on the street. Effective October 1, 2023, the [Pennsylvania Department of Human Services](#) expanded the provider types eligible to practice and bill for street medicine in Medicaid to include federally qualified health centers, peer support services, substances use disorder services, and mid-level providers. The ability for providers to be reimbursed for street based medical services can serve as a reliable source of funding to expand and sustain care for individuals with xylazine-associated wounds.

CMS also provides three resources for guidance to cover wound care services that can be applied to care for xylazine associated wounds. CMS’s “Local Coverage Determination: Wound Care” ([LCD ID L37228](#)) provides definitions for selective and non-selective debridement procedures and documentation that may be applied to wound care for xylazine-associated wounds. CMS’s “Billing and Coding: Wound Care and Debridement – Provided by a Therapist, Physician, NPP or as Incident to Services” ([Article ID A53046](#)) describes Current Procedural Terminology (CPT) codes for physical therapy evaluation of wounds and sharp selective debridement procedures. Lastly CMS’s “Billing and Coding: Wound Care” ([Article ID A55909](#)) provides the most comprehensive set of CPT codes for wound care billing, as well as international classification of disease (ICD) codes that support medical necessity. CPT codes 97597, 97598, 97602, 97605-97608 can be used to bill for active wound care management, and CPT codes 11000, 11001, 11004-11006, and 11042-11047 can be used to bill for surgical debridement. However, there is no ICD code specific for xylazine-associated wounds. Of note, CMS does not reimburse separately for dressing changes or topical applications, such as medications, ointments and dressings, which are included in the payment for procedure codes.

In some cases, providers have used CPT codes based on time to bill for wound care provided by nursing staff during an office visit, such as patient office visit codes (99212-99215): 99212 for 10-19 minutes; 99213 for 20-29 minutes; 99214 for 30-39 minutes; 99215 for 40-54 minutes.

Recommendations:

- 1) To be able to bill for RN services, providers may bill for time of visits and utilize RN staff for hands on wound care with appropriate oversight.
- 2) Provide staff with training on billing for wound care services.

Areas for future investigation:

- 1) Identifying appropriate ICD coding practices for xylazine-associated wounds

Housing and Nutrition

Individuals with xylazine-associated wound may be more likely to have health-related social needs, such as nutrition and housing. Inadequate nutrition can impair wound healing.⁶⁰ In addition, unstable housing can lead to challenges for individuals with xylazine-associated wounds to maintain their wound dressings and increase their risk of wound infection. Medical respite care for individuals with xylazine-associated wounds who are unhoused can lead to improved wound healing.²

Recommendations:

- 1) Protein- and mineral-rich food should be provided to individuals with xylazine-associated wounds who present for wound care.
- 2) Medical respite care for patients who are unhoused and have xylazine-associated wounds can improve wound care outcomes.

Patient Education

Individuals with xylazine-associated wounds can benefit from receiving education aimed at promoting wound healing and their overall wellbeing. Many people with xylazine-associated wounds who inject illicit substances may inject into their wounds. While injecting illicit substances directly into xylazine-associated wounds will not lead to improved wound healing, it is not clear that providing guidance to avoid injecting into xylazine-associated wounds will improve an individual's overall health. Recommending not injecting directly into wounds may lead to individuals injecting in locations that can cause serious complications such as developing new wound at their groin or neck. For individuals with xylazine-associated wounds who are actively injecting illicit substances, providers can help identify sites for injection that are not in the wound, review practices for safer injection, such as promoting venous access by applying warmth, and providing resources for accessing sterile injection supplies.

Individuals with xylazine-associated wounds may also access antibiotics without a prescription. Wound care providers may counsel patients to avoid antibiotics that are not prescribed to them, as this may lead to antibiotic resistance. In addition, wound care providers can offer individuals with xylazine-associated wounds wound care kits and provide education on best practices for dressing changes and how to prevent new wounds and infections. Wound care kits can include basic or individualized dressing change supplies (e.g. saline, petrolatum-based ointment, nonadherent gauze, gauze wrap, bandages); written/illustrated educational and follow-up information; products that aid in wound prevention (hand sanitizer, cleansing/bathing wipes, lotion/ointment, insect repellent, sunscreen, blister prevention, safer use supplies); products to help maximize successful venous access (tourniquets, hand warmers, water and/or electrolyte mix); protein bars, and socks.

Recommendations:

- 1) Wound care providers can educate patients on finding safer injection sites.
- 2) Wound care providers should counsel patients to avoid antibiotics that are not prescribed to them and support patients to complete regimens of antibiotics that are prescribed to them.
- 3) Wound care providers should educate patients on how to prevent new wounds and infections, and best practices for dressing changes.

Appendix: Contributing Authors

- Division of Substance Use Prevention and Harm Reduction, Philadelphia Department of Public Health
 - Daniel Teixeira da Silva, MD, MSHP, Medical Director
 - Rachel Neuschatz, RN, MSN, Harm Reduction Wound Care Field Nurse
 - Catherine Tomson, Urban Health Policy Fellow
- Substance Use Response, Guidance, and Education Program, Health Federation of Philadelphia
 - Catherine Abrams, Program Coordinator
 - Caroline Drob, Program Assistant
 - Jody Gilmore, ANP-BC, Consultant
- Select Clinician Review Committee
 - Kevin Banks PT, DPT, CWS, Physical Therapy Utilization Manager, Temple University Hospital
 - Raymond Bobb, DO, Medical Director, Merakey Parkside Recovery
 - Carrie Kovarik, MD, FAAD, Professor of Dermatology and Medicine, Perelman School of Medicine at the University of Pennsylvania
 - Rachel McFadden, MPH, BSN, RN, CEN, Wound Care Nurse; Prevention Point Philadelphia; Emergency Department Nurse, Hospital of the University of Pennsylvania; Penn Center for Addiction Medicine & Policy
 - Lisa Rae MD, MS, FACS, Chief of Burn Surgery, Medical Director, Temple Burn Center, Associate Professor of Surgery, Temple University Hospital
 - Sara K Schultz MD FACP FIDSA FCPP, Associate Professor of Medicine, Section of Infectious Diseases. Program Director, Infectious Diseases Fellowship, Lewis Katz School of Medicine at Temple University.
 - Monika Vansant, DO, Addiction Medicine Physician, Trinity Health Mid-Atlantic and Penn's Rock Primary Care
 - Lydia Williams, MSN, FNP-BC, CRNP, CWOCN, Family Nurse Practitioner, Project HOME

References:

1. D’Orazio J, Nelson L, Perrone J, Wightman R, Haroz R. Xylazine Adulteration of the Heroin–Fentanyl Drug Supply. *Ann Intern Med*. Published online October 10, 2023. doi:10.7326/M23-2001
2. McFadden R, Wallace-Keeshen S, Petrillo Straub K, et al. Xylazine-associated Wounds: Clinical Experience From a Low-barrier Wound Care Clinic in Philadelphia. *J Addict Med*. Published online November 29, 2023. doi:10.1097/ADM.0000000000001245
3. Center for Drug Evaluation and Research, U.S. Food and Drug Administration. FDA alerts health care professionals of risks to patients exposed to xylazine in illicit drugs. Published online November 8, 2022. Accessed December 21, 2023. <https://www.fda.gov/drugs/drug-safety-and-availability/fda-alerts-health-care-professionals-risks-patients-exposed-xylazine-illicit-drugs>
4. 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. doi:10.1016/j.forsciint.2014.03.015
5. Greene SA, Thurmon JC. Xylazine--a review of its pharmacology and use in veterinary medicine. *J Vet Pharmacol Ther*. 1988;11(4):295-313. doi:10.1111/j.1365-2885.1988.tb00189.x
6. Johnson J, Pizzicato L, Johnson C, Viner K. Increasing presence of xylazine in heroin and/or fentanyl deaths, Philadelphia, Pennsylvania, 2010-2019. *Inj Prev J Int Soc Child Adolesc Inj Prev*. 2021;27(4):395-398. doi:10.1136/injuryprev-2020-043968
7. Philadelphia Department of Public Health. Health Update: Xylazine (tranq) exposure among people who use substances in Philadelphia. *Phila Dep Public Health Health Alert Netw*. Published online December 8, 2022. https://hip.phila.gov/document/3154/PDPH-HAN_Update_13_Xylazine_12.08.2022.pdf/
8. 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. doi:10.1016/j.drugalcdep.2022.109380
9. Spadaro A, Connor KO, Lakamana S, et al. Self-reported Xylazine Experiences: A Mixed Methods Study of Reddit Subscribers. *MedRxiv Prepr Serv Health Sci*. Published online March 14, 2023:2023.03.13.23287215. doi:10.1101/2023.03.13.23287215
10. Wei J, Wachuku C, Berk-Krauss J, Steele KT, Rosenbach M, Messenger E. Severe cutaneous ulcerations secondary to xylazine (tranq): A case series. *JAAD Case Rep*. 2023;36:89-91. doi:<https://doi.org/10.1016/j.jdc.2023.04.016>
11. Malayala SV, Papudesi BN, Bobb R, Wimbush A. Xylazine-Induced Skin Ulcers in a Person Who Injects Drugs in Philadelphia, Pennsylvania, USA. *Cureus*. 2022;14(8). doi:10.7759/cureus.28160
12. Wallace L. A Case Of Skin Necrosis Caused By Intravenous Xylazine Abuse. *J Hosp Med*. Accessed December 21, 2023. <https://shmabstracts.org/abstract/a-case-of-skin-necrosis-caused-by-intravenous-xylazine-abuse/>
13. Ehrman-Dupre R, Kaigh C, Salzman M, Haroz R, Peterson LK, Schmidt R. Management of Xylazine Withdrawal in a Hospitalized Patient: A Case Report. *J Addict Med*. 2022;16(5):595-598.

14. Ahuja K, DeSena G. Xylazine: An Ulcerating Addiction. *SKIN J Cutan Med*. 2023;7(4):958-959. doi:10.25251/skin.7.4.24
15. Allaw F, Zakhour J, Kanj SS. Community-acquired skin and soft-tissue infections in people who inject drugs. *Curr Opin Infect Dis*. 2023;36(2):67-73. doi:10.1097/QCO.0000000000000902
16. Rose L, Kirven R, Tyler K, Chung C, Korman A. Xylazine-induced acute skin necrosis in two patients who inject fentanyl. *JAAD Case Rep*. 2023;36:113-115.
17. Zagorski CM, Hosey RA, Moraff C, et al. Reducing the harms of xylazine: clinical approaches, research deficits, and public health context. *Harm Reduct J*. 2023;20(1):141. doi:10.1186/s12954-023-00879-7
18. 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. doi:10.1016/j.jaad.2023.04.009
19. O'Malley PA. Rising Xylazine Drug Abuse in Humans: A Deep and Lingering High with Wounds, Amputations, and Death. *Clin Nurse Spec*. Published online August 2023:164-165. doi:10.1097/NUR.0000000000000758
20. Rodríguez N, Vidot JV, Panelli J, Colón H, Ritchie B, Yamamura Y. GC-MS confirmation of Xylazine (Rompun), a veterinary sedative, in exchanged needles. *Drug Alcohol Depend*. 2008;96(3):290-293. doi:10.1016/j.drugalcdep.2008.03.005
21. 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). <https://doi.org/10.58616/surgicoll.00002>
22. Warp PV, Hauschild M, Tookes HE, Ciraldo K, Serota DP, Cruz I. A Confirmed Case of Xylazine-Induced Skin Ulcers in a Person Who Injects Drugs in Miami, Florida, USA. *Res Sq*. Published online July 26, 2023. <https://doi.org/10.21203/rs.3.rs-3194876/v1>
23. Downton 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;00(00):1-3. doi:10.1097/ADM.0000000000001198
24. O'Neil J, Kovach S. Xylazine-Associated Skin Injury. *N Engl J Med*. 2023;388(24):2274. doi:10.1056/NEJMicm2303601
25. Soderquist M, Delgado G, Abdelfattah H, Thoder J, Solarz M. Necrotic Upper-Extremity Infections in People Who Inject Drugs: A Case Series. *J Hand Surg*. Published online May 12, 2023. doi:10.1016/j.jhsa.2023.04.001
26. Shang M, Jawa R. Illustration of Spectrum of Xylazine Wounds. Published 2023. Accessed October 13, 2023. <http://d-scholarship.pitt.edu/45422/>
27. Manna B, Nahirniak P, Morrison CA. Wound Debridement. In: *StatPearls*. StatPearls Publishing; 2023. Accessed September 21, 2023. <http://www.ncbi.nlm.nih.gov/books/NBK507882/>
28. Ramundo J, Gray M. Enzymatic wound debridement. *J Wound Ostomy Cont Nurs Off Publ Wound Ostomy Cont Nurses Soc*. 2008;35(3):273-280. doi:10.1097/01.WON.0000319125.21854.78

29. Bryant R, Nix D. *Acute and Chronic Wounds: Current Management Concepts*. 5th ed. Elsevier; 2015. Accessed November 7, 2023. <https://shop.elsevier.com/books/acute-and-chronic-wounds/bryant/978-0-323-31621-7>
30. Harris C, Coutts P, Raizman R, Grady N. Sharp wound debridement: patient selection and perspectives. *Chronic Wound Care Manag Res*. 2018;Volume 5:29-36. doi:10.2147/CWCMR.S146747
31. Rodd-Nielsen E, Harris CL. Conservative Sharp Wound Debridement: An Overview of Canadian Education, Practice, Risk, and Policy. *J Wound Ostomy Continence Nurs*. 2013;40(6):594. doi:10.1097/WON.0b013e3182a9ae8c
32. Higgins C, Smith BH, Matthews K. Evidence of opioid-induced hyperalgesia in clinical populations after chronic opioid exposure: a systematic review and meta-analysis. *Br J Anaesth*. 2019;122(6):e114-e126. doi:10.1016/j.bja.2018.09.019
33. Bowler PG, Duerden BI, Armstrong DG. Wound microbiology and associated approaches to wound management. *Clin Microbiol Rev*. 2001;14(2):244-269. doi:10.1128/CMR.14.2.244-269.2001
34. Lipsky BA, Berendt AR, Cornia PB, et al. 2012 infectious diseases society of america clinical practice guideline for the diagnosis and treatment of diabetic foot infections. *J Am Podiatr Med Assoc*. 2013;103(1):2-7. doi:10.7547/1030002
35. Spichler A, Hurwitz BL, Armstrong DG, Lipsky BA. Microbiology of diabetic foot infections: from Louis Pasteur to “crime scene investigation.” *BMC Med*. 2015;13:2. doi:10.1186/s12916-014-0232-0
36. Sadeghpour Heravi F, Zakrzewski M, Vickery K, G Armstrong D, Hu H. Bacterial Diversity of Diabetic Foot Ulcers: Current Status and Future Prospectives. *J Clin Med*. 2019;8(11):1935. doi:10.3390/jcm8111935
37. Ti L, Ti L. Leaving the Hospital Against Medical Advice Among People Who Use Illicit Drugs: A Systematic Review. *Am J Public Health*. 2015;105(12):e53-59. doi:10.2105/AJPH.2015.302885
38. Bryson-Cahn C, Beieler A, Chan J, Senter S, Harrington R, Dhanireddy S. A Little Bit of Dalba Goes a Long Way: Dalbavancin Use in a Vulnerable Patient Population. *Open Forum Infect Dis*. 2017;4(suppl_1):S336-S337. doi:10.1093/ofid/ofx163.800
39. Oliva A, Carbonara S, Cianci V, et al. Direct or early Discharge of Acute Bacterial Skin and Skin Structure Infection patients from the Emergency Department/Unit: place in therapy of dalbavancin. *Expert Rev Anti Infect Ther*. 2023;21(7):703-721. doi:10.1080/14787210.2023.2214727
40. Soriano A, Rossolini GM, Pea F. The role of dalbavancin in the treatment of acute bacterial skin and skin structure infections (ABSSSIs). *Expert Rev Anti Infect Ther*. 2020;18(5):415-422. doi:10.1080/14787210.2020.1746643
41. Menezes de Pádua CA, Schnuch A, Lessmann H, Geier J, Pfahlberg A, Uter W. Contact allergy to neomycin sulfate: results of a multifactorial analysis. *Pharmacoepidemiol Drug Saf*. 2005;14(10):725-733. doi:10.1002/pds.1117

42. Nímia HH, Carvalho VF, Isaac C, Souza FÁ, Gemperli R, Paggiaro AO. Comparative study of Silver Sulfadiazine with other materials for healing and infection prevention in burns: A systematic review and meta-analysis. *Burns J Int Soc Burn Inj*. 2019;45(2):282-292. doi:10.1016/j.burns.2018.05.014
43. Mohamed DS, Abd El-Baky RM, Sandle T, Mandour SA, Ahmed EF. Antimicrobial Activity of Silver-Treated Bacteria against other Multi-Drug Resistant Pathogens in Their Environment. *Antibiot Basel Switz*. 2020;9(4):181. doi:10.3390/antibiotics9040181
44. Melaiye A, Youngs WJ. Silver and its application as an antimicrobial agent. *Expert Opin Ther Pat*. 2005;15(2):125-130. doi:10.1517/13543776.15.2.125
45. Fuller FW. The side effects of silver sulfadiazine. *J Burn Care Res Off Publ Am Burn Assoc*. 2009;30(3):464-470. doi:10.1097/BCR.0b013e3181a28c9b
46. Manhapa A, Arias AJ, Ballantyne JC. The conundrum of opioid tapering in long-term opioid therapy for chronic pain: A commentary. *Subst Abuse*. 2018;39(2):152-161. doi:10.1080/08897077.2017.1381663
47. Gupta R, Holtgrave DR, Ashburn MA. Xylazine — Medical and Public Health Imperatives. *N Engl J Med*. 2023;388(24):2209-2212. doi:10.1056/NEJMp2303120
48. Harvey LH, Green TC, Park JN, Rich JD. Xylazine in the drug supply: A research agenda. *Int J Drug Policy*. 2023;120:104190. doi:10.1016/j.drugpo.2023.104190
49. Gomberg S. Partnerships to manage complications of xylazine use and linkage to treatment. Presented at: Emerging Drug Trends Symposium; November 9, 2023; Harrisburg, PA.
50. Thakrar AP, Uritsky TJ, Christopher C, et al. Safety and preliminary outcomes of short-acting opioid agonist treatment (sOAT) for hospitalized patients with opioid use disorder. *Addict Sci Clin Pract*. 2023;18(1):13. doi:10.1186/s13722-023-00368-z
51. Santos CJ, Shofer FS, Lowenstein M, Perrone J. Discharges “Against Medical Advice” in Patients With Opioid-related Hospitalizations. *J Addict Med*. 2021;15(1):49. doi:10.1097/ADM.0000000000000688
52. Braun HM, Potee RA. Individualizing methadone treatment with split dosing: An underutilized tool. *J Subst Use Addict Treat*. 2023;152:209096. doi:10.1016/j.josat.2023.209096
53. Gonzalez SR, Wolter KG, Yuen JC. Infectious Complications Associated with the Use of Integra: A Systematic Review of the Literature. *Plast Reconstr Surg Glob Open*. 2020;8(7):e2869. doi:10.1097/GOX.00000000000002869
54. Monteiro J, Phillips KT, Herman DS, et al. Self-treatment of skin infections by people who inject drugs. *Drug Alcohol Depend*. 2020;206:107695. doi:10.1016/j.drugalcdep.2019.107695
55. Gilbert AR, Hellman JL, Wilkes MS, Rees VW, Summers PJ. Self-care habits among people who inject drugs with skin and soft tissue infections: a qualitative analysis. *Harm Reduct J*. 2019;16(1):69. doi:10.1186/s12954-019-0345-z

56. French R, McFadden R, Stewart R, Christian H, Compton P. “I Just Need Proper Treatment”: Being Hospitalized for Endocarditis among Individuals Who Inject Drugs Being Hospitalized for Endocarditis. *J Gen Intern Med.* 2023;38(11):2470-2477. doi:10.1007/s11606-023-08133-3
57. Summers PJ, Hellman JL, MacLean MR, Rees VW, Wilkes MS. Negative experiences of pain and withdrawal create barriers to abscess care for people who inject heroin. A mixed methods analysis. *Drug Alcohol Depend.* 2018;190:200-208. doi:10.1016/j.drugalcdep.2018.06.010
58. Hatzenbuehler ML, Phelan JC, Link BG. Stigma as a fundamental cause of population health inequalities. *Am J Public Health.* 2013;103(5):813-821. doi:10.2105/AJPH.2012.301069
59. Harris RE, Richardson J, Frasso R, Anderson ED. Experiences with skin and soft tissue infections among people who inject drugs in Philadelphia: A qualitative study. *Drug Alcohol Depend.* 2018;187:8-12. doi:10.1016/j.drugalcdep.2018.01.029
60. Grada A, Phillips TJ. Nutrition and cutaneous wound healing. *Clin Dermatol.* 2022;40(2):103-113. doi:10.1016/j.clindermatol.2021.10.002