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ENHANCING WOUND HEALING THROUGH PLACENTAL TISSUE-BASED WOUND CARE AMONG INDIVIDUALS WITH XYLAZINE-ASSOCIATED WOUNDS

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Abstract: *Xylazine-adulterated opioids have created complex, treatment-resistant wounds among individuals with opioid use disorder (OUD), posing challenges that traditional wound care inadequately addresses. This study examines placenta-derived biomaterials as a therapeutic intervention for opioid-related chronic wounds, focusing on xylazine-induced tissue damage. A multidisciplinary analysis evaluated the scientific rationale, social implications, financial considerations, and medical applications of placental therapies for opioid-related wound care by synthesizing clinical studies and cost-effectiveness research. Placental tissues contain growth factors, anti-inflammatory cytokines, antimicrobial peptides, and extracellular matrix components that address the pathophysiology of xylazine-induced injuries. Dehydrated human amniotic/chorion membranes achieve 77-92% healing rates within 4-6 weeks, compared with negligible improvement with standard care. A cost analysis shows healing costs of $1,771 per wound with placental therapies, up to $8,800 with conventional treatments. Implementation barriers include inconsistent insurance coverage, social stigma, and limited provider education. Given the vulnerability of people who use drugs (PWUD), the ethical dimensions of informed consent, stigma reduction, and equitable implementation remain central to the adoption of placental therapies. Placental-derived biomaterials offer a cost-effective solution for chronic wounds in OUD. However, successful implementation requires policy interventions including expanded coverage, integration with harm-reduction programs, and enhanced provider training, to ensure equitable access.*

Keywords: *Placenta, Opioid Use Disorder, Xylazine, Chronic Wounds, and Tissue Regeneration.*

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INTRODUCTION

Xylazine, a vasoconstrictive veterinary sedative that has been extensively used as an adulterant in the opioid supply, has created a formidable public health challenge, characterized by complex soft-tissue wounds and painful damage that can expose underlying structures, such as muscles or bones. The cause of these wounds results from a multifactorial pathophysiology involving profound local vasoconstriction, direct chemical toxicity, and systemic effects, which are exacerbated by the social marginalization of people who use drugs (PWUD) (Newman, 2025). The Philadelphia Treatment Algorithm (Ilyas et al., 2025) offers an essential guide for managing these injuries by classifying xylazine-associated wounds into three stages. Each stage corresponds to increasing severity and depth of tissue injury, and each has its own treatment pathway (medical, nonoperative, or surgical). This classification helps determine when and how to intervene surgically, what type of reconstruction is possible, and under which circumstances providers should clinically intervene (e.g., patient compliance, cessation of xylazine use, and preserved function). Stage 1 involves mild wounds, with skin violation only; no muscle is engaged, and function is maintained, as illustrated in Figure 1. Treatment involves nonoperative wound care, including hygiene, cleaning, moist dressings, and enzymatic chemical debridement. Stage 2 involves moderate wounds with minor muscle necrosis, but with preserved function, as illustrated in Figure 2. Early surgical involvement is needed, followed by subsequent gentle debridement; reconstructive measures may then be required. Stage 3 is divided into two categories: 3A, a severe wound with intact function (Figure 3), or 3B, a severe wound without preserved function (Figure 4). Both scenarios involve extensive tissue destruction, including muscle, tendon, and even bone exposure, as illustrated. For 3A, the objective is to perform aggressive reconstruction aimed at preserving function, performed only after the patient is stabilized and is more likely to comply with recovery and infection-control protocols. In Stage 3B, amputation may need to be considered on a case-by-case basis and typically involves clear documentation, informed consent, and prosthetic planning (Ilyas et al., 2025).

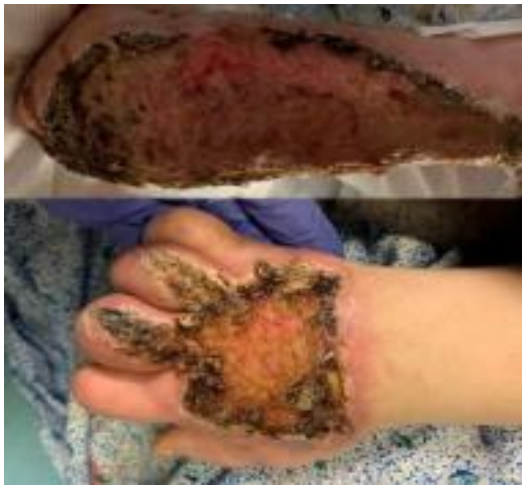

Figure 1: Stage 1 of xylazine-associated wounds (Ilyas et al., 2025).

Figure 2: Stage 2 of xylazine-associated wounds (Ilyas et al., 2025).

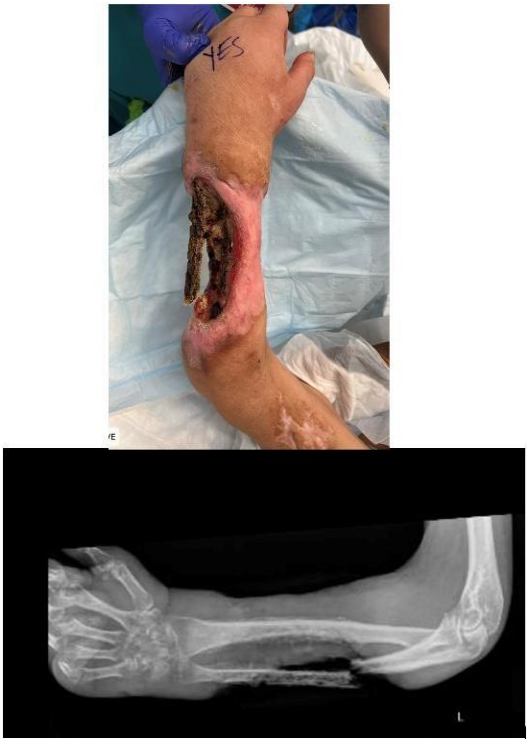

Figure 3: Stage 3A of xylazine-associated wounds (Ilyas et al., 2025).

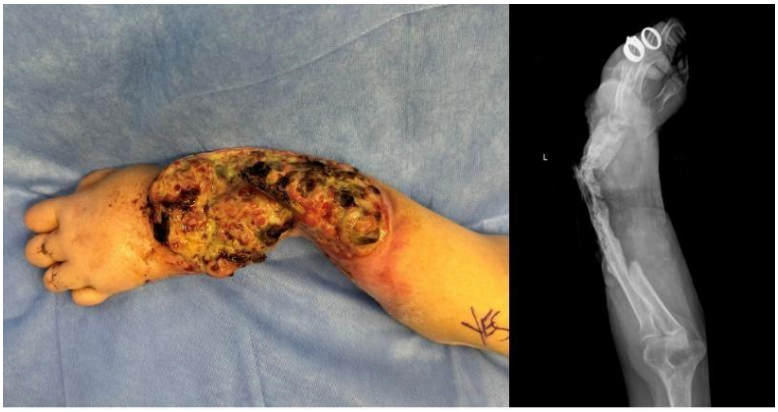

Figure 4: Stage 3B of xylazine-associated wounds (Ilyas et al., 2025).

Recent studies have highlighted the prevalence of these issues and the significant challenges they pose for care. As Jawa et al. (2024) reported in a survey of PWUD in Massachusetts, an overwhelming majority (87%) of participants with drug-related wounds were visually identified as consistent with xylazine exposure. The study further details profound treatment challenges, with 74% of those with xylazine wounds experiencing healthcare stigma and 58% receiving inadequate pain and withdrawal management when seeking medical care. Therefore, most patients resort to heterogeneous and even detrimental self-treatment practices, such as obtaining supplies primarily from syringe service programs rather than traditional healthcare settings. Even with optimal multidisciplinary support, healing of Stage 2 and 3 xylazine-associated wounds remains protracted and is associated with a high rate of complications and failure. The nature of these wounds creates a pathological wound bed that is notoriously hostile to standard reconstructive techniques, including skin grafts and local flaps, which often require a robust vascular supply for success (Ilyas et al., 2025). There is a need to investigate new regenerative therapies that can alter the wound environment, stimulate blood vessel growth, and facilitate healing, even in less-than-ideal circumstances.

Human placental membranes have emerged as a promising biologic scaffold in chronic wound care, owing to their rich composition of extracellular matrix, growth factors, cytokines, and stem cells, which confer potent immunomodulatory, anti-inflammatory, and pro-angiogenic effects. These characteristics make placental tissues a compelling therapeutic candidate for addressing the core pathophysiological driver of xylazine-induced tissue injury (Zhang et al., 2023). This paper aims to explore the scientific rationale for integrating placental tissue allografts into the multidisciplinary management algorithm for chronic wounds associated with xylazine exposure. In this discussion, the paper will examine the potential role of the placenta in overcoming the impediments to healing posed by tissue ischemia and toxicity, ultimately improving functional outcomes in its vulnerable patient population.

SCIENTIFIC BACKGROUND

The placenta is the lifeline between the fetus and the mother during pregnancy. This unique organ provides the developing fetus with nutrients and oxygen, along with many growth factors and immunological barriers necessary for a successful full-term pregnancy. These functions make the placenta rich in nutrients, proteins, and cells required for fetal repair and development.

Physiology of Wound Healing

Angiogenesis is the body's natural process of forming blood vessels throughout the cardiovascular system and is essential for repairing damaged tissue in the deep layers of the skin. The dermis requires access to these blood vessels for oxygen, vital nutrients, and immunologic molecules, as well as for the removal of waste products from wounds, thereby promoting the regrowth of healthy tissue. Illicit drugs are being mixed with xylazine, a tranquilizer, pain reliever, and central nervous system depressant approved by the FDA for veterinary medicine (NIDA, 2022). The rising prevalence of xylazine in drugs is causing sores and wounds to form due to decreased perfusion at

injection sites (Malayala et al., 2022). With xylazine, the scars can extend deep into the dermis and cause hypoperfusion in the affected area. This causes inflammation, which is necessary for clearing damaged tissue and bacteria, but if prolonged, it can damage tissues and delay healing, thus increasing scar formation. When the skin is damaged and blood vessels fail to deliver sufficient oxygen to tissues, the hypoxia-inducible factor (HIF) is activated. The hypoxia-induced HIF-α protein binds HIF-β to form a transcriptional complex (Hong et al., 2014). This complex binds to cellular DNA, triggering genes that adjust cellular functions in response to hypoxic conditions. One gene activated by HIF promotes angiogenesis (Hong et al., 2014). During fetal development, angiogenesis is crucial for establishing a mature vascular network and for forming endothelial cells in the skin. Vascular endothelial growth factor (VEGF) is present throughout development, whereas HIF levels decline as pregnancy progresses (Chen & Zheng, 2014).

HIF and VEGF continue to support vascular repair and growth in adults as needed. VEGF expression is induced in cells by low oxygen via HIF (Apte et al., 2019). VEGF-A activates both VEGFR-1 and VEGFR-2, promoting angiogenesis and endothelial cell proliferation. VEGFR-1's precise role remains under investigation, though it is known to contribute to angiogenesis. VEGFR-2 activates the PLCγ-PKC-MAPK pathway, which triggers DNA synthesis and cell division (Wong & Jin, 2005). VEGF-D binds to VEGFR-3 and is present in lymphatic endothelial cells, promoting lymphangiogenesis and lymphatic vessel formation. VEGF is vital for wound repair and can be supplemented with placental components, which contain high concentrations of fetal endothelial proteins required for vascular and lymphatic cell development.

Cytokines are signaling molecules — primarily proteins — that regulate inflammation by activating immune cells in response to infection. When wounds form, the first phase of healing, hemostasis, begins with platelet activation. Platelets aggregate and, when exposed to collagen fibers, trigger clotting pathways (Wong et al., 2025). During hemostasis, cytokines such as TNF-α, interleukin (IL)-1, and IL-6 are released, prompting endothelial cells to secrete additional proinflammatory mediators that signal the next stage. The inflammatory phase begins with the recruitment of lymphocytes and the recognition of molecular patterns from damaged cells (Wong et al., 2025). Cytokines, including TGF-β and TNF-α, recruit neutrophils and macrophages to the injury site, where they phagocytose debris and pathogens and release reactive oxygen species to destroy them. The proliferation phase follows and involves re-epithelialization, angiogenesis, and granulation tissue formation (Wong et al., 2025). During proliferation and angiogenesis, growth factors such as VEGF are released to form new blood vessels. Growth factors stimulate fibroblasts to produce matrix metalloproteinases (MMPs) that degrade clots, promote cell migration, and create additional extracellular matrix (ECM) components. M2 macrophages release anti-inflammatory cytokines such as IL-4, IL-10, IL-13, and TGF-β to reduce reactive oxygen species production and neutrophil recruitment, thereby facilitating healing. Finally, the remodeling phase strengthens collagen fibers and organizes new tissue. During remodeling, ECM deposition is balanced with MMP activity to increase tensile strength, and this process is regulated by cytokines such as TGF-β, IL-4, IL-10, and IL-22.

During pregnancy, the placenta regulates inflammatory processes between maternal and fetal tissues by releasing pro- and anti-inflammatory mediators. In preeclamptic pregnancies, proinflammatory cytokines are elevated (Raghupathy, 2013). Placental trophoblasts, macrophages, and stromal cells produce these proinflammatory cytokines. Levels vary from the first trimester to term and are influenced by maternal factors. Most inflammatory cytokines (IL-2, IL-6, IL-8, and IL-17) peak in the first trimester, decline in the second trimester, and rise again later in pregnancy. Conversely, anti-inflammatory cytokines, such as IL-13, increase throughout gestation (Jarmund et al., 2021).

The extracellular matrix (ECM) is present throughout the body, provides structural support, facilitates cell communication, and participates in wound healing. It plays a crucial role in tissue homeostasis by regulating cellular differentiation and apoptosis. Additionally, it controls growth factors, receptors, hydration, and pH, and serves as a reservoir for growth factors, chemokines, and cytokines (Diller & Tabor, 2022).

Collagen is the most abundant protein in the skin, providing tensile strength and elasticity. Skin damage triggers the formation of scar tissue through physiological repair processes. In scar tissue, collagen fibers are thinner and straighter, reducing tensile strength (Diller & Tabor, 2022). This reduced strength and altered mechanobiology can lead to pathological fibrosis, compromising tissue function.

Proteoglycans promote cell adhesion to the ECM by binding proteins and growth factors, with major contributors including hyaluronan (hyaluronic acid), decorin, versican, and dermatopontin (Diller & Tabor, 2022). Proteoglycans bind water and cations, increasing tissue lubrication and supporting cell migration and communication. Versican aggregates with elastic fibers, influencing migration, while decorin regulates collagen

fibril organization (Diller & Tabor, 2022). Hyaluronic acid plays a key role in wound healing and hydration and also influences inflammation, collagen expression, and myofibroblast migration. Fibronectin, the second-most-abundant ECM protein, contains binding sites that facilitate cell movement and tissue organization. Dermatopontin improves skin elasticity and tensile strength and enhances collagen fiber formation (Diller & Tabor, 2022). Together, these proteins and proteoglycans repair damaged collagen fibers and promote cell migration, supporting healthy tissue growth.

Placental Healing Properties

Human placental extract has demonstrated healing properties. In recent years, placental tissues have been used for skin grafts, reconstructive surgery, and burn care because of their regenerative effects (Silini et al., 2015). These properties were not well understood until the twentieth century, when studies of placental hormones and endocrinology began. Research expanded on the role of the placenta in supporting maternal physiological adaptation during pregnancy (Napso et al., 2018), leading to advances in fertility treatments.

Placenta exhibits potent anti-inflammatory properties essential for fetal development and wound healing. It maintains a balance between pro- and anti-inflammatory cytokines, preventing immune rejection of the fetus while protecting against infection. The anti-inflammatory effect is often attributed to melatonin produced in the placenta, which inhibits the NLRP3 inflammasome, a key driver of chronic inflammation, and reduces oxidative stress by scavenging reactive oxygen species (ROS) (Joseph, 2024). In chronic wounds, such as those caused by xylazine-induced hypoxia or diabetes, persistent inflammation and ROS damage impair healing. Placental-derived therapies, including melatonin, help modulate immune responses and protect cells from oxidative injury. Studies have shown that placental extracts reduce inflammation by up to 49% in preclinical models, indicating their potential to accelerate wound closure and minimize scar formation (Suk TK et al., 2003). These anti-inflammatory effects can improve healing outcomes for many individuals with chronic wounds. Clinicians can thus address the underlying inflammatory dysregulation that impedes healing, offering an alternative to traditional treatments.

Placental tissues also possess antimicrobial properties that support fetal protection. Epithelial and immune cells within the human chorionic membrane (hCM) and the human amniotic membrane (hAM) secrete antimicrobial peptides (AMPs) into the human amniotic fluid (hAF), which provide antibacterial, antifungal, antiviral, and antiprotozoal protection, as well as immunomodulatory functions (Ramuta et al., 2021).

Human beta-defensins (HBD 1–3) are produced throughout the human amniochorion membrane (hACM) and released into hAF (King et al., 2007). These peptides inhibit microbial biosynthesis by modulating innate and adaptive immune responses, thereby reducing the risk of fetal infection. Human neutrophil peptides (HNP 1–3), members of the α-defensin family, are abundant during inflammatory phases of pregnancy and function similarly to HBDs while also regulating inflammation.

Secretory leukocyte protease inhibitor (SLPI) is present in hAF and hACM, particularly in trophoblasts and amniotic epithelial cells. Elafin has been identified in trophoblasts and the chorionic mesenchyme of the hCM, as well as in epithelial cells of the hAM. SLPI inhibits the activation of the transcription factor NFκB, which regulates immune gene expression and cytokine and chemokine production (King et al., 2007). Elafin and SLPI regulate inflammation and participate in wound healing and tissue remodeling (King et al., 2007). Cathelicidin, found exclusively in amniotic fluid, responds to intra-amniotic infection by activating multiple immune pathways (Tambor et al., 2013).

Placental-derived materials are effective for wound healing and scar reduction in multiple murine studies. Felor Biniazan et al. (2022) simulated ischemia-reperfusion injury in mice, similar to wounds caused by xylazine, and treated them with human amniotic epithelial cells (hAECs). Wound closure in the hAEC-treated group was significantly improved in two and three weeks compared with untreated mice. New tissue volume was considerably higher in weeks one through three with hAEC treatment, indicating enhanced regeneration. Serological results showed reduced neutrophils and increased fibroblasts and basal cells in the hAEC group, supporting ECM development, angiogenesis, and re-epithelialization. Western blot analysis showed reduced TGF-β1 and increased TGF-β3 at week two. Elevated TGF-β1 in late healing increases scarring, whereas increased TGF-β3 promotes scarless remodeling. This inverse pattern suggests therapeutic potential for minimizing scar tissue in ischemia-reperfusion injuries.

Placental tissues possess diverse therapeutic potential that is often overshadowed by other biological components (Pogozhykh et al., 2018). Placenta-derived products include cord blood cells, placental extracts, cord blood serum, isolated placental cells, amniotic and chorionic membranes, placental tissue fragments, and amniotic fluid. Each component contributes unique healing properties and is currently used in wound care. Dehydrated human

amniotic/chorion membranes (dHACM) are one example of a regenerative tool derived from the placenta. Isolated mesenchymal stromal cells (MSCs) from amniotic or chorionic tissues demonstrate anti-inflammatory and immunomodulatory effects and release growth factors that promote tissue regeneration. Together, placental components regulate the fetal immune system and regenerate damaged tissue, a critical capability sometimes overlooked in clinical practice. Despite these benefits, some healthcare providers discard placentas due to concerns about potential hazards (Baergen et al., 2013). However, these concerns are not supported by current evidence. Placental therapies may be especially beneficial for chronic wound care in individuals with opioid use disorder (OUD). MSCs help regulate immune responses that activate FoxP3, which suppresses excessive immune activation and chronic inflammation, thereby supporting tissue repair (Kim et al., 2018). The rich cellular composition of the placenta makes it a valuable resource for improving chronic wound treatment.

Placental Processing

Before preservation, donors and tissues must be screened. After obtaining informed consent, the placenta is delivered to a processing facility. The U.S. Food and Drug Administration (FDA) provides recommendations for tissue banks and hospitals. Donors must be free of relevant communicable diseases and of risks associated with allotransplantation, and must test negative or nonreactive for infectious markers (U.S. Food and Drug Administration, 2007). Diseases screened include: HIV types 1 and 2, HBV, HCV, human transmissible spongiform encephalopathy (TSE), Creutzfeldt-Jakob disease (CJD), Treponema pallidum (syphilis), human T-lymphotropic virus types I and II, Chlamydia trachomatis, and Neisseria gonorrhoeae. Additional screening for West Nile virus, sepsis, and vaccinia is recommended. Placentae must be tested using FDA-licensed assays performed according to the manufacturer's instructions. After meeting the guidelines, the placenta is preserved.

Standard preservation methods include lyophilization, dehydration, and cryopreservation, all of which aim to minimize ice-crystal formation, which can damage cells, organelles, and tissue structure. Cryoprotective agents (CPAs) such as glycerol, dimethyl sulfoxide (DMSO), and trehalose help limit this damage (Chen et al., 2023). Lyophilization involves freezing tissues to −80°C and using sublimation to remove water, with CPAs stabilizing proteins and enabling room-temperature storage. Dehydration uses air or heat to preserve structure and biochemical activity while preventing microbial growth (Protzman et al., 2023). It also allows room-temperature storage and enables terminal sterilization, thereby reducing disease transmission. Cryopreservation is the most widely used method. It begins by cooling the tissue with CPAs at 1°C/min to prevent cell damage, followed by freezing to −80°C and storage below −135°C to halt molecular activity (Baust & Corwin, 2011). When needed, tissues are rapidly thawed to reduce hypothermic injury, refreshed with CPAs, and stored again at −80°C.

Safety Regulation

Transplant establishments must register with the FDA and undergo routine inspections to ensure regulatory compliance. States may impose additional requirements. Laboratories must meet biosafety level 3 standards to test for listed diseases. Biosafety level 2 practices are required, including the use of biosafety cabinets for infectious agents, hands-free sinks and eyewash stations, directional airflow, and interlocking laboratory entry doors (U.S. Department of Health and Human Services, n.d.). Personnel must undergo a security risk assessment and training on the collection, processing, and storage of tissues, while adhering to OSHA laboratory standards. Maintaining a sterile laboratory environment and following federal infectious disease guidelines minimize the risk of disease transmission and donor-related complications.

MEDICAL ANALYSIS

The placenta has long been recognized for its therapeutic potential in wound healing. Ancient medical practices used placental tissue for its regenerative and antimicrobial properties, applying it as a natural dressing to treat burns, wounds, and ulcers (Silini, 2015). Placentophagia—the practice of ingesting the placenta and afterbirth—has been a maternal behavior for centuries, driven by hypothesized health benefits, including newborn weight gain, reduced postpartum depression, and increased breast milk production (Mota-Rojas, 2020). In 1593, the Compendium of Materia Medica by Chinese expert Li ShiZhen included a section devoted entirely ("zi he chi") to the medical use of the placenta. In the 20th century, the placenta was incorporated into healing ointments because of its high content of natural growth factors (Silini, 2015).

Early 20th-century physicians provided further evidence supporting these uses, particularly for severe burn injuries. John Staige Davis, a Johns Hopkins surgeon in 1910, used the amniotic sac lining for skin transplantation, with limited success. In 1913, Nicholas Sabella reported success applying intact amniotic membranes, covered with

dressings, to burned and ulcerated skin surfaces. 2 days later, upon removal of the dressings, they noted that the amniotic membrane had integrated with the patient's tissues. They reported a lack of infection (shielding from environmental contaminants), significant pain reduction, and an increased rate of re-epithelialization. These studies pioneered this field of interest, prompting many contemporary investigatory applications of placental-based medicine to augment wound healing (Silini, 2015).

Amniotic membrane grafts, harvested from the innermost layer of the placenta, have demonstrated success across multiple medical specialties. These grafts are rich in cytokines and growth factors that promote cellular proliferation and tissue regeneration. Additionally, the graft tissues produce anti-inflammatory cytokines that modulate the recipient's local inflammatory processes, thereby preventing tissue rejection.

Amniotic membrane transplants (AMT) have played an essential role in reconstructive eye surface surgery since 1995. Disorders of the cornea, such as corneal ulceration with persistent epithelial defect (following burns or trauma), are among the most common indications for AMT. If left untreated, corneal defects can lead to scar formation, permanently impairing vision. With AMT, an amniotic membrane is sutured to the corneal basement membrane, allowing nearby recipient epithelial cells to migrate onto the membrane and facilitating closure of the defect (Silini, 2015). Some techniques have success rates of 65% to 80% (Meller, 2011).

Neurosurgeons have also used amniotic membrane grafts in their specialty. Several neurosurgical procedures require a dural substitute to cover the exposed brain, most commonly following a craniectomy. Studies have shown that the use of amniotic membrane grafts was comparable to autologous dural substitutes in preventing postoperative complications, such as CSF leak, meningitis, hydrocephalus, and pseudomeningocele (Shah, 2022).

Most notably, human amniotic membranes have been successfully used in modern wound management. Amniotic membrane grafts can be applied as biological dressings to wounds. Epifix, a dehydrated amniotic membrane allograft, received FDA approval in 2022 for the treatment of diabetic foot ulcers (DFU), venous leg ulcers, and other chronic wounds (Silini, 2015).

Placental extracts represent a promising therapeutic option, rich in bioactive compounds such as epidermal growth factors, hyaluronic acid, and fibronectin—key molecules involved in angiogenesis, tissue repair, and the regulation of inflammation (Silini, 2015). These extracts are under investigation for a range of applications, including topical agents for wound healing and skincare products with potential anti-aging properties. They have also been researched as an injectable agent to slow the progression of osteoarthritis by preserving joint cartilage (Moghassemi, 2025).

Despite their therapeutic potential, placenta-derived therapies, including amniotic membrane grafts and placental extracts, face several limitations. Processing and storage present significant challenges, as cryopreservation and dehydration methods require strict standardization to maintain bioactivity and product consistency. Cost also remains a barrier, with some placental grafts priced at up to $3,000 per square centimeter, limiting accessibility. Ethical considerations further complicate their use, necessitating careful sourcing practices and clear donor consent protocols. Additionally, regulatory oversight imposes constraints, as the FDA classifies placental products as tissue products rather than medical devices or biologics, restricting the extent of processing and innovation (Food, 2001). These factors collectively highlight the need for ongoing research, standardized practices, and updated regulatory frameworks to fully realize the clinical potential of placenta-derived therapies (Moghassemi, 2025).

A meta-analysis conducted in 2017 analyzed data from 5 randomized controlled trials (311 patients) comparing amniotic products with the standard of care for the healing of DFU. As of 2025, in the United States, diabetes has a prevalence of over 9.3%, and approximately 25% of diabetics will develop a DFU during their lifetime. DFU are notoriously difficult to treat, owing to impaired wound-healing processes and a higher risk of infection. Approximately two-thirds of all non-traumatic foot amputations performed in the US are a result of diabetic foot wounds (Haugh, 2017). In these five studies, the outcome measure was the proportion of patients with complete wound re-epithelialization. The overall relative risk (RR) for complete wound healing with amniotic products, compared with standard care, was 2.75, indicating a statistically significant improvement in wound closure rates ($p<0.001$). These findings suggest that the use of amniotic products to augment healing in DFU holds considerable promise for future patients (Haugh, 2017).

Similarly, vascular ulcers are one of the leading causes of chronic skin changes in the industrialized world. Venous disease is responsible for 60-80% of these ulcers. Approximately 10% result from arterial disease, and 20-30% from mixed venous/arterial disease. Skin grafting is a commonly utilized method to assist wound healing in this patient population. Revascularization in patients with vascular disease is often not feasible due to the distal features of the wounds and frequent comorbid conditions in patients, rendering surgery contraindicated. Amniotic

membranes have been explored in various studies for their role in optimizing vascular wounds prior to skin grafting, with mixed results. In several studies reviewed, pre-treatment (before skin grafting) with fresh amniotic membrane appeared to decrease time before grafting but did not seem to make a difference in the long-term outcomes of these patients. In one study, wound recurrence rate and time-to-recurrence showed no improvement despite pre-treatment with amniotic membrane. In one study, wound recurrence within 1 year was estimated at around 50%. The limited studies available on the use of amniotic membranes for venous wounds are very heterogeneous, and few randomized controlled studies exist (Pesteil, 2024).

Future applications of placenta-derived therapies are being actively explored across many fields of medicine. The opioid epidemic has increased the prevalence of complex, difficult-to-treat wounds at injection sites. Placental-derived therapies show potential for addressing these challenges through their antimicrobial, growth-stimulating, and balanced inflammatory-modulating effects. Various formulations of placental extracts have been researched for the treatment of chronic hepatitis (Moghassemi, 2025). In Japan, a pharmaceutical-grade placental extract, rich in estrogen and progesterone, is indicated for the treatment of menopause (Kitanohara, 2017). Otolaryngologists have even explored intranasal injections for the management of chronic atrophic rhinitis (Wo, 2023). One of the most promising areas of research for placental extracts is their potential for treating hair loss. Proposed mechanisms have been hypothesized to promote hair follicle stimulation (Moghassemi, 2025). These diverse applications underscore the placenta's potential to support innovative therapeutic strategies across multiple medical fields.

Placenta-derived therapies have demonstrated potential in wound healing and tissue regeneration across multiple medical disciplines. From historical applications to modern innovations, innovative therapies such as amniotic membrane grafts and placental extracts, have been utilized with success due to their anti-inflammatory, antimicrobial, and regenerative properties (Silini, 2015). Clinical studies have shown promising results, though challenges such as cost, ethical considerations, and regulatory constraints remain. As research continues, the versatility of placental products may expand therapeutic applications, offering new solutions for conditions ranging from neurosurgical reconstruction to hair loss treatment. With ongoing advancements in processing and standardization, placenta-based medicine holds great promise for future clinical practice (Moghassemi, 2025).

SOCIAL ANALYSIS

Public understanding of placenta-based treatments is often limited, leading to misconceptions about their safety and efficacy. A 2017 study by Buser et al. found that many individuals associate the use of placenta with pseudoscience or unproven medical practices, despite its FDA approval for specific clinical applications. Many people hold negative views regarding placenta-derived products, influenced by cultural values and ethical concerns surrounding their use. Despite these misconceptions, placenta-based treatments have been approved for specific medical applications, such as wound healing and tissue regeneration, highlighting their potential therapeutic benefits when properly regulated (Zhang et al., 2023).

The U.S. FDA has approved certain placenta-derived products for specific medical uses. For instance, in March 2023, the FDA cleared Innova Burn, a placental extracellular matrix medical device, for the management of partial-thickness second-degree burns (Convatec, 2023). This approval underscores the potential of placental biomaterials in promoting wound healing by providing an extracellular matrix scaffold for tissue repair (Zhang et al., 2023). Despite these advancements, public skepticism persists, partly due to the association of placental products with unapproved and unregulated therapies. The FDA has issued warnings about unapproved regenerative medicine products, including those derived from placental tissues, emphasizing that such products require FDA licensure or approval for marketing to consumers (FDA, 2023). This regulatory stance protects consumers from potential risks associated with unproven treatments.

Moreover, cultural practices such as placentophagy and postpartum placenta consumption have contributed to public misconceptions. Advocates claim benefits such as improved mood and increased energy; however, scientific evidence supporting these claims is limited. The Centers for Disease Control and Prevention (CDC) has advised against placentophagy due to potential health risks, including bacterial infections (Buser et al., 2017). Enhancing public understanding is crucial to distinguish between scientifically validated medical applications of placental derivatives and unproven or potentially unsafe practices.

Beyond social stigma, economic and geographic barriers significantly impact access to placenta-based wound care, particularly among underserved populations. Advanced wound care treatments, including placental skin grafts, are often expensive, placing them out of reach for many patients who lack adequate insurance coverage or financial resources (Kaur et al., 2019). Individuals with OUD are particularly vulnerable to these barriers, as they often face economic instability. Singh et al. in 2019 reported that approximately 24.6% of individuals who suffered fatal opioid overdoses were living below the poverty line, compared to 11.7% of the general population. Additionally, 29.1% of fatal opioid overdose victims were uninsured, further limiting their access to advanced medical treatments. These financial constraints make it difficult for vulnerable populations, including those affected by opioid-related wounds, to receive optimal care. When individuals cannot afford such treatments, they often resort to basic wound care methods, which may be less effective in preventing infection and promoting tissue regeneration. Community-based health programs and government-subsidized initiatives may help address these financial disparities by expanding access to affordable or free treatment options.

Community-based initiatives that offer early wound care services demonstrate how such therapies can be effectively deployed. A Chicago-based syringe exchange program (SEP) study found that 24% of all clinical encounters involved wound complaints, highlighting a significant unmet need in this population (Huyck et al., 2020). However, because placenta-derived wound products require prescription and physician oversight, they cannot be directly dispensed within syringe exchange programs as over-the-counter interventions. Instead, SEPs could serve as critical points of screening, triage, and referral, partnering with licensed medical providers or wound care clinics to evaluate eligible patients for advanced therapies such as placental extracts. Integrating structured referral pathways into these low-barrier environments could improve wound outcomes while decreasing the burden on emergency and inpatient care facilities. Public health systems can reduce disease transmission, lower complication rates, and improve long-term outcomes for high-risk individuals by facilitating early, clinically supervised treatment.

Geographic barriers further limit access to placental wound care, especially in rural and medically underserved areas. Many advanced wound care facilities are concentrated in urban centers, making specialized care difficult for individuals in remote areas to access. Telemedicine has emerged as a potential solution, enabling healthcare providers to guide wound management remotely (Kaur et al., 2019). Moreover, opioid overdose death rates vary significantly across states, with per capita costs ranging from $1,204 in Hawaii to $7,247 in West Virginia (Singh et al., 2019). These variations highlight the need for targeted interventions that consider economic and geographic factors to ensure equitable access to advanced wound care treatments, including placenta-based therapies. Mobile clinics and community health worker programs can also help bridge the gap by bringing essential wound care services to populations without access. Addressing these socioeconomic and geographic challenges is critical to ensuring equitable access to placenta-based treatments for opioid-related wounds.

A critical yet often overlooked barrier to equitable access to and acceptance of placenta-based wound care is the lack of public health literacy and healthcare provider training. Health literacy, defined as the ability to understand and use health information, is essential for patients to make informed decisions regarding wound care options. Unfortunately, many individuals with chronic wounds or opioid-related injuries lack sufficient understanding of advanced treatment options, including the therapeutic use of placental-derived biomaterials (Callender et al., 2021). This knowledge gap can lead to underutilization of effective, FDA-approved therapies due to misinformation or distrust.

Patients who are unaware of the science behind placental treatments may conflate these therapies with fringe or unregulated practices, reinforcing existing stigma. As emphasized by Protzman et al. (2023), when placental-derived materials are appropriately regulated and used , they offer immense therapeutic potential, promoting angiogenesis, tissue regeneration, and infection control. Educating patients on these mechanisms can empower them to seek out and adhere to more effective treatments. Furthermore, tailored, patient-centered education programs have been shown to improve wound-healing outcomes and promote treatment adherence (Callender et al., 2021). These

programs must be culturally competent and designed to meet the needs of diverse populations, especially those disproportionately affected by chronic wounds and socioeconomic barriers.

On the provider side, inadequate training in advanced wound care remains a global challenge. Many clinicians, particularly those practicing in underserved regions, lack formal education on newer technologies such as placental grafts (Gould & Herman, 2025). As wound care evolves through innovations such as 3D-printed placental bioinks, there is a pressing need to integrate these developments into standard medical education. Bashiri et al. demonstrate that these bioinks significantly enhance wound healing outcomes by improving vascularization and cellular proliferation, suggesting that provider familiarity with these innovations can directly impact patient outcomes.

Efforts to improve provider education must also address systemic limitations, such as the availability of continuing education in rural and low-resource settings. Online training modules, clinical guidelines, and tele-education platforms can bridge this gap by making advanced wound care knowledge accessible to practitioners across geographic boundaries. Ultimately, increasing educational awareness at both the patient and provider levels is essential to ensure the successful implementation of placenta-based therapies. Without these educational interventions, the benefits of scientific advancements in wound healing may remain inaccessible to the very populations most in need.

The broader implementation of placenta-based wound care has the potential to yield significant benefits for community health while also reducing healthcare expenditures. For populations disproportionately affected by chronic wounds, such as individuals with OUD and PWUD, timely access to effective treatments is critical. Placental-derived therapies, including FDA-cleared products like Innova Burn, offer regenerative benefits such as enhanced angiogenesis, reduced inflammation, and accelerated tissue healing (Protzman et al., 2023). Integrating these therapies into public health interventions could reduce complications associated with untreated wounds, such as infections, sepsis, and amputations, which contribute to high morbidity and mortality rates in underserved populations.

Community-based initiatives that offer early wound care services demonstrate how such therapies can be effectively deployed. Although placenta-derived wound products require prescription and physician oversight, syringe exchange programs (SEPs), such as the Chicago-based program described by Huyck et al. (2020), could function as screening and referral hubs, connecting eligible patients with licensed wound care providers. Structured referral partnerships may improve wound outcomes while decreasing the burden on emergency and inpatient care facilities. Public health systems can reduce disease transmission, lower complication rates, and improve long-term outcomes for high-risk individuals by treating wounds early and effectively in low-barrier environments.

Importantly, regulatory oversight plays a vital role in ensuring that public health investments are directed toward safe and effective products. The U.S. FDA has issued warnings about unapproved regenerative medicine products, including specific placental-derived therapies, reinforcing the need for evidence-based implementation (FDA, 2023). Adhering to regulatory standards not only protects patients but also ensures that healthcare resources are allocated to interventions with proven efficacy.

In summary, placenta-based wound care holds significant promise for improving community health and reducing healthcare expenditures. When implemented through community health initiatives and regulated frameworks, these therapies can address both clinical and economic challenges associated with chronic wounds in vulnerable populations.

FINANCIAL ANALYSIS

Traditional wound care methods differ significantly from the utilization of placental tissue for wound management. Analysis of the financial implications of using placental tissue is multifaceted and requires a comprehensive analysis of both the clinical outcomes and cost-effectiveness. Modern-day wound care interventions involve advanced therapies that are often prohibitively expensive. For instance, the cost of standard wound care

products can increase rapidly, particularly for chronic wounds such as DFU, where the average cost to closure can exceed $2,700 per wound when using conventional treatments (Zelen et al., 2014). In contrast, placental-derived products, particularly dHACM, have demonstrated a significantly lower cost to closure, averaging around $1,771 per healed wound (DiDomenico et al., 2018). This drastic cost difference affects the availability and allocation of wound care resources, favoring dHACM as a more cost-effective option for acute wound care management.

Extensive research and literature have documented the utility and clinical efficacy of placental tissue in wound care. Studies have shown that dHACM can achieve 77% and 92% healing rates within 4 and 6 weeks, respectively, in treating DFU, compared with negligible healing rates with standard care (Koob et al., 2014). This recovery rate offers benefits beyond the cost of the placental intervention and, in turn, reduces hospitalization rates and complications, critical factors in overall healthcare expenditures (Zelen et al., 2014). Incorporating placental tissue into modern wound care management protocols offers enhanced healing outcomes, efficacious wound management, and a more cost-effective intervention, ultimately supporting the current growing healthcare landscape of value-based care.

Cryopreservation and dehydration are two preservation methodologies that play a vital role in the financial viability of placental tissue. These methods maintain the biological properties of the tissue while extending shelf life and reducing the risk of disease transmission (Gibbons, 2015). The ability to store these placental tissues for long periods without loss of functionality and clinical efficacy enables healthcare providers to manage inventory more effectively, thereby reducing waste and associated costs. Furthermore, the placental tissues' inherent biocompatibility and regenerative properties will allow them to serve as anti-inflammatory and antimicrobial therapeutics, thereby contributing to wound healing and leading to shorter treatment durations, fewer patient visits, and lower overall costs (Frykberg, 2024; Johnson et al., 2017).

In addition to costs, the financial analysis must also consider the broader implications of wound care strategies on patient quality of life and long-term health outcomes. Advanced wound care therapies that promote faster healing improve patient satisfaction and reduce the likelihood of complications such as infections, amputations, and prolonged disability, which can incur substantial costs to the healthcare system (Zelen et al., 2014). Hence, placental-derived products are not only cost-effective as direct treatment interventions but also contribute to improved patient outcomes and reduced overall healthcare costs.

One major concern with the use of products such as dHACM is the variability and effectiveness of placental tissue between donors and recipients. However, recent studies indicate that such variability does not significantly affect healing efficiency, suggesting that the benefits of using placental membranes are consistent across different preparations (Horváth et al., 2023). This consistency improves the reliability of placental products and promotes their utility as a standard intervention for wound management. An overall cost comparison between placental tissue and the traditional wound care management system must account for current standards for multiple visits, extensive dressing changes, and various adjunct therapies. Patients with chronic wounds that require long-term treatment would therefore have significant cumulative costs (Zelen et al., 2016). In contrast, placental interventions reduce the frequency of visits, the need for additional therapies, and overall costs.

Substance-induced wounds, particularly in Kensington, Philadelphia, Pennsylvania, require a specific financial analysis of the wound care treatment modalities and costs. The prevalence of chronic wounds in this demographic is significant, and the associated healthcare costs can be substantial. Traditional wound care methods often involve frequent clinic visits, dressing changes, and various adjunct therapies, which can accumulate significant expenses over time. For example, the average cost of managing a DFU can range from $2,140 for a healed wound to $8,800 for an unhealed wound, demonstrating the financial burden of chronic wound management (Guest et al. 2017). Substance-induced injuries are prevalent in Kensington, Philadelphia, Pennsylvania, resulting in an increasing frequency of medical visits to clinics and hospitals. For patients requiring advanced wound care, the average number of visits can reach 20 over a treatment period, with each costing approximately $150 to $300, depending on the wound's complexity and required interventions (Nussbaum et al., 2018). This results in a total expenditure of $3,000

to $6,000 for outpatient care alone, not including the costs of dressings, medications, and potential complications arising from untreated or poorly managed wounds. On the other hand, placental-derived products, such as dHACM, can reduce the number of patient visits due to their rapid and enhanced healing properties. Studies indicate that dHACM can achieve healing rates of 77% within 4 weeks, potentially reducing the total number of visits to as few as 5-10 over the same period (Koob et al., 2014; Nussbaum et al., 2018).

When examining the overall treatment costs of placental tissue use for wound care, the average cost to closure using dHACM is approximately $1,771 per healed wound, significantly lower than the costs associated with traditional wound care methods. This cost includes the price of the placental product, which typically ranges from $500 to $1,000 per application, and the reduced need for follow-up visits and additional therapies. On the other hand, traditional treatments may require multiple dressing changes per week, each costing between $20 and $100, leading to cumulative costs that can exceed $5,000 over the course of treatment (Gueltzow et al., 2018).

The management of untreated wounds can lead to increased hospitalizations and additional complications, increasing healthcare costs. For instance, the cost of managing a putatively infected wound can reach up to $11,200, while the cost of managing an uninfected wound is significantly lower, at around $4,000 (Guest et al., 2018). This disparity underscores the importance of effective wound management strategies that not only promote healing but also minimize the risk of complications. In Kensington specifically, the nature of substance-induced wounds requires a tailored approach to the community that considers both the clinical and economic outcomes and effects. The use of placental tissues could potentially reduce the overall cost burden on the healthcare system by promoting faster healing and reducing the need for extensive outpatient care.

Looking ahead, the integration of telemedicine across all aspects of medicine, including wound care, has shown promise in reducing costs and improving patient outcomes. Studies indicate that structured telemedicine models for chronic wound management involve scheduled remote follow-up visits in which home care nurses or primary providers capture standardized digital photographs of wounds, document wound dimensions and characteristics, and transmit this information to wound care specialists for review and treatment recommendations (Goff-Pronost et al., 2018). In this protocol, specialists provide ongoing guidance regarding debridement, dressing selection, and advanced therapies without requiring frequent in-person visits. Such a model could be particularly valuable when implementing placental extract-based wound therapies, as remote specialist oversight could help ensure appropriate patient selection, monitor graft integration and wound healing progression, identify early signs of infection or graft failure, and adjust treatment plans in real time. In resource-limited settings such as Kensington, where access to specialty wound care is often limited, a structured telemedicine protocol could facilitate the safe administration and monitoring of placental-derived wound treatments while reducing barriers to transportation, cost, and clinical availability.

In conclusion, the financial implications of implementing dHACM and other placental tissue modalities for wound care is significantly superior compared to the traditional wound care methods. The lower cost to closure, combined with enhanced healing rates and reduced complications, positions placental derived coproducts as a cost-effective alternative in the management of chronic wounds. The growing emphasis of value-based care in healthcare will support the integration of placental tissues into wound care protocols, not only for clinical efficacy but also economic benefits.

ETHICAL ANALYSIS

Research and clinical practice involving placental-derived products intersect with several inherently vulnerable groups: postpartum tissue donors and PWUD with OUD. These vulnerable groups face unique ethical challenges that require careful assessment, analysis, and consideration, particularly regarding autonomy, consent, and protection from harm. The provider-patient-donor triad necessitates ethical and procedural oversight to protect all parties involved in this complex healthcare setting. Discussions of ethics in working with vulnerable populations are

imperative to minimize risk, maximize participant autonomy, and ensure justice in access to care, particularly when marginalized communities require serious medical attention (Clark, 2017; Addison et al., 2025). The synthesis in this paper aligns with existing conditions and medical interventions that also require attention to consent, equity, and stigma in health care delivery. We can expand placental-derived wound care by emphasizing voluntary, informed consent processes for donors and recipients, along with equitable access to placenta-based therapies for PWUD (Clark, 2017; Addison et al., 2025).

Placental tissues used in clinical medicine and regenerative therapies are sourced from postpartum donors who undergo screening and informed consent procedures. The ethical procurement of placental tissue requires informed consent from donors, comprehensive screening for infectious risks, and appropriate regulatory oversight to minimize the risk of transmitting infectious diseases and maintain safety. The ethical literature on tissue banking and regenerative medicine emphasizes the necessity of donor autonomy, informed consent, and transparent governance of tissue banking procedures as central to public trust and patient safety (Boers et al., 2016; Olson et al., 2011; Singh et al., 2024). Tissue banks should adhere to accepted biomaterial handling practices, risk assessment, and regulatory steps that reflect the novel and rapidly changing use of placenta-derived products (Boers et al., 2016; Olson et al., 2011). Therefore, the donor consent framework should explicitly address the purpose of placenta use, the potential future uses beyond the immediate wound-healing indication, privacy and data protection, and the right to withdraw consent when a participant requests (Boers et al., 2016; Olson et al., 2011).

PWUD with OUD experience stigma in health care settings and often face barriers to accessing advanced wound care and novel therapies. Stigma can stifle physician-patient trust, influence the voluntariness of consent, and may bias clinical decision-making and resource allocation. Research on stigma in the care of PWUD highlights how health care providers' perceptions of drug use can affect the quality of care, patient engagement, and the willingness of patients to be adherent to treatment (Biancarelli et al., 2019; Febres-Cordero et al., 2023). Research and clinical practices involving vulnerable populations require enhanced safeguards to prevent patient coercion, misunderstanding of therapeutic outcomes and effects, or undesired exploitation, particularly with novel interventions. Ethical guidance on vulnerable populations, particularly in emergencies, emphasizes respect for persons, non-maleficence, and beneficence, while acknowledging the vulnerability of the communities (Clark, 2017; Quest & Marco, 2003). These insights support an approach in which PWUD with OUD receive clear information about potential health benefits and risks, with patient-centered decision-making, respect for autonomy, and an emphasis on patient comprehension of the therapy (Clark, 2017; Biancarelli et al., 2019).

Federal regulation of tissue donation is rooted in a system in which the collection, storage, and distribution of human tissues for transplantation and research are governed by national health agencies, specifically the U.S. FDA which oversees tissue banking procedures. The American Association of Tissue Banks (AATB) offers standards and accreditation to ensure safety, ethical practice, and traceability. Government tissue banks are regulated for safety and ethical purposes, and FDA regulations extend to tissue banking practices, including donor consent and protection of donors' rights. It is particularly pertinent in the case of placental tissue for wound healing, where ethical procurement and appropriate clinical use are highlighted. These usually include skin, bone, cartilage, and blood products, though placental tissue is also regulated for use in wound care. These tissues are utilized for transplantation, research toward the development of new therapies, and medical education for resident physician training. There are ethical issues related to informed consent, ensuring that donors are aware of how their tissue is utilized, and overall surveillance to promote transparency in tissue banking operations and to preserve donor anonymity and rights under regulatory oversight.

The ethical justification for placenta-derived therapies is supported by the potential to improve wound healing outcomes and reduce suffering in a population facing treatment-resistant wounds and high morbidity and mortality. Regenerative medicine literature emphasizes that benefits should be weighed against risks, with ongoing monitoring and transparency regarding the care. Ethical analysis underscores the importance of establishing an evidence base through clinical oversight, while acknowledging the potential of placental biomaterials to modulate inflammation,

promote angiogenesis, and facilitate tissue remodeling in wounds. Contemporary research emphasizes the need for governance incorporating bioethics, translational science, and patient engagement to maintain safety, public trust, and equitable access (Boers et al., 2016; Olson et al., 2011; Singh et al., 2024). Tissue biobanking, tissue development, and the immunomodulatory properties of placental tissue underscore the ethical importance of obtaining, storing, and using biologic materials containing living cells (Boers et al., 2016; Olson et al., 2011). Therefore, the placenta-based approach is ethically justifiable when performed with explicit and documented donor consent, transparent risk communication, appropriate regulatory oversight, and proactive attention to equity in access (Boers et al., 2016; Olson et al., 2011; Singh et al., 2024).

A primary ethical concern is whether placenta-derived therapies will be equitably accessible to PWUD with OUD, who often experience financial instability, insurance coverage gaps, and geographic barriers to healthcare. The ethical pillar of justice in health care requires attention to equitable access, affordability, and distribution of novel therapies. Current legislative policies in medicine emphasize the need to align industry innovation with social justice by integrating therapy frameworks and public health strategies that allow therapeutics to reach marginalized populations (Singh et al., 2024; Addison et al., 2025; Febres-Cordero et al., 2023). For example, embedding wound care services within syringe exchange programs can facilitate access to advanced therapies, address immediate health needs, and potentially reduce downstream costs associated with chronic wound complications. Therefore, clinical benefits can be intertwined with equity considerations by delivering the placental-based wound care initiative alongside an existing social service for marginalized populations (Febres-Cordero et al., 2023). Innovations should not exacerbate health and economic disparities. Instead, therapeutic innovations should be accompanied by training, education, and infrastructural support to ensure diverse care and appropriate implementation (Singh et al., 2024; Addison et al., 2025).

Effective and ethically conscious translation of placenta-based therapies into standard practice requires careful alignment with regulatory safeguards, biosafety considerations, and transparent communication about the limits of current evidence. Donor screening for infectious risks, traceability of tissue, storage and preservation methods, and clear guidelines for permissible uses are paramount for maintaining participant trust and public trust (Boers et al., 2016; Olson et al., 2011). Additionally, transparent reporting of clinical outcomes and adverse events is pivotal (Singh et al., 2024; Olson et al., 2011). Public perceptions of placenta-derived products vary and continue to be influenced by cultural and ethical factors, as well as media attention.

To utilize placental-derived products for managing substance-induced wounds in PWUD with OUD, we believe the following ethical framework should be implemented. The initial step is to obtain informed consent from placenta donors, providing them with clear information about potential current and future uses, alongside donor screening and privacy protections (Boers et al., 2016; Olson et al., 2011). Next, screen PWUD for consent capacity, providing plain-language information about benefits, risks, and uncertainties of placenta-derived therapies, and maintain ongoing consent processes and respect for patient autonomy (Clark, 2017; Biancarelli et al., 2019). On a larger scale, it is important to design implementation plans that address geographic, financial, and insurance barriers for vulnerable populations (Singh et al., 2024; Febres-Cordero et al., 2023). Healthcare teams must embrace a precision public health approach that weighs population-level benefits and harms, considers data governance and privacy, and fosters trust through transparency and community involvement (Boers et al., 2016; Olson et al., 2011).

To educate wound care specialists in tissue-based wound care strategies, employing the Organ Procurement Organization (OPO) education model will allow us to emphasize formal training, awareness, collaborative workshops, and ongoing education, following tested OPO educational models (Goodarzi et al., 2014; Manyalich et al., 2011). Having training that covers the reasons for donation of tissue, the procurement and processing procedure, and how to approach families will enhance clinicians' knowledge and confidence. This can be delivered either by face-to-face sessions or web-based platforms to reach a large audience (Siminoff et al., 2022, Sedgwick et al., 2014). Healthcare education campaigns that highlight the potential of tissue donation to enhance patients' and communities' lives are critical for promoting clinician commitment and support for tissue-based therapies (ShieldsPirri, 2016;

Fahrenwald & Stabnow, 2005). Interactive transplant ethicist-donor family workshops expose clinicians to diverse perspectives and hands-on experiences in donation, a valuable element of effective clinician education programs (Goodarzi et al., 2014; Manyalich et al., 2011). Recurrent Continuing Medical Education (CME) activities are necessary to maintain clinicians' familiarity with the latest best practices and evolving regulatory guidance. Evidence shows that sustained knowledge acquisition through repeated testing and education is effective (Sedgwick et al., 2014; Álvarez-Márquez et al., 2024). For the achievement of scalability and sustainability of such initiatives, training-of-trainers strategies, such as the European Training Program on Organ Donation (ETPOD), have proven to extend coverage and standardize competencies at facilities, with activities focusing on strengthening dissemination as well (Goodarzi et al., 2014; Manyalich et al., 2011). Finally, use of interactive modalities, such as simulation-based communication education to practice donor discussions and web-based modules to facilitate learning, is associated with improved knowledge, attitudes, and donor-consent outcomes, substantiating the promise of multimodal training in the education of wound care professionals performing tissue-based therapies (Siminoff et al., 2022; Álvarez-Márquez et al., 2024).

The ethical examination of placenta-derived biomaterials for opioid-related wound care must be anchored in donor-informed consent, patient autonomy, non-maleficence, beneficence, and justice. Given the vulnerability of PWUD and the potential public health benefits of reducing wound burden and improving healing, the ethical pathway forward rests on transparent consent procedures, careful risk-benefit assessment, equitable access, public health regulatory oversight, and ongoing engagement with affected communities. The integration of placenta-based therapies into wound care for PWUD with OUD, when implemented ethically, aligns with the broader aims of community preventative medicine public health ethics: to deliver beneficial care while safeguarding individuals and communities against harm, exploitation, and inequitable access (Clark, 2017; Boers et al., 2016; Illes et al., 2017; Olson et al., 2011; Singh et al., 2024).

DISCUSSION SECTION

After an overview of social, financial, medical, and ethical perspectives on the use of the placenta as a wound care technique, it is essential to emphasize how these scenarios can be applied to patient care and how physicians can more effectively utilize them. The following case presents a 43-year-old homeless woman with severe opioid use. She had already experienced three overdoses and had a history of injecting both fentanyl and cocaine. The patient arrived at a wound care clinic, where “she reported ulcers on bilateral upper extremities” (Warp, 2023). From her description, the wounds were in the closed areas of hypopigmentation; they would then gradually open to produce smelly, yellow drainage (see Fig. 5: 1a, 1b). Over time, they would also become painful and red, approximately 4 cm in diameter. After the team cleaned the wounds with saline and dressed them with petroleum-impregnated gauze, the patient was instructed to clean the wounds with soap and water daily, replace the petroleum-impregnated gauze dressing, and ensure the wounds did not worsen. She was also prescribed a course of doxycycline for a potential bacterial infection. After seven weeks, she presented to the clinic once again for wound care, where her wounds progressed due to her injecting drugs. The wounds were warm, red, and painful, and she had a subjective fever (see Fig 5: 2a, 2b). On the physical exam, she had multiple extensive ulcerations to her bilateral forearms with surrounding hyperpigmentation, plus a necrotic center on the lateral aspect of her bilateral knees. The patient noted that she did not inject anything into her knees. Her urine was also tested for xylazine, which came out positive, indicating the presence of xylazine in her body. Once again, her wounds were cleaned similarly to her first visit, and she was given the same antibiotic prescription and wound care instructions (Warp et al., 2023).

From a medical perspective, the foul-smelling drainage and signs of infection reflect the first stage of xylazine wounds, as defined by the Philadelphia Treatment Algorithm (Ilyas et al., 2025). Placental products, such as dHACM, offer a targeted solution through multiple mechanisms. Growth factors (EGF, FGF) stimulate epithelialization of her 4 cm ulcers, anti-inflammatory cytokines modulate chronic inflammation, and antimicrobial

peptides combat infection. At the same time, the extracellular matrix scaffolds support structured regeneration. Evidence from studies on diabetes ulcers shows a 2.75 times higher healing rate with placental therapy. It also showed a 93.6% reduction in wound size progression, as recently documented (Frykberg et al., 2014). For this patient, placental therapy represents a biological solution by breaking the cycle of ineffective wound care and hospitalization, and a sobering reminder of systematic obstacles that prevent equitable access to advanced wound technologies for marginalized populations.

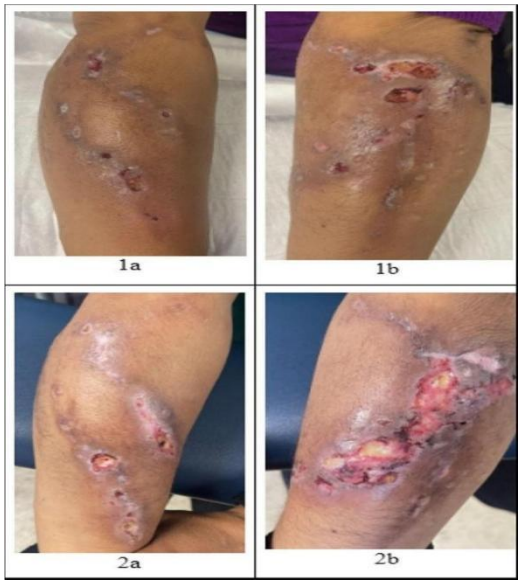

Figure 5: Xylazine-induced wounds after the first (1a, 1b) and second(2a,2b) visit (Warp et al, 2023)

The social aspect of placenta therapies also presents its challenges. Although the FDA has approved specific applications, such as Innova Burn, for burn treatment, significant stigma still surrounds placenta wound care, leading many providers and patients to view placenta as an unproven alternative medicine rather than evidence-based care (Buser et al., 2017). The stigma is compounded if the patient is a part of a marginalized population, as in the case of the case study, who already face discrimination in a healthcare setting due to substance abuse. Potential placental therapies could improve outcomes in such cases and play a crucial role in shifting perceptions of current wound care practices.

One way to provide placental wound care is through harm-reduction programs that standardize care. As reported by SEPs, nearly a quarter of clinical encounters involve complaints about wounds (Huyck et al., 2020). Integrating structured referral for placental therapies within such services could significantly improve outcomes while ensuring that treatments remain physician-supervised and clinically appropriate. Increasing placenta-based wound care through community partnerships, mobile clinics, and telemedicine models could improve geographic accessibility and promote provider training in trauma-informed and harm-reduction approaches. Such wide integration may reduce stigma by embedding advanced wound care within patient-centered, low-barrier settings that are specifically designed to serve individuals with SUD, thereby offering greater understanding and continuity of care than traditional emergency departments, where high volume and acute demands may limit sustained, relationship-based care.

Cultural associations regarding placental uses and postpartum practices may pose challenges for patient populations. Many healthcare providers lack training in advanced wound care techniques and may therefore feel hesitant to adopt a new approach. People in rural areas may further complicate the issue, as they often lack facilities to administer placental treatments and require trained personnel to oversee them. Even in urban settings, with better access to care, fragmentation of services among marginalized populations creates dangerous obstacles to consistent treatment.

The financial burden of conventional wound care is substantial, particularly for chronic conditions such as diabetic ulcers. The standard treatment includes debridement, antibiotics, regimens, and dressing changes, which typically cost up to $8,800 per wound (Guest et al., 2017). When infections occur and hospitalization is required, costs escalate. For vulnerable groups, such as people experiencing opioid use, these costs create an insurmountable barrier to care. This is evident in the case of a 43-year-old homeless woman. Her untreated wounds progressed to painful ulcers, leading to a costly visit to the emergency department. Placenta therapies, however, offer a more financially sustainable alternative in this case. The dHACM is often more cost-effective, averaging around $1,771 per healed wound, compared with a maximum of $8,800 (Didomenico et al., 2018). With early intervention using placenta therapy, the patient in the case study could have prevented infected ulcers, saved thousands of dollars, and avoided a second hospitalization. These costs suggest that, in opioid crisis areas like Kensington, the public impact could be significant. Faster healing times translate into reduced strain on emergency services, lower hospital costs, and fewer hospital stays for patients and workers alike.

Both the financial and social aspects of placental wound care present opportunities and challenges. On the one hand, the overall cost burden of care could be reduced through national implementation, thereby normalizing placenta-based therapies and potentially reducing stigma associated with their use. Moreover, various studies on the efficacy of dHACM and other placenta-derived tissue grafts show faster wound healing, shorter time to wound closure, and reduced need for advanced wound care. As dHACM treatment becomes part of routine wound management, it is expected that its implementation on a wider scale will result in a reduction in stigma experienced by patients with chronic and substance-associated wounds, as well as a decrease in costs associated with newer wound care therapies (Zelen et al., 2014; Gould et al., 2015). Without implementation efforts that address financial and social barriers, placental treatment may be inconsistent across populations and ineffective. In the case study, although placental therapy would be effective and cost-efficient, the current hospital system faces numerous obstacles that prevent such care. Policy interventions can bridge the gap. A training program for providers could build the confidence they need to perform these therapies. Additionally, public education campaigns that present facts and benefits of placental use can accelerate cultural competence toward placental use. This would greatly apply to the patient in the case study, whose life would have significantly changed if policies encouraging and insurance covering placental use were in place.

Placental-derived wounds show a promising solution for high-risk patients, such as the 43-year-old homeless woman with opioid-related ulcers. Medically, placental therapeutics address core challenges of chronic wounds through their unique combination of growth factors, anti-inflammatory properties, and antimicrobial effects. Thus, it offers faster healing and fewer complications than standard care. Financially, they present a cost-effective alternative that could alleviate the burden on emergency services and hospitals. However, systemic barriers like inconsistent insurance coverage, social stigma, and gaps in provider training limit equitable access to advanced treatments. To realize the full potential of placental wound care, policy reform is needed to expand Medicaid coverage, integrate harm-reduction programs such as SEPs, and provide targeted education about the placenta. These changes could significantly impact vulnerable patients suffering from OUD, such as those experiencing chronic suffering and recovery. Bridging the implementation gap is not only a clinical imperative but also a moral one, ensuring that scientific progress translates into tangible improvements for society's vulnerable populations.

CONCLUSION

The emergence of xylazine-adulterated opioids has created a crisis that challenges conventional medical approaches. This interdisciplinary study demonstrates that placenta-derived material provides an economical, evidence-based approach to treating these complex wounds. According to the evidence, dHACM reduce treatment costs from up to $8,800 per wound to approximately $1,771, achieving healing rates of 77-92% within 4-6 weeks, compared with minimal improvement with standard care. The placenta has therapeutic potential due to its unique combination of growth factors, anti-inflammatory cytokines, antimicrobial peptides, and extracellular matrix components that address the pathophysiology of xylazine-induced tissue damage. Still, significant obstacles stand in the way of successful implementation, including uneven insurance coverage, gaps in provider knowledge, social stigma, and limited geographic access to such care.

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