International Wound Journal

WILEY | IWJ

ORIGINAL ARTICLE OPEN ACCESS

A Retrospective Real-World Data Analysis of Pressure Ulcer Healing With Nitric Oxide-Delivering Foam Among Older Adults

Rhonda Sullivan[1] | Zwelithini Mzwandile Tunyiswa[2] | Windy Cole[3] | Lisa Gould[4] | Mervin Low[5]

[1]iWOC Nursing Foundation, Villa Rica, Georgia, USA | [2]Open Wound Research, LLC, Puyallup, Washington, USA | [3]Director of Wound Care Research, Kent State University College of Podiatric Medicine, Independence, Ohio, USA | [4]Director of Research, South Shore Health Center for Wound Healing, Weymouth, Massachusetts, USA | [5]CEO Newport Wound, Newport Beach, California, USA

Correspondence: Rhonda Sullivan (iwocnurse@gmail.com)

Received: 21 November 2025 | **Revised:** 9 March 2026 | **Accepted:** 2 April 2026

ABSTRACT

Pressure ulcers remain a major cause of morbidity in skilled nursing facility populations, where frailty and comorbid conditions hinder healing. Numerous studies have established Nitric oxide's role in tissue repair, angiogenesis, and infection control, suggesting therapeutic potential for nitric oxide in chronic wound healing. A retrospective observational cohort study was conducted using de-identified data from skilled nursing patients presenting with pressure ulcers. Two matched cohorts (200 patients per group) were compared: Those treated with a nitric oxide–delivering foam and historical controls receiving standard of care. Propensity score matching accounted for baseline wound size, stage, sex, comorbidities, and treatment start date. The primary endpoint was complete closure (epithelialized or had an area of zero) within 12 weeks. Bayesian hierarchical hurdle–gamma regression estimated treatment effects using posterior means and 95% credible intervals. Within 12 weeks, closure or resolution rates had a significant benefit in the treatment group across most stages: 94% versus 79% for Stage 1, 80% versus 45% in Stage 2, 64% versus 28% in Stage 3, 39% versus 12% in unstageable, 34% versus 10% in Stage 4, and 67% versus 31% for Deep Tissue Pressure Injuries. Overall, 63% (95% CrI 50%–75%) of NODF-treated wounds healed compared with 34% (21%–47%) of SOC wounds. Posterior probabilities of superior healing with NODF exceeded 99% for most comparisons.

1 | Introduction

In 2019, the National Pressure Injury Advisory Panel (NPIAP) defined pressure ulcers (PrUs) as localized injuries to the skin and underlying tissues, typically caused by intense or prolonged pressure at bony prominences or from medical devices [1]. PrUs are denoted by six distinct stages, Stage 1–4, unstageable, and deep tissue pressure injury. Stage 1 is characterized by non-blanchable erythema with no open wound while Stage 4 PrUs are characterized by exposed bone, muscle or fascia and may be complicated by osteomyelitis. PrUs have documented high morbidity and mortality and greatly affect patients' quality of life [2]. The implementation of early prevention strategies, standardized care protocols, and prompt treatment can significantly decrease both incidence and mortality rates [3, 4]. However, the global prevalence of PrUs continues to rise, increasing from approximately 300 000 cases in 1990 to over 645 000 by 2021, with the majority occurring in adults aged 60 years and older [5]. Prevalence estimates vary across care settings: up to 23% in acute care, 11% in long-term care, and 2%–5% in the community [6]. Importantly, older adults bear a disproportionate burden. One study found that 70% of PrUs occur in individuals over the age of 70, whereas prevalence among nursing home residents with advanced dementia can reach nearly 39% [7].

Despite advances in wound care, PrUs remain highly resistant to treatment and are associated with poor outcomes. Healing of PrUs is often protracted and incomplete. In the general

Key Points

- Pressure ulcer healing remains a major unmet need in older adults, especially in skilled nursing facilities.
- Nitric oxide-delivering foam was associated with substantially better healing than standard of care.
- The treatment benefit was seen across most pressure ulcer stages.
- The findings are biologically credible because nitric oxide supports multiple phases of wound healing.
- This study provides compelling real world evidence to support further clincial adoption and study of NODF.

population, retrospective data indicate that only 35.6% of patients achieve healing at discharge or death [8]. Among older adults, healing outcomes are worse. One U.S. cohort study across skilled nursing facilities found that only 45.5% of stage 2 PrUs healed within 1 year, with healing times ranging from 33 days for small wounds to 73 days for large wounds [9].

Older adults are particularly vulnerable to delayed healing due to multiple, interacting factors. Physiological changes associated with aging, including reduced dermal thickness, diminished angiogenesis, impaired immune function, and altered inflammatory responses, compromise wound repair [10]. Frailty, immobility, malnutrition, and comorbidities such as diabetes and vascular disease contribute to both the development and chronicity of PrUs [10]. Although PrUs are common among residents of skilled nursing facilities, research on therapeutic interventions in this population remains limited. These factors collectively predispose older adults to recurrent, non-healing wounds. The global aging population, combined with the rising prevalence of chronic conditions such as hypertension, diabetes, and cardiovascular diseases, has led to a significant increase in PrUs. This trend, particularly evident in aging societies, necessitates urgent and comprehensive strategies to address this growing health concern. The combination of rising incidence, poor healing outcomes, and serious consequences of PrUs emphasizes the need for innovative approaches to wound treatment, especially for older adults. There is a critical demand for a novel, multi-dimensional wound treatment that offers individualized care to meet the specific needs of each wound and patient.

Importantly, although PrUs are common in skilled nursing facilities, evidence to guide effective, scalable therapeutic interventions in this population remains limited. Current standard-of-care approaches often rely on combinations of pressure redistribution, moisture management, debridement, infection control, and advanced dressings, yet healing remains inconsistent, and many wounds persist for months or even years. As PrU prevalence rises alongside population aging and increasing multimorbidity, there is a growing need for treatments that can accelerate healing in real-world settings and reduce the clinical and operational burden of chronic wounds in older adults.

Nitric Oxide (NO) is essential to wound healing processes. NO bioavailability is reduced with age, increasing vulnerability and impeding wound healing capability in older adults [11]. Delivery of nitric oxide stands out as a promising solution, facilitating essential processes in all phases of wound healing. NO plays an important role in numerous aspects of the wound healing process, including: platelet aggregation, modulation of inflammation, infection management, debridement, biofilm disruption, vasculogenesis, collagen synthesis, angiogenesis, cellular proliferation, granulation formation, wound contraction, and epithelialization [12].

Therefore, this study was designed to address the clinical question: Among older adults with pressure ulcers treated in real-world care settings, is treatment with a clinician-applied nitric oxide–delivering foam associated with improved pressure ulcer healing outcomes compared with standard of care? Herein, we present findings from a retrospective observational study evaluating the effectiveness of a clinician-applied nitric oxide–delivering foam on pressure ulcer healing in older adults.

2 | Materials and Methods

2.1 | Study Design and Setting

A retrospective, observational cohort study was conducted to evaluate healing outcomes of PrUs in skilled nursing facility (SNF) patients treated with a nitric oxide–delivering foam compared with historical Standard of Care (SOC) using a Bayesian method for estimating treatment effects. F686 regularized behavior as it relates to pressure ulcers in nursing homes, including proper documentation of staging and measurements, standardized offloading, and staffing assessments, which help mitigate secular variance between the historical and current cohorts. The study utilized de-identified data from SNF patients with PrUs. The Nitric Oxide Delivering Foam (NODF; NoxyDERM; NOxy Health Products Inc.) cohort was drawn from a de-identified sponsor-maintained registry, and SOC patients were identified from de-identified records of post-acute facilities during a comparable period (Table 1). For Stage 1

TABLE 1 | Registry (pre-matched) demographics.

	NODF registry	LiftOff registry
Subject summary		
Subjects	217	9898
Age (Mean)	82.0	72.9
Diabetic	66	1247
Wounds	217	15 686
Wound summary		
Deep tissue injury	45 (20.7%)	21 (0.1%)
Stage 1	29 (13.4%)	0 (0.0%)
Stage 2	61 (28.1%)	15 (0.1%)
Stage 3	32 (14.7%)	7471 (47.6%)
Stage 4	11 (5.1%)	3242 (20.7%)
Unstageable	39 (18.0%)	4937 (31.5%)

pressure ulcers, for whom exact matches did not exist in the SOC registry, the model used information from DTI and Stage 2 primarily to generate estimates. Other wound area strata estimates were regularized toward adjacent means, and then in turn toward the global mean of the estimand. The overall treatment effect (ATE) is thus a weighted estimate, which naturally down-weights stages lacking overlap, or stages with less observed units. The difference between the SNF quality star rating between treatment and control was within one (1) star, on average. The Five-Star Quality Rating System is a Centers for Medicare & Medicaid Services (CMS) public reporting system available on Medicare Care Compare. It is intended to help consumers compare nursing homes and to help facilities identify improvement areas. While a one-star difference between facilities can reflect meaningful variation in staffing, care processes, and protocol adherence, which may translate into clinically important differences in prevention of complications and healing outcomes, matching facilities within a one-star rating difference was deemed sufficient to ensure comparable baseline care quality and operational capacity across study arms. All clinical decisions regarding wound care, including where NODF was clinically indicated, were made by the treating SNF teams, independent of the study sponsor.

2.2 | Sponsor Involvement and Data Governance

The sponsor designed the registry structure (including prompts and validation logic) but did not enter, edit, or adjudicate any clinical data. All patient and wound variables were entered exclusively by participating facility administrative or clinical staff as part of routine documentation, independent of the sponsor, using a sponsor-initiated real-world wound registry implemented on the Qualtrics platform.

To enhance data integrity and minimize selective updating, entries were completed retrospectively only after case termination (healing, discharge, death, or treatment discontinuation), and interim or partial entries were not permitted.

Prior to analysis, a limited quality control review was performed to remove a small number of records with obvious entry errors (e.g., implausible wound dimensions or inconsistent dates). No outcome-based exclusions were applied, and no clinical variables were modified or imputed by the sponsor.

A pre-specified analytic protocol defined inclusion/exclusion criteria and conservative handling rules for incomplete or ambiguous records (e.g., requiring wound stage, baseline and follow-up measurements, healing status, and minimum exposure duration). These criteria were established before outcome analysis and applied uniformly across treatment groups.

2.3 | Study Population

Eligible participants were adults (≥18 years) with documented PrUs treated in SNFs between April 1, 2024, and May 31, 2025. Inclusion criteria required a baseline wound stage (1–4, unstageable, or deep tissue pressure injury) and a wound area measurement at first assessment. The SOC arm comprised 200 historical control patients treated during a contemporaneous time interval and in comparable nursing homes. The NODF arm included 200 patients (Table 2). Inclusion criteria required patients in the treatment arm to receive at least two applications of NODF over a 7-day period. Wounds were required to have closure or resolution status or follow-up wound area recorded at discharge or treatment discontinuation. Patients lacking baseline or follow-up wound measurements, or with missing treatment dates, were excluded.

Although wound care practices can vary across facilities, pressure ulcer management in the United States (US) nursing homes follows standardized federal requirements under F686: Treatment/Services to Prevent and Heal Pressure Ulcers (42 CFR §483.25[b]), which mandate evidence-based prevention and treatment protocols. Moreover, the Minimum Data Set (MDS), Section M operationalizes these standards by requiring uniform documentation of pressure ulcer presence, stage, and healing. This structured reporting framework effectively normalizes assessment and care expectations across nursing homes, supporting comparability in real-world data. To ensure comparability between groups, 1:1 propensity score matching was applied on baseline covariates including wound area at first measurement, wound stage (1–4, deep-tissue pressure injuries, and unstageable), patient sex, major comorbidities, and treatment-start date (±30 days). Sensitivity analyses employed non-informative and informative priors, and alternative weighting schemes.

2.4 | Pressure Ulcers

Patients enrolled presented with PrUs of varying clinical severities and anatomical sites. Wounds were staged according

TABLE 2 | Matched subject demographics and raw unadjusted data.

	Matched NODF	Matched control
Subjects		
Subjects	200	200
Age	81.8	85.3
Diabetic	59	59
Starting wound area	12.5	12.6

	Wounds		Healed	
	NODF	SOC	NODF	SOC
Deep tissue injury	41	5	27 (65.9)%	2 (40.0)%
Stage 1	26	0	26 (100.0)%	0 (0.0)%
Stage 2	57	7	49 (86.0)%	0 (0.0)%
Stage 3	31	34	17 (54.8)%	13 (38.2)%
Stage 4	10	15	3 (30.0)%	1 (6.7)%
Unstageable	35	139	14 (40.0)%	16 (11.5)%
All stages	200	200	136 (68.0)%	32 (16.0)%

to International Guidelines for Pressure Injury Prevention and Management (Stage 1–4, deep tissue pressure injury, and unstageable) [1]. Each patient's data was entered directly into the registry by a designated clinician at the skilled nursing facility once wound healing was achieved, at discharge, or at treatment discontinuation.

2.5 | Co-Morbid Conditions and Co-Variants

The analytic framework incorporated patient diabetic status and demographic factors (sex, age) as baseline covariates. To account for potential heterogeneity across sites, analyses also considered time of treatment initiation. A sensitivity analysis was performed using quantitative bias analysis across 21 scenarios and the treatment effect remained robust even under extreme cases where hidden factors were simulated to be twice as powerful as factors that were included in modeling.

TABLE 3 | NODF dosing frequency by basic baseline.

	Subjects	Age (mean)	Diabetic	Wound area mean
Other dosage	54 (27.0%)	79.1	15 (25.4%)	15.5
3 doses (per week)	123 (61.5%)	83.0	35 (59.3%)	11.0
7 doses (per week)	23 (11.5%)	81.8	9 (15.3%)	13.6

2.6 | Treatment Groups

The NODF arm consisted of patients managed with over-the-counter nitric oxide–delivering foam, alone or in combination with adjuncts. Patients received at least two applications of the NODF within 7 days, as recorded in the registry (Table 3). The use of adjunct therapy alongside NODF ranged from 2% to 28% and included zinc oxide paste (zinc), medical honey, debriding agents, antimicrobial wash, alginate, hydrophilic paste, and negative pressure therapy (Table 4). Overall use of adjuncts remained similar before and after the introduction of NODF, with 22% of patients receiving an active adjunct prior to NODF and 24% afterward (Table 5). However, the number of different adjunctive therapies employed declined following NODF introduction. The SOC cohort comprised patients treated with conventional wound management, including saline cleansing, debridement if indicated, dressings, and antimicrobial/honey as ordered (Table 6). All patients received appropriate pressure offloading and individualized nutritional support, including supplementation when indicated, based on each resident's nutritional status (e.g., intake adequacy, weight trends, and risk of malnutrition), in accordance with best-practice nutrition standards and each skilled nursing facility's policy. MDS Section K (Nutritional Assessment) normalizes behavior at the nursing home level. However, adherence to these interventions could not be directly confirmed and was treated as a potential source of residual confounding.

2.7 | Endpoints

The probabilistic primary study endpoint was complete wound closure or resolution within 12 weeks of treatment initiation.

TABLE 4 | Breakdown of adjunct therapies used with NODF arm.

	Zinc	Honey	Debriding agent	Anti-microbial	Alginate	Triad	Wound vac
Deep tissue injury	0.0%	2.0%	0.0%	9.0%	0.0%	0.0%	0.0%
Stage 1	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Stage 2	3.0%	2.0%	0.0%	0.0%	3.0%	3.0%	0.0%
Stage 3	3.0%	28.0%	9.0%	0.0%	6.0%	6.0%	0.0%
Stage 4	10.0%	0.0%	10.0%	10.0%	0.0%	0.0%	20.0%
Unstageable	0.0%	8.0%	16.0%	3.0%	5.0%	0.0%	0.0%

TABLE 5 | Historical care for the wounds in the NODF Arm, before the introduction of NODF.

	Zinc	Honey	Debriding agent	Anti-microbial	Alginate	Triad	Wound vac
Deep tissue injury	0.0%	2.0%	0.0%	5.0%	2.0%	0.0%	0.0%
Stage 1	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	4.0%
Stage 2	5.0%	8.0%	5.0%	0.0%	2.0%	3.0%	2.0%
Stage 3	3.0%	19.0%	6.0%	6.0%	0.0%	3.0%	0.0%
Stage 4	0.0%	0.0%	20.0%	0.0%	0.0%	0.0%	10.0%
Unstageable	0.0%	18.0%	8.0%	0.0%	13.0%	0.0%	0.0%

TABLE 6 | Breakdown of adjuncts used with standard of care.

	Zinc	Honey	Triad	Debridement agent	Alginate	Anti-microbial	Wound vac
Deep tissue injury	0.0%	0.0%	0.0%	0.0%	0.0%	100.0%	0.0%
Stage 2	0.0%	16.7%	0.0%	0.0%	0.0%	0.0%	0.0%
Stage 3	0.0%	10.8%	0.0%	9.2%	4.6%	5.4%	0.0%
Stage 4	0.0%	0.0%	0.0%	0.0%	20.8%	20.8%	0.0%
Unstageable	0.0%	10.3%	0.0%	16.4%	0.9%	27.6%	0.0%

Patients who were discharged before wound closure or resolution were censored, with healing progress quantified by change in wound area, consistent with prior pressure ulcer research [13]. Secondary outcomes included continuous wound area change analysed with hurdle–gamma models and exploratory analyses stratified by wound stage and age group.

2.8 | Bayesian Analysis

Bayesian methods were selected to provide a coherent probabilistic framework for estimating treatment effects and for propagating uncertainty across both the matching and outcome stages. Bayesian inference generates full posterior distributions that quantify uncertainty in estimated treatment effects within the matched sample [14, 15]. Several prior applications have demonstrated the advantages of Bayesian propensity score modeling for observational causal inference [16–18]. The Bayesian framework also allows flexible hierarchical modeling of clustered data, partial pooling, and robust estimation under limited overlap or small sample conditions. Together, these features make Bayesian methods particularly appropriate for real-world wound data, where treatment assignment is nonrandom, empirical wound-area distributions are mixtures, and patient and wound heterogeneity is expected.

Propensity score matching was performed using a Bayesian normal-logistic regression adjusting for baseline wound area [19] among other baseline covariates. Bayesian hierarchical models were employed to estimate treatment effects, an approach well-suited to real-world datasets with substantial heterogeneity [20, 21]. The primary analysis used a Bayesian hierarchical hurdle–gamma regression model, in which the hurdle component modeled binary healing outcomes and the gamma component modeled percent area reduction (PAR) among non-healed wounds. Posterior means and 95% credible intervals were reported for marginal and at-the-distributional-mean treatment effects. Hierarchical modeling allowed borrowing of information across wound stages and facilities, thereby improving estimation precision in smaller or unbalanced subgroups [21, 22].

Analyses were performed in Python (PYMC, BAMBI packages), with noninformative priors applied unless otherwise specified. Posterior convergence and model adequacy were confirmed by standard diagnostics. Bayesian inference was chosen for its flexibility and interpretability, as a 95% credible interval can be directly interpreted as the probability that the parameter lies within the interval, conditional on the data and model [20].

Despite good covariate balance on patient-level factors, wound stage remained imbalanced after matching due to limited overlap in stage distribution between treatment arms. This imbalance reflects a structural characteristic of the data rather than a failure of the matching procedure. The greedy matching algorithm prioritized overall similarity on the propensity score, which summarizes multidimensional covariate information, over exact categorical alignment, a strategy that is appropriate and commonly recommended when certain strata are sparsely populated or non-overlapping. Because wound stage is an ordered, monotonic measure of severity, enforcing exact matching on each category would have eliminated a substantial portion of treated cases, reduced overlap, and undermined generalizability of the treatment effect.

Instead of discarding observations, we retained the full matched sample and addressed residual stage imbalance analytically. The post-matching hierarchical model incorporated wound stage as a random effect, enabling partial pooling across adjacent stages to stabilize estimates for categories with few observations. This approach allows information sharing between clinically proximal wound stages and propagates uncertainty associated with sparse or missing strata. Consequently, the treatment effect estimation reflects both the underlying ordinal structure of wound severity and the observed imbalance, providing a principled adjustment without imposing restrictive or data-destructive matching constraints.

Because treatment was assigned at the patient level, matching needed to occur on patient-level characteristics to preserve causal alignment. Matching on individual wounds would ignore within-patient dependence and allow wounds from biologically and contextually distinct patients to be compared as if independent, introducing pseudo-replication and confounding. Patient-level matching therefore ensures that comparisons are made between individuals with comparable underlying risk profiles, whereas subsequent modeling of wound-level outcomes captures local heterogeneity without violating the unit of treatment assignment.

3 | Results

3.1 | Baseline Characteristics

The matched cohorts (200 NODF; 200 SOC) were well balanced on prespecified baseline factors (mean age 85.2 ($\sigma = 10.4$) years in SOC arm and 81.8 ($\sigma = 9.5$) in NODF arm, 39.5% male in both arms, average starting area of 12.6cm^2($\sigma = 18.95$) in SOC arm

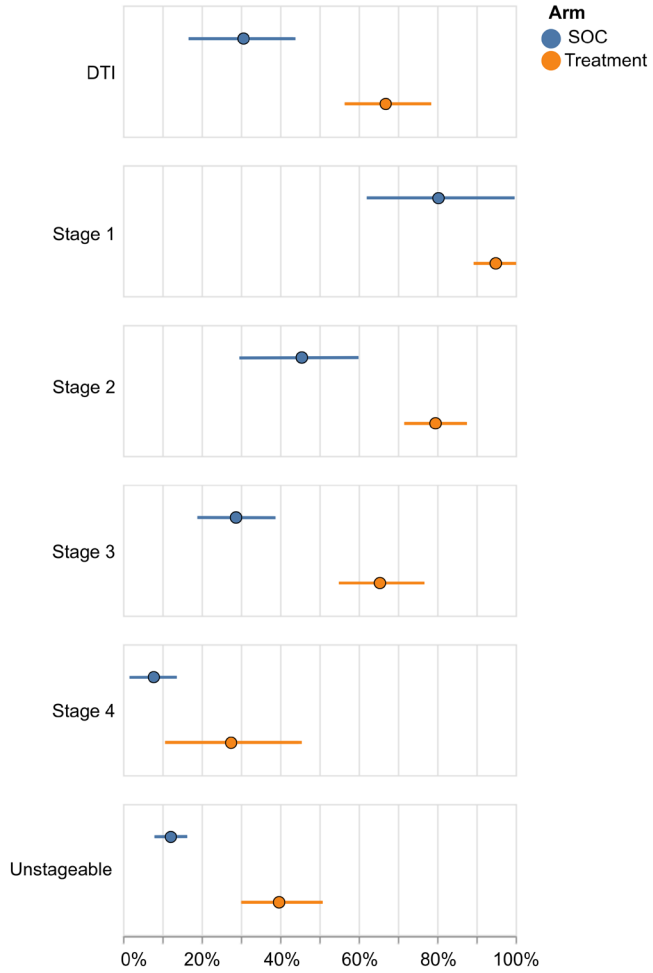

FIGURE 1 | Posterior mean 12-week average treatment effect (ATE) by stage (with 95% CrI) contrasts.

and 12.5cm^2($\sigma = 18.99$) in NODF arm, and a similar distribution of wound stages in each arm), supporting exchangeability of treatment groups for comparative effectiveness inference.

3.2 | Primary Endpoint: Complete Closure (Epithelialized or Had an Area of Zero) by 12 Weeks

Across all PrUs, the posterior 12-week average treatment effect (ATE) was 63% (95% CrI, 50%–75%) with NODF versus 34% (21%–47%) with SOC, a 29-percentage-point absolute improvement, or a risk ratio of 1.9 (1.6–2.5) (Figure 1). The stage-stratified posterior estimates are reproduced, and derived effect sizes and the significance assessment are shown (Table 7).

Posterior probability (Bayesian, 95% CrI rule):

- Significant NODF benefit (non-overlapping 95% CrIs): Stage 2, Deep Tissue Pressure Injury, Stage 3, Unstageable, and All PrUs (overall).
- Uncertain with the available summaries (overlapping 95% CrIs despite large point differences): Stage 1 and Stage 4. These could still be significant when assessed on the joint

TABLE 7 | Posterior mean 12-week average treatment effect (ATE) and effect sizes by stage (with 95% CrI).

	NODF healed	SOC healed	Absolute risk difference	Risk ratio	Odds ratio	NNT	Credible interval
Deep tissue injury	67.2% (57.0%–78.1%)	30.5% (17.7%–43.0%)	36.7% (35.1%–39.2%)	2.2 (1.8–3.2)	4.7 (4.7–6.1)	2.7 (2.5–2.8)	✓
Stage 1	94.4% (88.5%–100.0%)	79.0% (60.1%–100%)	15.4% (0.0%–28.4%)	1.2 (1.0–1.5)	4.4 (1.5–5.1)	6.5 (3.5–20000.0)	Uncertain
Stage 2	79.5% (72.0%–87.3%)	45.1% (31.4%–60.1%)	34.4% (27.2%–40.6%)	1.8 (1.5–2.3)	4.7 (4.6–5.6)	2.9 (2.5–3.7)	✓
Stage 3	64.4% (53.8%–75.1%)	27.6% (18.2%–37.0%)	36.8% (35.6%-38.2)	2.3 (2.0–3.0)	5.2 (4.7–5.2)	2.7 (2.6–2.8)	✓
Stage 4	33.7% (14.8%–51.0%)	10.0% (3.0%–17.1%)	23.7% (11.8%–34.0%)	3.4 (3.0–5.0)	5.1 (4.6–5.7)	4.2 (2.9–8.5)	Uncertain
Unstageable	39.0% (28.9%–49.4%)	11.7% (7.7%–15.2%)	27.3% (21.1%–34.2%)	3.3 (3.2–3.7)	4.8 (4.8–5.4)	3.7 (2.9–4.7)	✓
All PI's (Any)	63.0% (50.4%–75.1%)	34.0% (20.5%–46.7%)	29.0% (28.4%–29.9%)	1.9 (1.6–2.5)	3.4 (3.3–3.9)	3.4 (3.3–3.5)	✓

Note: Criteria: ✓ denotes non-overlapping 95% CrIs between groups (conservative indicator that the 95% CrI of the treatment difference would exclude 0). "Uncertain" indicates overlapping group CrIs—final significance should be determined from the joint posterior for the contrast.

posterior of the treatment difference; confirmation requires the model's contrast-level CrIs.

The evidence supports a clinically and statistically credible improvement in 12-week healing with NODF for most wound categories and overall. Stages 1 and 4 show large absolute benefits (15–24 percentage points) but overlapping group CrIs in the available summaries; reporting the contrast-level posterior summaries (risk difference or hazard ratio with 95% CrI) will clarify significance for these two strata.

4 | Discussion

Pressure ulcers represent a significant clinical and economic burden. Clinically, they may be associated with pain, infection, sepsis, prolonged hospital stays, reduced functional status, and increased mortality [5, 10]. Financially, the impact is staggering: in the United States alone, the annual cost of pressure ulcer-related care exceeds $26.8 billion, driven by extended hospitalizations, surgical interventions, and the management of complications [23]. As healthcare systems grapple with the demands of an aging population, these costs are projected to rise even further.

In this large real-world cohort of skilled nursing facility patients with PrUs, treatment with a nitric oxide–delivering foam demonstrated significantly improved healing outcomes compared to standard of care. At 12 weeks, a markedly higher proportion of NODF-treated wounds achieved complete closure (epithelialized or had an area of zero) across all stages of pressure ulcer. Rather than excluding sparse strata entirely or reporting unstable frequentist estimates (which would be undefined with zero events in a comparison group), partial pooling provides principled estimation by borrowing strength from adjacent wound stages while allowing Stage 1 to retain its own estimate. Additionally, wound stage was specified as an ordinal covariate, enabling the model to borrow more information from clinically adjacent stages (Deep Tissue and Stage 2), which is appropriate given the severity continuum. Bayesian analyses reinforced the robustness of these findings, with high probabilities indicating that the observed differences were unlikely to be due to chance.

The observed benefits of NODF are consistent with prior preclinical and clinical investigations highlighting the role of nitric oxide in wound biology. Nitric oxide is known to regulate multiple repair pathways, including angiogenesis, collagen synthesis, and the modulation of inflammatory responses [12]. Preclinical models have demonstrated enhanced tissue granulation and epithelialization in the presence of nitric oxide donors [24]. Clinical studies in chronic ulcers have further supported the beneficial effects of nitric oxide, with evidence of improved wound healing following topical delivery [25, 26]. The present findings build on this body of evidence by confirming that foam-based nitric oxide therapies can be effective in a large, heterogeneous cohort of SNF patients with PrUs, thus providing translational evidence that supports its clinical utility in routine practice.

These promising results suggest that integrating nitric oxide delivery into wound care protocols may not only accelerate healing in this high-risk population but also help reduce the overall financial burden on healthcare systems. Faster wound closure can lead to shorter hospital stays, fewer surgical interventions, and lower rates of complications: Factors that collectively have the potential to curb escalating costs and improve resource allocation in long-term care settings.

5 | Limitations

Several limitations should be acknowledged when interpreting these findings. First, the retrospective observational design introduces potential for residual confounding despite careful propensity score matching and sensitivity analyses. This retrospective observational design leverages real-world clinical data and is subject to the limitations of non-randomized studies, notwithstanding our attempts to ameliorate said limitations. Although Bayesian hierarchical modeling improves robustness, unmeasured factors, such as nutritional status, pressure offloading practices, or staff-to-patient ratios may still have influenced outcomes. Second, reliance on registry-based data limited the precision of wound assessments to those routinely collected in SNFs, and inter-rater variability in staging or measurement cannot be excluded. Third, the SOC arm used historical controls, which may introduce bias from temporal changes in wound care practices and facility protocols. Despite consistent eligibility criteria and analytic methods, residual confounding from unmeasured or incompletely captured factors (e.g., nutritional status, adherence to offloading, debridement frequency, staffing levels, and other facility-specific practices) must be considered. We acknowledge that using a weighted treatment affect does not fully resolve the methodological challenges posed by the wound stage's complexity. However, alternative PSM strategies; either ignoring stage or enforcing exact baseline stage balance may introduce less quantifiable bias. Marginal structural models (MSMs) have been proposed as an alternative, and we plan to explore their application in wound-care research in future work. Finally, the study follow-up was limited to 12 weeks, and long-term durability of healing, recurrence rates, and cost-effectiveness were not assessed. These constraints underscore the need for well-controlled prospective trials to validate and extend the present findings.

6 | Future Research

Given the strength of the findings in this real-world dataset, further evaluation of NODF in prospective randomized controlled trials is warranted. Such studies could refine estimates of efficacy, explore optimal treatment frequency and duration, and assess cost-effectiveness across different health-care settings. If confirmed, nitric oxide–delivering foams may become an important adjunct in pressure ulcer treatment and logically will apply to a wide variety of complex wounds.

Acknowledgements

The authors gratefully acknowledge the skilled nursing facility staff and registry coordinators for their dedication to accurate data collection and documentation. We also thank the independent data management

and statistical teams for their contributions to data extraction, cleaning, and analysis. The study was conducted with the oversight of the sponsor, and all analyses were performed in a secure, access-controlled environment to ensure data integrity and confidentiality.

Funding

This study was supported by NOxy Health Products Inc. The sponsor provided access to the de-identified registry and funded the statistical analyses. The sponsor had no role in clinical decision-making or patient care at participating skilled nursing facilities.

Ethics Statement

The study used fully de-identified registry and historical control data in accordance with institutional privacy standards. Participant consent was obtained in compliance with institutional policy. Institutional Review Board (IRB) review was sought from Advarra (IRB# 00000971; Protocol ID# PRO00086251, June 16, 2025) with exemption status determined based on de-identification. Data extraction and cleaning were performed by an independent third party, and all analyses were conducted under strict confidentiality protocols.

Conflicts of Interest

The authors declare no conflicts of interest. Author 1 is a former employee of the sponsor, developed the data registry during her employment, and contributed medical writing support for the manuscript. The authors declare that they have all received consulting fees for various roles in the development and preparation of this manuscript.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

1. European Pressure Ulcer Advisory Panel, National Pressure Injury Advisory Panel, & Pan Pacific Pressure Injury Alliance, *Prevention and Treatment of Pressure Ulcers/Injuries: Clinical Practice Guideline. The International Guideline*, ed. E. Haesler (EPUAP/NPIAP/PPPIA, 2019).

2. J. Kottner, J. Cuddigan, K. Carville, et al., "Pressure Ulcer/Injury Classification Today: An International Perspective," *Journal of Tissue Viability* 29, no. 3 (2020): 197–203.

3. L. J. Gould, J. Alderden, R. Aslam, et al., "WHS Guidelines for the Treatment of Pressure Ulcers-2023 Update," *Wound Repair and Regeneration* 32, no. 1 (2024): 6–33.

4. E. Roussou, G. Fasoi, A. Stavropoulou, et al., "Quality of Life of Patients With Pressure Ulcers: A Systematic Review," *Med Pharm Reports* 96, no. 2 (2023): 123–130, https://doi.org/10.15386/mpr-2531.

5. S. Zhang, G. Wei, L. Han, W. Zhong, Z. Lu, and Z. Niu, "Global, Regional and National Burden of Decubitus Ulcers in 204 Countries and Territories from 1990 to 2021: A Systematic Review," *Front Public Health* 26, no. 13 (2025): 1–11.

6. S. Graziadio, A. Serafin, N. Sanaeifar, et al., "An Unbrella Review of Systematic Reviews and Meta-Analysis of Prevalence and Incidence of Pressure Injuries in the United States," *Journal of Wound Management* 26, no. 3 (2025): 212–244.

7. P. McAuliffe, E. Winter, A. Talwar, et al., "Pressure Ulcer Trends in the United States: A Cross-Sectional Assessment from 2018-2019," *American Surgeon* 89, no. 12 (2023): 5609–5618.

8. A. Karahan, A. Abbasoglu, S. Isik, et al., "Factors Affecting Wound Healing in Individuals with Pressure Ulcers: A Retrospective Study," *Ostomy Wound Manage* 68, no. 3 (2022): 246–253.

9. H. Mohammed, D. Mannion, A. Cassata, and R. D. Fraser, "Trends in Pressure Injury Prevalence Rates and Average Days to Healing Associated with Adoption of a Comprehensive Wound Care Program and Technology in Skilled Nursing Facilities in the United States," *Wounds* 31, no. 1 (2024): 23–33.

10. B. Duluklu, J. Ivory, A. McElvaney, et al., "Frailty and Comorbidity in Older Adults With and Without Diabetes and Chronic Leg Ulcer: A Cross-Sectional Study," *Internal Wound Journal* 22, no. 1 (2025): 1–17.

11. S. M. Andrabi, N. S. Sharma, A. Karan, et al., "Nitric Oxide: Physiological Functions, Delivery, and Biomedical Applications," *Advanced Science* 10, no. 30 (2023): e2303259, https://doi.org/10.1002/advs.202303259.

12. D. A. Bell, C. M. Miller, and R. Sullivan, "A Continuous Mode of Action of Nitric Oxide in Hard-To-Heal Wound Healing," *Journal of Wound Care* 33, no. 12 (2024): 912–925, https://doi.org/10.12968/jowc.2024.0004.

13. P. M. Sheean, A. G. Gonzalez-Feliciano, A. Wong, and N. A. Stotts, "Pressure Ulcer Healing Trajectories and Factors Influencing Healing in a Long-Term Care Population," *Journal of Gerontological Nursing* 43, no. 1 (2017): 20–28.

14. L. C. McCandless, P. Gustafson, and A. R. Levy, "Bayesian Sensitivity Analysis for Unmeasured Confounding in Observational Studies," *Statistics in Medicine* 28, no. 8 (2009): 1062–1080.

15. C. M. Zigler and F. Dominici, "Uncertainty in Propensity Score Estimation: Bayesian Methods for Variable Selection and Model-Averaged Causal Effects," *Journal of the American Statistical Association* 109, no. 505 (2014): 95–107.

16. D. Kaplan and J. Chen, "Bayesian Propensity Score Analysis for Observational Studies," *Educational and Psychological Measurement* 72, no. 5 (2012): 863–880.

17. F. Li, K. L. Morgan, and A. M. Zaslavsky, "Balancing Covariates via Propensity Score Weighting," *Journal of the American Statistical Association* 110, no. 510 (2015): 741–754.

18. D. Talbot, J. Massé, A. Desgagné, and F. Légaré, "Bayesian Estimation of Causal Effects Using Propensity Score Functions in the Presence of Non-Overlap," *Statistics in Medicine* 34, no. 21 (2015): 3089–3104.

19. J. A. Tooze, G. K. Grunwald, and R. H. Jones, "Analysis of Repeated Measures Data With Clumping at Zero," *Statistical Methods in Medical Research* 11, no. 4 (2002): 341–355.

20. D. J. Spiegelhalter, K. R. Abrams, and J. P. Myles, *Bayesian Approaches to Clinical Trials and Health-Care Evaluation* (John Wiley & Sons, 2004).

21. A. Gelman, J. Hill, and A. Vehtari, *Regression and Other Stories* (Cambridge University Press, 2020).

22. R. McElreath, *Statistical Rethinking: A Bayesian Course With Examples in R and Stan*, 2nd ed. (CRC Press, 2020).

23. W. V. Padula and B. A. Delarmente, "The National Cost of Hospital-Acquired Pressure Injuries in the United States," *International Wound Journal* 16, no. 3 (2019): 634–640, https://doi.org/10.1111/iwj.13071.

24. M. B. Witte and A. Barbul, "Role of Nitric Oxide in Wound Repair," *American Journal of Surgery* 183, no. 4 (2002): 406–412.

25. R. Ahmed, R. Augustine, M. Chaudhry, et al., "Nitric Oxide-Releasing Biomaterials for Promoting Wound Healing in Impaired Diabetic Wounds: State of the Art and Recent Trends," *Biomedicine & Pharmacotherapy* 149 (2022): 112707, https://doi.org/10.1016/j.biopha.2022.112707.

26. M. J. Malone-Povolny, S. E. Maloney, and M. H. Schoenfisch, "Nitric Oxide Therapy for Diabetic Wound Healing," *Advanced Healthcare Materials* 8, no. 12 (2019): e1801210, https://doi.org/10.1002/adhm.201801210.