EFFECT OF WOUND EXUDATE SEVERITY ON TIME TO COMPLETE HEALING IN DIABETIC FOOT ULCERS: A REAL-WORLD LONGITUDINAL ANALYSIS (ExAct STUDY)

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INTRODUCTION

Diabetic foot ulcers are associated with substantial morbidity, healthcare utilization, and risk of amputation. Chronic wound exudate may reflect an inflammatory, protease-rich wound environment that disrupts extracellular matrix integrity, growth factor signaling, granulation, and epithelialization.

Although exudate management is a core component of wound care, the magnitude of delay in diabetic foot ulcer healing associated with increasing exudate severity has not been well quantified in real-world clinical practice.

OBJECTIVE

To quantify the association between wound exudate amount and time to complete healing among adults with diabetic foot ulcers treated in U.S. outpatient wound care centers.

METHOD

Design and data source: Retrospective cohort study using deidentified Net Health WoundExpert electronic health record data from U.S. outpatient wound care centers, 2002-2020.
Study population: Adults with eligible diabetic foot ulcers. Wounds were followed from first documented clinic visit until complete healing or censoring. Patients could contribute more than one wound.
Exposure: Exudate amount, assessed during routine care and categorized as none, mild, moderate, or heavy. Exudate was modeled as a time-varying exposure.
Outcome: Complete wound healing, defined as wound status recorded as closed, healed, resolved, or treatment complete.
Analysis: Marginal structural models with stabilized inverse probability of treatment and censoring weights were used to address time-varying confounding and informative censoring. Weighted Royston-Parmar flexible parametric survival models estimated hazard ratios, healing probabilities, and restricted mean survival time. Confidence intervals were estimated using patient-level clustered bootstrap procedures.

RESULTS

The analytic cohort comprised 8,176 patients contributing 14,743 diabetic foot ulcers, with patient and wound characteristics summarized in Table 1. The cohort was broadly representative of a real-world outpatient DFU population: mean age was 62.4 years, 66.5% of patients were male, 52.6% were obese, and diabetes was documented in 81.0%. The mean initial wound area was 12.0 cm², and Grade 1 and Grade 2 wounds were the most common wound stages, representing 32.0% and 31.0% of wounds, respectively (Table 1). The estimated probability of complete healing was 32.2% at 12 weeks, 55.2% at 24 weeks, and 69.1% at 36 weeks, indicating that a substantial proportion of ulcers remained unhealed for several months even before stratification by exudate severity (Table 1).

Table 1. Cohort Characteristics *(8,176 patients contributed 14,743 DFUs)*

Characteristic	Value
Mean age at initial visit	62.4 years
Male	66.5%
Obese	52.6%
Diabetes recorded	81.0%
Mean initial wound area	12.0 cm²
Most common wound grades	Grade 1: 32.0%; Grade 2: 31.0%

In the marginal structural Royston–Parmar flexible parametric survival model, increasing exudate severity was associated with progressively lower hazards of complete healing compared with wounds without exudate (Table 2). Mild exudate was associated with an adjusted hazard ratio of 0.11, moderate exudate with a hazard ratio of 0.06, and heavy exudate with a hazard ratio of 0.012, corresponding to approximately 89%, 94%, and 99% lower instantaneous healing rates, respectively, relative to no exudate (Table 2). This monotonic pattern supports the interpretation that exudate amount is not simply a descriptive wound feature, but a strong marker of delayed healing trajectory in DFU care.

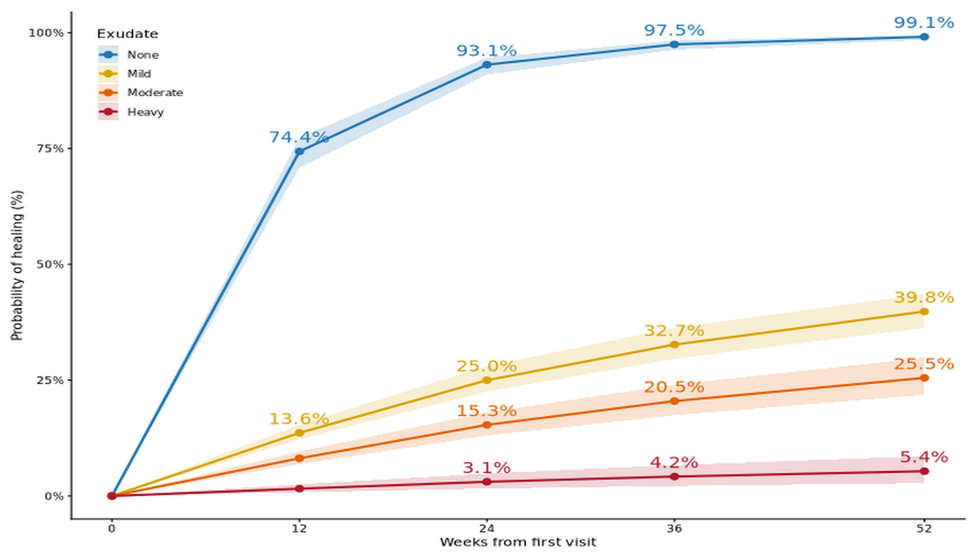
Table 2. Exudate severity and healing hazard

Exudate amount vs none	Adjusted hazard ratio	95% CI	Interpretation
Mild	0.11	0.09-0.12	~89% lower healing rate
Moderate	0.06	0.05-0.07	~94% lower healing rate
Heavy	0.012	0.006-0.019	~99% lower healing rate

Restricted mean survival time estimates provide an absolute measure of time spent unhealed and may be particularly useful for clinical and health-economic interpretation. The consistency of the hazard ratios, counterfactual healing curves, and restricted mean survival time estimates supports a clear severity gradient in which greater exudate burden is associated with substantially slower DFU healing.

These results should be interpreted in the context of routinely collected electronic health record data. Exudate was clinician-assessed using non-standardized categorical documentation, and residual confounding, informative visit patterns, coding variability, and unmeasured competing events such as amputation or death cannot be fully excluded. Nevertheless, the large sample size, time-varying exposure approach, inverse probability weighting, and complementary reporting of relative and absolute estimands strengthen the clinical interpretability of the findings.

Figure 1. Counterfactual healing curves under hypothetical scenarios with exudate level fixed as none, mild, moderate, or heavy



CONCLUSIONS

- Higher wound exudate levels were strongly associated with substantially slower diabetic foot ulcer healing.
- The association showed a clear severity gradient: mild, moderate, and heavy exudate were each associated with progressively lower healing rates, lower model-estimated healing probabilities, and longer duration unhealed.
- Exudate amount may serve as a clinically meaningful prognostic marker and a modifiable target within comprehensive diabetic foot ulcer care pathways.

HEOR and Clinical Implications

- Delayed healing associated with higher exudate burden may increase clinic visits, dressing changes, debridement, advanced therapy use, infection risk, hospitalization, and amputation-related costs.
- Restricted mean survival time provides an absolute measure of delayed healing that can support health economic modeling, cost-effectiveness analyses, and payer decision-making around targeted exudate assessment and management.

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