Health Economic Assessment of Skin Substitute Graft Use for Diabetic Foot Ulcers in Hospital Outpatient Departments

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INTRODUCTION

Diabetic foot ulcers (DFUs) present a major clinical and economic challenge, often leading to prolonged care and increased healthcare costs.[1] Advanced wound care modalities such as skin substitutes as adjuncts to standard care have demonstrated well-established clinical benefits including improved healing rates, reduced amputation risk, and shorter time to closure.[2,3] Despite a wide variety of available skin substitutes, ranging from cellular and tissue-based constructs to acellular dermal matrices, their comparative cost-effectiveness remains insufficiently characterized, especially within outpatient care settings. As healthcare systems increasingly emphasize value-based care, identifying higher-value skin substitutes that optimize both clinical outcomes and cost efficiency has become essential for payers, providers, and policy makers. DFU care is intensive and costly, with clinical outcomes and treatment costs directly influencing product selection, and reimbursement decisions, especially considering recent Centers for Medicare and Medicaid Services (CMS) policy changes. This study evaluated the cost-effectiveness of 11 skin substitutes for DFU management in hospital outpatient departments (HOPDs), based on healing outcomes and CMS treatment costs.

METHODS

A literature review identified published clinical data with healing rates and number of applications for each skin substitute in patients with Wagner grade 1-2 DFUs: (Wagner 3-4 or similar for deep wound studies wherever available), Dermacell AWM® (LifeNet Health®, VA, USA)[4,5], TheraSkin® (LifeNet Health®, VA, USA)[6], Kerecis® Omega 3 (Kerecis LLC, VA, USA)[7,8], Grafix® Core (Smith & Nephew, England, UK)[9,10], OASIS® wound matrix (Smith & Nephew, England, UK)[11], OASIS® trilayer wound matrix (Smith & Nephew, England, UK)[12], GraftJacket™ (Wright Medical, TN, USA)[4], Integra® DRT (Integra LifeSciences, NJ, USA)[13], EPIFIX® (MIMEDX Group, Inc., GA, USA)[14], Apligraf® (Organogenesis Inc., MA, USA)[14], and Dermagraft® (Organogenesis Inc., MA, USA)[15]. Cost-effectiveness analyses compared reported 12-week and 16-week healing rates wherever available to total cost of treatment in HOPDs. Cost data were derived from Q3 2025 CMS Hospital Outpatient Prospective Payment System (OPPS) and Physician Fee Schedule (PFS) rates using product-specific HCPCS and CPT codes. A standardized effectiveness measure (DFUs healed per 100 patients per $1,000 spent) was calculated to allow direct comparison across products with varying unit sizes and pricing structures. Incremental cost-effectiveness with respect to Dermacell was also measured. Cost per additional DFU healed was calculated as the incremental cost-effectiveness ratio by dividing the difference in per-patient cost by the difference in healing rates compared to Dermacell.

RESULTS

Healing rates at 12 weeks ranged from 30% to 62%, while the average cost per DFU treated varied from $2,304 to $16,702. A standardized effectiveness analysis showed substantial differences in economic value, ranging from 3.4 to 23.0 DFUs healed per 100 patients per $1,000 spent. Using Dermacell as the reference comparator, incremental cost-effectiveness analysis demonstrated that TheraSkin exhibited minimal incremental cost ($1,593 per patient) with a 7.4 percentage point improvement in 12-week healing rates. Kerecis Omega 3, Grafix, and OASIS Ultra incurred high (> $4000) incremental cost per patient while achieving a higher percentage point improvement in 12-week healing rates. GraftJacket, Integra DRT, EPIFIX, Apligraf, Oasis wound matrix, and Dermagraft demonstrated an unfavorable cost-effectiveness profile, i.e., they cost more per patient than Dermacell and achieved lower healing rates at 12 weeks. For 16-week healing outcomes and 12-week healing outcomes in DFUs with deep wounds such as exposed structures (bones, tendons, etc.), evaluated products demonstrated minimal or no additional healing benefit compared to Dermacell, despite requiring higher treatment costs.

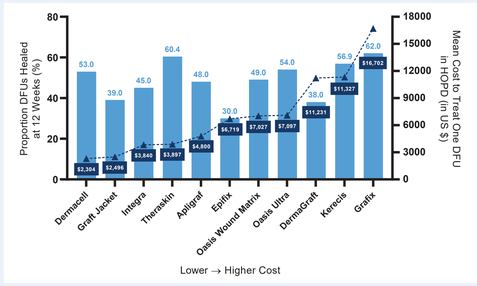


Figure 1: 12- week healing rate with average cost in HOPDs. Cost-effectiveness analysis based on published 12- week healing rates, published number of applications and Q3 2025 CMS data for treating DFUs in HOPDs. Triangle markers show the average cost of treating one DFU.

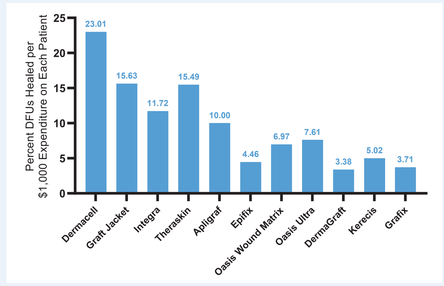
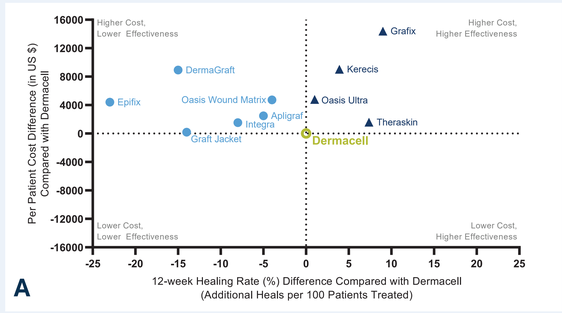
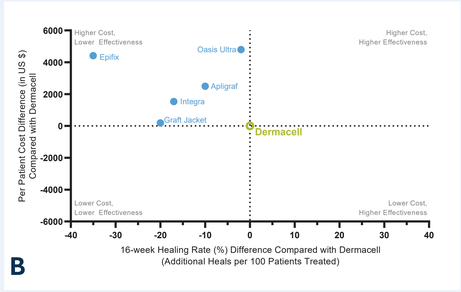


Figure 2: Ratio of patients healed per $1000. The estimated number of DFUs healed in 12 weeks out of 100 DFUs per $1000 expenditure with each patient.





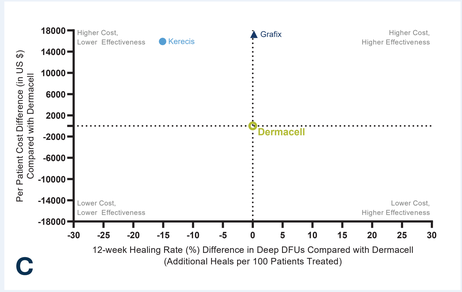


Figure 3: Incremental cost-effectiveness of skin substitutes relative to Dermacell for DFU management in HOPD settings. The x-axis represents the difference in **(A)** 12-week healing rates **(B)** 16-week healing rates whenever available in literature (additional heals per 100 patients treated), **(C)** 12-week healing rates for deep wound DFUs (Not all products are included in this figure due to lack of published data points for those products). The y-axis shows the difference in cost per patient. Products positioned in the upper-left quadrant indicate higher cost with lower effectiveness. The upper-right quadrant represents higher cost with higher effectiveness. Lower-left quadrant represents lower cost with lower effectiveness and lower-right quadrant represents lower cost with higher effectiveness. Inherent methodological variation may impact the accuracy of comparisons.

DISCUSSION

Healing outcomes and CMS treatment costs varied substantially among skin substitutes used to treat DFUs in HOPDs. Dermacell demonstrated favorable cost-effectiveness as a reference comparator, with TheraSkin showing comparable cost-effectiveness with minimal incremental cost. Other products showed higher incremental expenditures, ranging from $160,000 to $479,000 per additional DFU healed, while several alternatives achieved lower healing rates at higher costs (e.g., lower-value). These findings highlight the importance of HOPD and physician selection of higher-valued skin substitute products that are able to achieve both clinical and economic efficacy. This study is limited by the absence of sensitivity analysis and by inherent cross-study heterogeneity in trial designs, patient populations, and wound characteristics. Future studies incorporating long-term outcomes, quality-adjusted life years, amputation rates, and real-world effectiveness data would strengthen the evidence base for resource utilization decisions in DFU management.

CONCLUSION

Skin substitutes for DFU treatment in the HOPD setting demonstrated varied cost-effectiveness profiles. Integrating healing outcomes with direct cost data reveals that higher expenditure on skin substitutes may not always result in better healing rates, highlighting that more expensive products are not necessarily more effective on an incremental basis.

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REFERENCES

1. Armstrong DG, Boulton AJM, Bus SA. Diabetic Foot Ulcers and Their Recurrence. *New England Journal of Medicine*. 2017;376(24):2367–2375. doi:doi:10.1056/NEJMra1615439
2. Gordon AJ, Alfonso AR, Nicholson J, Chiu ES. Evidence for Healing Diabetic Foot Ulcers With Biologic Skin Substitutes: A Systematic Review and Meta-Analysis. *Ann Plast Surg*. Oct 2019;83(4S Suppl 1):S31–s44. doi:10.1097/sap.0000000000002096
3. Sui L, Xie Q, Jiang H-t, Li X-d. Effectiveness and safety of dermal matrix used for diabetic foot ulcer: a systematic review and meta-analysis of randomized controlled trials. *BMC Endocrine Disorders*. 2024;24(1):23.
4. Cazzell S, Vayser D, Pham H, et al. A randomized clinical trial of a human acellular dermal matrix demonstrated superior healing rates for chronic diabetic foot ulcers over conventional care and an active acellular dermal matrix comparator. Wound Repair and Regeneration. 2017;25(3):483–497. doi:https://doi.org/10.1111/wrr.12551
5. Cazzell S, Moyer PM, Samsell B, Dorsch K, McLean J, Moore MA. A Prospective, Multicenter, Single-Arm Clinical Trial for Treatment of Complex Diabetic Foot Ulcers with Deep Exposure Using Acellular Dermal Matrix. *Advances in skin & wound care*. Sep 2019;32(9):409–415. doi:10.1097/01.ASW.0000569132.38449.c0
6. Landsman AS, Cook J, Cook E, et al. A retrospective clinical study of 188 consecutive patients to examine the effectiveness of a biologically active cryopreserved human skin allograft (TheraSkin®) on the treatment of diabetic foot ulcers and venous leg ulcers. *Foot & ankle specialist*. Feb 2011;4(1):29–41. doi:10.1177/1938640010387417
7. Lantis Ii JC, Lullove EJ, Liden B, et al. Final efficacy and cost analysis of a fish skin graft vs standard of care in the management of chronic diabetic foot ulcers: a prospective, multicenter, randomized controlled clinical trial. *Wounds : a compendium of clinical research and practice*. Apr 2023;35(4):71–79. doi:10.25270/wnds/22094
8. Dardari D, Piaggesi A, Potier L, et al. Intact Fish Skin Graft to Treat Deep Diabetic Foot Ulcers. *NEJM Evid*. Dec 2024;3(12):EVIDoa2400171. doi:10.1056/EVIDoa2400171
9. Lavery LA, Fulmer J, Shebetka KA, et al. The efficacy and safety of Grafix(®) for the treatment of chronic diabetic foot ulcers: results of a multi-centre, controlled, randomised, blinded, clinical trial. *International wound journal*. Oct 2014;11(5):554–60. doi:10.1111/iwj.12329
10. Frykberg RG, Gibbons GW, Walters JL, Wukich DK, Milstein FC. A prospective, multicentre, open-label, single-arm clinical trial for treatment of chronic complex diabetic foot wounds with exposed tendon and/or bone: positive clinical outcomes of viable cryopreserved human placental membrane. International wound journal. Jun 2017;14(3):569–577. doi:10.1111/iwj.12649
11. Niezgoda JA, Van Gils CC, Frykberg RG, Hodde JP. Randomized clinical trial comparing OASIS Wound Matrix to Regranex Gel for diabetic ulcers. *Advances in skin & wound care*. Jun 2005;18(5 Pt 1):258–66. doi:10.1097/00129334-200506000-00012
12. Cazzell SM, Lange DL, Dickerson JE, Jr., Slade HB. The Management of Diabetic Foot Ulcers with Porcine Small Intestine Submucosa Tri-Layer Matrix: A Randomized Controlled Trial. *Advances in wound care*. Dec 1 2015;4(12):711–718. doi:10.1089/wound.2015.0645
13. Driver VR, Lavery LA, Reyzelman AM, et al. A clinical trial of Integra Template for diabetic foot ulcer treatment. *Wound repair and regeneration : official publication of the Wound Healing Society [and] the European Tissue Repair Society*. Nov–Dec 2015;23(6):891–900. doi:10.1111/wrr.12357
14. Kirsner RS, Sabolinski ML, Parsons NB, Skornicki M, Marston WA. Comparative effectiveness of a bioengineered living cellular construct vs. a dehydrated human amniotic membrane allograft for the treatment of diabetic foot ulcers in a real world setting. *Wound repair and regeneration : official publication of the Wound Healing Society [and] the European Tissue Repair Society*. Sep 2015;23(5):737–44. doi:10.1111/wrr.12332
15. Kraus I, Sabolinski ML, Skornicki M, Parsons NB. The Comparative Effectiveness of a Human Fibroblast Dermal Substitute versus a Dehydrated Human Amnion/Chorion Membrane Allograft for the Treatment of Diabetic Foot Ulcers in a Real-world Setting. *Wounds : a compendium of clinical research and practice*. May 2017;29(5):125–132.

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