COMPARATIVE EFFECTIVENESS FOR MEDICARE BENEFICIARIES WITH DIABETIC FOOT ULCERS (DFUs) TREATED WITH AND WITHOUT ADVANCED SKIN SUBSTITUTE PRODUCTS

Urvi Desai, PhD;[1] J. Bradford Rice, PhD;[1] Jian-Yu E , ScD;[1] Serena Kongara, MPH;[1] Justin Chun, MHS;[1] Robert S. Kirsner, M.D., PhD[2]

[1]Analysis Group Inc., Boston, MA USA, [2]Director, University of Miami Hospital and Clinics Wound Center, University of Miami Miller School of Medicine, Miami, FL USA

INTRODUCTION

- DFUs are a costly complication of diabetes contributing to significant morbidity and mortality due to hospital admissions and risk of lower-limb amputations[1]
- Among all costs associated with diabetes, at least 33% were linked to the treatment of DFUs[2], affecting nearly 13% of the US population with diabetes[3]
- Effective intervention is crucial for reduction of major amputations and the improved treatment of acute and chronic wounds, which will in turn increase quality of life, and decrease DFU-related costs[2]
- Advanced skin substitutes included living technology (Apligraf[(a)], Dermagraft[(a)]), placental allografts (Affinity[(a)], Epifix, Grafix Core, Grafix Prime, Nushield[(a)]), collagen dressings (Oasis, PriMatrix, PuraPly AM[(a)]) and cadaveric skin grafts (TheraSkin). Non-skin substitutes include debridement, negative pressure wound therapy, drainage, use of offloading devices, compression therapy, and hyperbaric oxygen therapy.
- Skin substitute use has been supported by the results of randomized clinical trials[4] but there is limited information about the real-world clinical and economic outcomes associated with using skin substitutes in patients with DFUs
- [(a)]Organogenesis Inc., Canton, MA

OBJECTIVE

- To better understand the profiles of patients receiving skin substitutes versus patients not receiving skin substitutes (non-skin substitutes) for DFUs
- To compare the real-world rates of non-traumatic lower-limb amputations, all-cause medical use, and number of DFU-related medical events for patients with DFUs receiving skin substitutes versus non-skin substitutes

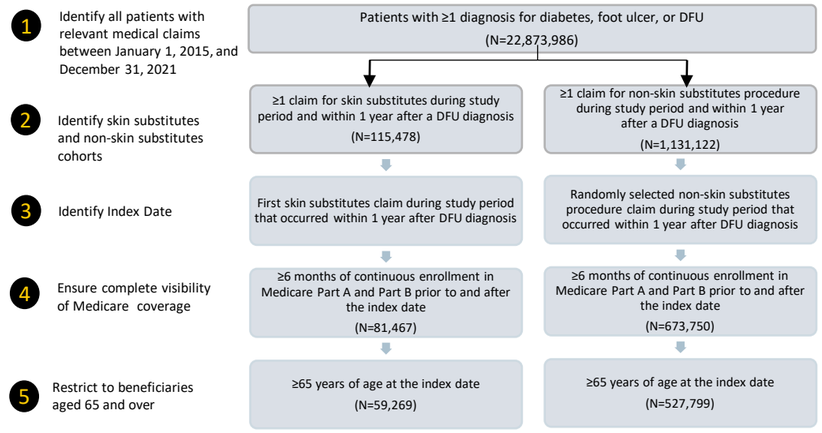
DATA SOURCE AND STUDY DESIGN

- The study used de-identified administrative claims data for the 100% sample of fee-for-service Medicare beneficiaries (Q1 2015-Q4 2021)
- The analysis is based on an "intent to treat" design with patients assigned to mutually exclusive categories based on whether or not they were treated with skin substitutes in 2016 or later years
- The first observed claim for skin substitutes or a randomly selected non-skin substitutes procedure during the study period that occurred within 1 year after a DFU diagnosis was designated as the index date
- Beneficiaries receiving skin substitutes were matched 1:1 to those not receiving skin substitutes using propensity score matching algorithm which accounted for baseline differences in patient characteristics outlined in Table 1
- The baseline and follow-up periods each consisted of the 6 months prior to and following the index date, respectively

STUDY MEASURES

- Baseline differences in demographics, comorbid conditions, wound severity, and healthcare resource use (HCRU) by place of service (outlined in Table 1) were compared before matching using Wilcoxon rank-sum tests for continuous measures and chi-square tests for categorical measures
- Baseline characteristics, rates of non-traumatic lower limb amputation, and HCRU over 6 months post-index were compared for matched cohorts using Wilcoxon sign-rank tests for continuous measures and McNemar's tests for categorical measures

SAMPLE SELECTION



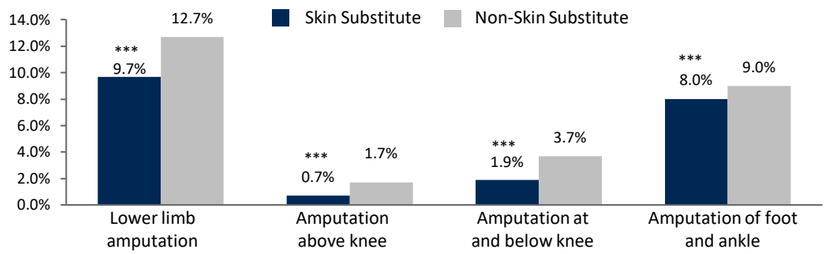
Note: Procedures qualifying for non-skin substitutes include debridement, negative pressure wound therapy, drainage, use of offloading devices, compression therapy, hyperbaric oxygen therapy.

TABLE 1. BASELINE SAMPLE CHARACTERISTICS

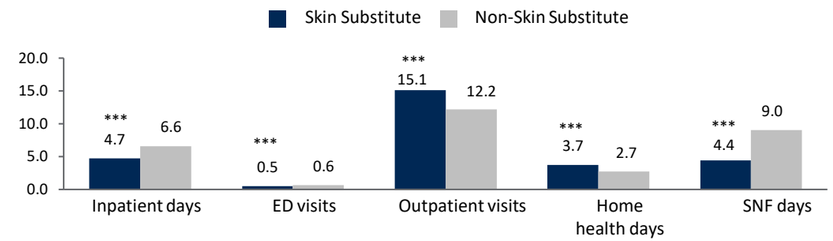
Selected characteristics	Pre-match			Post-match		
	Skin substitutes (N=59,269)	Non-skin substitutes (N=527,799)	P-value	Skin substitutes (N = 58,491)	Non-skin substitutes (N= 58,491)	P-value
Patient Demographics/Comorbidities						
Age, mean	75.9	77.5	<0.001	75.9	75.9	0.290
Male	62.0%	53.9%	<0.001	61.9%	62.7%	0.002
Charlson comorbidity index, mean	3.1	2.9	<0.001	3.1	3.2	<0.001
Select comorbid conditions, %						
Diabetes with complications	78.7%	66.2%	<0.001	78.5%	76.6%	<0.001
Peripheral vascular disease	69.8%	52.2%	<0.001	69.6%	63.5%	<0.001
Cerebrovascular disease	21.4%	22.0%	<0.001	21.3%	23.6%	<0.001
Congestive heart failure	39.7%	34.3%	<0.001	39.7%	39.0%	0.013
COPD	23.1%	21.8%	<0.001	23.1%	23.5%	0.114
Renal disease	46.5%	38.6%	<0.001	46.4%%	45.4%	0.001
Myocardial infarction	16.1%	12.2%	<0.001	16.1%	15.8%	0.185
Number of unique DFU diagnosis, mean	16.5	5.0	<0.001	15.8	14.4	<0.001
Severity						
Months of active ulceration	5.5	3.4	<0.001	5.5	5.9	<0.001
DFU related infections	68.2%	47.4%	<0.001	67.8%	69.7%	<0.001
Non-traumatic lower limb amputation	12.6%	6.4%	<0.001	12.4%	12.8%	0.037

RESULTS

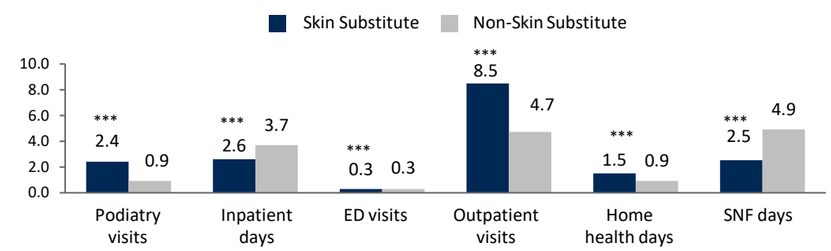
Non-traumatic lower-limb amputations during 6-month follow-up period after matching



All-cause medical use during 6-month follow-up period after matching



Number of DFU-related medical events during 6-month follow-up period after matching



Statistical significance of difference between skin substitutes and non-skin substitutes: *P<0.05, ** P<0.01, ***P<0.001.

LIMITATIONS AND CONCLUSIONS

- While the study controlled for numerous proxies for wound severity, clinical measures (e.g., wound size and depth) were not directly observable in the database
- Study findings are limited to fee-for-service Medicare beneficiaries aged ≥65 years
- Skin substitutes are disproportionately used in more complex patients, with more severe DFU
- Despite this, use of skin substitutes is associated with improved patient outcomes and healthcare resource utilization – particularly with respect to inpatient and SNF use over the 6 months post-treatment compared with not using skin substitutes in patients with DFUs

REFERENCES

1. Jodheea-Jutton A et al. *The Foot*. 2022:101909. **2.** Driver VR et al. *J Am Podiatr Med Assoc*. 2010;100(5):335-341. **3.** Zhang P et al. *Ann Med*. 2017;49(2):106-116. **4.** Santema TK et al. *Wound Repair*. 2016;24(4):737-744.

ORGANOGENESIS

Presented at Symposium on Advanced Wound Care Fall, November 2-5, 2023.

Acknowledgements and Financial Disclosures
Research funding provided by Organogenesis, Inc.
Dr. Kirsner serves as a scientific adviser for Organogenesis.