

INPLASY202560038
doi: 10.37766/inplasy2025.6.0038
Received: 9 June 2025
Published: 9 June 2025

Corresponding author:
Zwelithini Tunyiswa

zweli@openwoundresearch.com

Author Affiliation:
Open Wound Research LLC.

Bayesian hierarchical meta-analysis of CAMPS versus standard of care for diabetic foot ulcer covered products: A protocol for systematic review of evidence from Medicare’s 2024 final Local Coverage Determinations

Tunyiswa, Z; Frykberg, RG; Dirks, R.

ADMINISTRATIVE INFORMATION

Support - All funding was provided by Open Wound Research LLC. Open-access publication fees were supported by Biostem Technologies.

Review Stage at time of this submission - The manuscript is being written.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202560038

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 9 June 2025 and was last updated on 9 June 2025.

INTRODUCTION

Review question / Objective PICOS Framework: Population (P): Adults with diabetic foot ulcers (DFUs), as enrolled in the RCTs listed in Table 1 (Evidence for Covered Products for DFU) of the 2024 Skin Substitute Grafts/Cellular and Tissue-Based Products for the Treatment of Diabetic Foot Ulcers and Venous Leg Ulcers Local Coverage Determinations(LCD's). Intervention (I): Cellular and/or Tissue-Based Products (CAMPS) listed as covered in the LCD (Table 1: Evidence for Covered Products for DF). Comparator (C): Standard of Care (SOC) Outcomes (O): Primary outcome—complete wound healing by final follow-up; Additional outcome—individual study sample size per arm. Study Design (S): Randomized Controlled Trials (RCTs) listed in the Medicare LCD evidence table.

Rationale The 2024 Medicare LCDs applied GRADE ratings but did not statistically synthesize

healing effect sizes or sample size across covered products covered for DFU. This meta-analysis addresses that evidence gap using a principled, probabilistic approach.

Condition being studied Chronic diabetic foot ulcers (DFUs).

METHODS

Search strategy Not applicable. All studies are pre-specified from in Table 1 (Evidence for Covered Products for DFU) of the 2024 Skin Substitute Grafts/Cellular and Tissue-Based Products for the Treatment of Diabetic Foot Ulcers and Venous Leg Ulcers Local Coverage Determinations(LCD's).

Participant or population Adults with DFUs enrolled in Table 1 (Evidence for Covered Products for DFU) of the 2024 Skin Substitute Grafts/Cellular and Tissue-Based Products for the Treatment of

Diabetic Foot Ulcers and Venous Leg Ulcers Local Coverage Determinations(LCD's).

Intervention CAMPS products listed as covered in Table 1 (Evidence for Covered Products for DFU) of the 2024 Skin Substitute Grafts/Cellular and Tissue-Based Products for the Treatment of Diabetic Foot Ulcers and Venous Leg Ulcers Local Coverage Determinations(LCD's).

Comparator Standard of Care (SOC) arms in Table 1 (Evidence for Covered Products for DFU) of the 2024 Skin Substitute Grafts/Cellular and Tissue-Based Products for the Treatment of Diabetic Foot Ulcers and Venous Leg Ulcers Local Coverage Determinations(LCD's).

Study designs to be included Randomized Control Trials (RCTs).

Eligibility criteria Inclusion: Randomized Control Trials with CAMPS arms in Table 1 (Evidence for Covered Products for DFU) of the 2024 Skin Substitute Grafts/Cellular and Tissue-Based Products for the Treatment of Diabetic Foot Ulcers and Venous Leg Ulcers Local Coverage Determinations(LCD's).

Information sources Sole source: Table 1 (Evidence for Covered Products for DFU) of the 2024 Skin Substitute Grafts/Cellular and Tissue-Based Products for the Treatment of Diabetic Foot Ulcers and Venous Leg Ulcers Local Coverage Determinations(LCD's).

Main outcome(s) Complete wound healing at final follow-up (typically 12–20 weeks).

Additional outcome(s) Individual study total sample size.

Data management Two-reviewer extraction with resolution by consensus. Data and code managed in GitHub. Analysis in Python using Bambi and ArviZ.

Quality assessment / Risk of bias analysis GRADE ratings from Table 1 (Evidence for Covered Products for DFU) of the 2024 Skin Substitute Grafts/Cellular and Tissue-Based Products for the Treatment of Diabetic Foot Ulcers and Venous Leg Ulcers Local Coverage Determinations(LCD's).LCD Table 1 used as-is. No additional risk of bias tools applied.

Strategy of data synthesis Quantitative analysis will use a Bayesian hierarchical (mixed-effects) beta-binomial model with uninformative priors.

Binomial outcome (healed / total). Effect measure: Risk Ratio with 95% credible intervals. Random intercepts for product and study. Missing SOC arms will be simulated using posterior predictive distributions conditioned on the model structure to generate synthetic SOC comparators for single-arm CAMPS studies.

Subgroup analysis

By individual study.

By individual CAMPS product.

Sensitivity analysis

Sensitivity to prior specification will be tested:

- Non-informative priors
- Informative priors
- Skeptical priors

Posterior distributions and model diagnostics will be compared to evaluate robustness.

Language restriction English-only.

Country(ies) involved United States of America.

Other relevant information Public GitHub repository will host data, code, figures.

Keywords Bayesian meta-analysis; diabetic foot ulcer; wound healing; CAMPS; Medicare LCD; hierarchical model; beta-binomial.

Dissemination plans Manuscript will be submitted to The International Journal of Tissue Repair. Results will be disseminated via journal publication, conference presentations, GitHub repository, and communication with wound care stakeholders.

Contributions of each author

Author 1 - Zwelithini Tunyiswa - Conceptualization, modeling, manuscript writing.

Email: zweli@openwoundresearch.com

Author 2 - Robert Frykberg - Conceptualization, modeling, manuscript writing.

Email: rgfdpm@openwoundresearch.com

Author 3 - Ryan Dirks - Clinical interpretation.

Email: ryandirks@unitedwoundhealing.com