

Supplementary Table S1

Supplementary Table S1. Adjusted linear mixed-effects models for patient-reported outcomes (intention-to-treat population, N = 90)

Panel A: Patient Empowerment (IR-DES-28)

Model specification: Linear mixed-effects model with participant-level random intercepts and unstructured covariance structure. Restricted maximum likelihood (REML) estimation. Adjusted for age (continuous, years), duration of diabetes (continuous, years), body mass index (continuous, kg/m²), HbA1c (continuous, %), and baseline infection severity (categorical: mild vs. moderate). Missing outcome data handled under the missing-at-random assumption using all available observations.

Fixed effect	β	SE	95% CI	df	t	P value
Intercept	68.42	4.87	58.85 to 77.99	82.3	14.05	<0.001
Group (Intervention vs. Control)	1.52	1.79	−2.01 to 5.05	83.1	0.85	0.398
Time (Post-intervention vs. Baseline)	3.24	1.18	0.92 to 5.56	164.7	2.75	0.007
Time (Two-month follow-up vs. Baseline)	4.35	1.17	2.05 to 6.65	164.9	3.72	<0.001
Group × Time (Post-intervention)	4.31	1.35	1.66 to 6.96	165.2	3.19	0.002
Group × Time (Two-month follow-up)	6.58	1.36	3.91 to 9.25	165.4	4.84	<0.001
Age (years)	−0.08	0.11	−0.30 to 0.14	82.7	−0.73	0.468
Duration of diabetes (years)	0.05	0.22	−0.38 to 0.48	82.5	0.23	0.819
BMI (kg/m ²)	0.14	0.19	−0.23 to 0.51	83.0	0.74	0.462
HbA1c (%)	−0.62	0.68	−1.96 to 0.72	82.8	−0.91	0.365
Baseline infection severity (Moderate vs. Mild)	−2.15	1.71	−5.52 to 1.22	82.9	−1.26	0.211

Variance components:

- Random intercept variance: 41.28 (SE = 6.82)
- Residual variance: 22.15 (SE = 2.47)
- Intraclass correlation coefficient (ICC): 0.65

Model diagnostics:

- $-2 \log$ likelihood: 1756.42
- Akaike information criterion (AIC): 1780.42
- Bayesian information criterion (BIC): 1824.75
- Residual normality (Shapiro–Wilk test on standardized residuals): $W = 0.991$, $P = 0.38$
- Homoscedasticity (Levene's test on residuals by time point): $P = 0.67$

Interpretation: After adjustment for covariates, the treatment-by-time interactions remained statistically significant at both post-intervention ($P = 0.002$) and two-month follow-up ($P < 0.001$). The adjusted estimates were slightly larger than the unadjusted estimates (4.31 vs. 4.24 at post-intervention; 6.58 vs. 6.47 at two-month follow-up), indicating that covariate adjustment did not attenuate the treatment effect.

Panel B: Diabetic Foot Self-Care (DFSQ-UMA)

Model specification: Identical to Panel A.

Fixed effect	β	SE	95% CI	df	t	P value
Intercept	49.87	4.23	41.55 to 58.19	82.4	11.79	<0.001
Group (Intervention vs. Control)	0.38	1.58	−2.73 to 3.49	83.2	0.24	0.811
Time (Post-intervention vs. Baseline)	4.48	1.10	2.32 to 6.64	164.8	4.07	<0.001
Time (Two-month follow-up vs. Baseline)	6.35	1.11	4.17 to 8.53	165.0	5.72	<0.001
Group $\times$ Time (Post-intervention)	0.15	1.26	−2.32 to 2.62	165.3	0.12	0.905
Group $\times$ Time (Two-month follow-up)	0.92	1.27	−1.57 to 3.41	165.5	0.72	0.472
Age (years)	0.06	0.10	−0.14 to 0.26	82.6	0.60	0.550

Duration of diabetes (years)	−0.03	0.19	−0.40 to 0.34	82.5	−0.16	0.873
BMI (kg/m²)	0.08	0.16	−0.23 to 0.39	83.1	0.50	0.618
HbA1c (%)	−0.35	0.58	−1.49 to 0.79	82.9	−0.60	0.550
Baseline infection severity (Moderate vs. Mild)	−1.82	1.45	−4.68 to 1.04	83.0	−1.26	0.211

Variance components:

- Random intercept variance: 35.74 (SE = 5.91)
- Residual variance: 19.62 (SE = 2.19)
- Intraclass correlation coefficient (ICC): 0.65

Model diagnostics:

- −2 log likelihood: 1698.86
- Akaike information criterion (AIC): 1722.86
- Bayesian information criterion (BIC): 1767.19
- Residual normality (Shapiro–Wilk test on standardized residuals): W = 0.987, P = 0.24
- Homoscedasticity (Levene's test on residuals by time point): P = 0.71

Interpretation: After adjustment for covariates, the treatment-by-time interactions for foot self-care remained non-significant at both post-intervention (P = 0.905) and two-month follow-up (P = 0.472), consistent with the unadjusted analyses. The adjusted estimates were similar in magnitude to the unadjusted estimates (0.15 vs. 0.13 at post-intervention; 0.92 vs. 0.87 at two-month follow-up), confirming that covariate adjustment did not materially change the findings.

Summary of Adjusted vs. Unadjusted Treatment Effects

Outcome	Time point	Unadjusted β (95% CI)	Adjusted β (95% CI)	Change in β
IR-DES-28	Post-intervention	4.24 (1.63 to 6.86)	4.31 (1.66 to 6.96)	+0.07
IR-DES-28	Two-month follow-up	6.47 (3.85 to 9.09)	6.58 (3.91 to 9.25)	+0.11
DFSQ-UMA	Post-intervention	0.13 (−2.30 to 2.57)	0.15 (−2.32 to 2.62)	+0.02

DFSQ- UMA	Two-month follow-up	0.87 (−1.57 to 3.31)	0.92 (−1.57 to 3.41)	+0.05
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Conclusion: Adjustment for age, duration of diabetes, BMI, HbA1c, and baseline infection severity did not materially change the direction, magnitude, or statistical significance of the treatment effects for either patient-reported outcome. The robustness of the findings to covariate adjustment supports the validity of the primary longitudinal conclusions.

Supplementary Table S2. Baseline demographic and clinical characteristics of the per-protocol population (n = 85)

Characteristic	Ozonated olive oil (n = 42)	Standard care (n = 43)	P value
Age, years	57.5 ± 8.1	55.6 ± 8.7	0.31
Male sex, n (%)	27 (64.3)	25 (58.1)	0.58
BMI, kg/m ²	28.4 ± 4.6	27.9 ± 4.3	0.60
Educational level, n (%)			0.71
Primary or less	14 (33.3)	16 (37.2)	
Secondary	19 (45.2)	20 (46.5)	
Tertiary or above	9 (21.4)	7 (16.3)	
Duration of diabetes, years	10.6 ± 4.1	10.1 ± 4.0	0.56
HbA1c, %	8.2 ± 1.4	8.0 ± 1.3	0.50
Ulcer duration, days, median (IQR)	21 (14–35)	24 (14–32)	0.68
Ulcer area, cm ²	3.8 ± 2.1	3.6 ± 1.9	0.64
Ulcer location, n (%)			0.82
Plantar surface	19 (45.2)	18 (41.9)	
Toes	14 (33.3)	16 (37.2)	
Dorsal surface	6 (14.3)	5 (11.6)	
Other	3 (7.1)	4 (9.3)	

Peripheral neuropathy, n (%)	33 (78.6)	32 (74.4)	0.65
Peripheral arterial disease, n (%)	9 (21.4)	10 (23.3)	0.84

Values are presented as mean $\pm$ SD, median (IQR), or n (%). Percentages are based on the per-protocol denominators (42 and 43). BMI = body mass index; HbA1c = glycated hemoglobin; IQR = interquartile range.