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Early PUSH Response, Maintenance, and Short-term Wound Dynamics: A Secondary Landmark Analysis of the RISE_UP Randomized Trial

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Abstract

Introduction. Serial assessment with the Pressure Ulcer Scale for Healing (PUSH) supports monitoring of pressure ulcers, but the interpretation of early improvement and short-term fluctuations remains uncertain. This study examined whether day-7 and day-14 PUSH improvement was associated with improvement at approximately 4 weeks, whether early responses were maintained, and whether early improvement identified faster subsequent change.

Methods. This exploratory post hoc landmark analysis used data from the RISE_UP randomized trial, which compared standard care with or without adjunctive blue-light photobiomodulation

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in 48 rehabilitation inpatients with stage 2 or stage 3 pressure ulcers. Assessments through day 35 were included. Early and week-4 responses were defined as any PUSH reduction from baseline. Documented closure was carried forward as PUSH = 0; other missing outcomes were not imputed in the main analysis. Risk ratios were adjusted for treatment group, ulcer stage, and baseline PUSH. Additional analyses examined response maintenance, incremental post-landmark change, subsequent slopes, and visit-to-visit worsening.

Results. Forty-three participants contributed to both landmark analyses. At day 7, 23/25 early responders (92.0%) remained improved at week 4, compared with 9/18 nonresponders (50.0%; adjusted risk ratio, 1.86; 95% confidence interval, 1.10–3.14). At day 14, corresponding proportions were 25/29 (86.2%) and 7/14 (50.0%; adjusted risk ratio, 1.89; 95% confidence interval, 1.003–3.573). Among early responders, 64.0% at day 7 and 75.9% at day 14 remained below baseline at every subsequent assessment. Early change showed negligible correlations with incremental post-landmark improvement, and adjusted slope analyses provided no clear evidence of faster subsequent improvement. Across all 48 participants, 38 (79.2%) experienced at least one visit-to-visit PUSH increase of ≥1 point, affecting 78/432 transitions (18.1%).

Discussion. Early response was associated with improvement at follow-up but did not clearly identify faster subsequent improvement. Delayed responses and frequent fluctuations limit the interpretation of isolated assessments. The small, single-centre sample, exploratory design, and response threshold without established clinical importance warrant cautious interpretation. Early PUSH changes should be interpreted within serial wound assessments. Absence of early improvement alone does not establish treatment failure. Prospective external validation is required before early-response thresholds can guide clinical decisions.

Keyword: Pressure Ulcer, Wound Healing, Wound Assessment, Prognosis, Photobiomodulation Therapy, Rehabilitation

Introduction

Pressure ulcers (PUs), also termed pressure injuries, remain common among hospitalized and mobility-limited adults and can prolong care, impair rehabilitation, and require sustained clinical resources. Their incidence varies across hospital settings and patient populations but remains a substantial safety and care-quality problem (Afzali Borojeny et al., 2020). Because healing is often slow and heterogeneous, assessment at a single endpoint provides limited information for clinical decision-making. Serial assessment is needed to determine whether a wound is progressing, static, or deteriorating and whether an observed improvement is sustained.

The Pressure Ulcer Scale for Healing (PUSH) was developed for this purpose. It combines wound surface area, exudate amount, and tissue type into a score ranging from 0 to 17, with lower values indicating a more favourable wound status (Stotts et al., 2001). Prospective evidence indicates that PUSH scores decrease over time in healing pressure ulcers and distinguish healing from nonhealing ulcers (Gardner et al., 2005), while a larger observational study confirmed the instrument's responsiveness across acute and chronic wound types (Choi et al., 2016).

PUSH trajectories have also been related to time to healing in neuropathic diabetic foot ulcers (Gardner et al., 2011). These properties support longitudinal use of the instrument, but they do not establish how much clinical weight should be assigned to a small change at a single early assessment.

Early wound trajectories may provide prognostic information before complete closure is observed. In venous leg ulcers and diabetic foot ulcers, area-based healing rates and trajectories measured during the first 4 weeks were strongly associated with later closure (Cardinal et al., 2008). In pressure ulcers among patients with spinal cord injury, the rate of dimensional reduction during the first 4 weeks similarly identified wounds likely to continue along a faster or slower course (van Asbeck & Post, 2015). However, most previous work has focused on wound area or on a 4-week observation period. Less is known about whether a composite PUSH response as early as day 7 or day 14 is associated with short-term outcome, whether that response is maintained, and how often apparent improvement is interrupted by temporary worsening.

This question is particularly relevant when an adjunctive treatment is added to standard care. The broader evidence for photobiomodulation in pressure-ulcer management has been characterized by heterogeneous treatment parameters and generally limited methodological quality (Petz et al., 2020). For blue-light photobiomodulation specifically, preliminary clinical reports have described improvement in peristomal skin disorders (Antonini & Gasperini, 2023) and in a heterogeneous series of pediatric skin injuries (Nicolosi et al., 2025). The RISE_UP randomized trial subsequently evaluated blue light in stage 2 and stage 3 pressure ulcers and found more favourable PUSH change and healing-trajectory patterns in the intervention group (Dollaku et al., 2025). The parent report, however, addressed treatment efficacy over the complete 4-week period rather than the interpretation of early within-patient response.

The aim of this exploratory secondary analysis was therefore to determine whether PUSH improvement at day 7 or day 14 was associated with improvement at approximately 4 weeks in participants from the RISE_UP trial. Secondary aims were to examine whether early improvement was maintained, distinguish early response from the rate of subsequent change, and quantify temporary visit-to-visit worsening. The analysis was intended to characterize short-term wound dynamics and generate clinically testable hypotheses, not to establish a definitive prognostic threshold or to re-estimate the efficacy endpoint of the parent trial.

Methods

Study design and reporting framework

This study was a post hoc, exploratory secondary analysis of individual-participant data from the RISE_UP trial, a single-centre, prospective, parallel-group, open-label randomized controlled trial that evaluated blue-light photobiomodulation in addition to standard care for stage 2 or stage 3 pressure ulcers. The design and primary findings of the parent trial have been reported previously (Dollaku et al., 2025). The present analysis addressed a distinct temporal question: whether early changes in Pressure Ulcer Scale for Healing (PUSH) scores were associated with improvement at approximately 4 weeks, whether early improvement was maintained, and how frequently PUSH scores worsened temporarily between consecutive assessments. Reporting was developed with reference to the CONSORT 2025 statement where applicable to a secondary analysis of a randomized trial (Hopewell et al., 2025). These analyses were not specified as efficacy endpoints in the original protocol and were therefore considered exploratory.

Setting, participants, randomization, and intervention

Participants were recruited between December 2021 and February 2024 at an inpatient rehabilitation hospital in Italy. The principal eligibility criteria were age 50 years or older; a stage 2 or stage 3 pressure ulcer located on the sacrum or lower limb; wound area of at least 2 cm^2; expected length of stay of at least 30 days; and a Braden Scale score of at least 11. Principal exclusions included clinical infection requiring systemic antibiotic therapy, stage 3 ulcers with undermining, tunnelling, or eschar, pregnancy, photosensitivity, active neoplastic disease, cytostatic treatment, high-dose intravenous corticosteroid therapy, and a life expectancy

shorter than 30 days.

Participants were randomized 1:1 to standard care alone or standard care plus blue-light photobiomodulation, with stratification by ulcer stage and diabetes status. Standard care was delivered three times weekly for 4 weeks and included cleansing, debridement when indicated, and dressing according to the study protocol. In the intervention group, EmoLED v.1 (Emoled S.r.l., Florence, Italy), a class IIa non-contact device emitting blue light at 410–430 nm with an optical power density of 120 mW/cm^2, was applied for 60 seconds at a distance of 40 ± 10 mm before dressing. Device and procedural details are available in the parent report (Dollaku et al., 2025).

Data source and wound assessment

The secondary dataset contained the 48 randomized participants and all recorded wound assessments. Nurses trained in the protocol evaluated each wound approximately three times per week. At every assessment, the PUSH instrument summarized wound surface area, exudate amount, and tissue type into a total score ranging from 0 to 17, with lower scores indicating a more favourable wound status and a score of 0 indicating closure (Stotts et al., 2001). The present analysis used PUSH assessments recorded from baseline through day 35, allowing a 7-day tolerance around the planned week-4 assessment. Six assessments occurring after day 35 were excluded. Patient identifiers were standardized across source sheets. One visit-level PUSH total that was inconsistent with its three recorded component scores was recalculated as the component sum before analysis. Source measurements were otherwise retained unchanged.

Landmark definitions and outcomes

Landmark assessments were defined at day 7 and day 14. For day 7, the assessment closest to the target day within days 4–10 was selected; for day 14, the closest assessment within days 11–17 was selected. When two observations were equally distant from the target, the earlier assessment was used. The week-4 outcome was the observation closest to day 28 within days 21–35. If a participant reached PUSH = 0 before a landmark or before the week-4 window and the database documented wound closure, the original wound was considered closed and a score of 0 was carried forward as an absorbing state. No values were carried forward for participants who discontinued follow-up without documented closure.

Early PUSH change was calculated as baseline PUSH minus landmark PUSH; positive values therefore indicated improvement. Consistent with the responder definition used in the parent trial, the primary binary definition of early response was any reduction greater than 0 points. Week-4 response was defined analogously as any reduction from baseline greater than 0 points. Because a universally established minimal clinically important difference for PUSH change was not assumed, reductions of at least 2 and at least 3 points were examined only as more stringent sensitivity thresholds and were not labelled clinically important.

Each participant was classified into one of four temporal patterns: early response maintained at week 4; early response subsequently lost; delayed response, defined as no early response followed by improvement at week 4; or no response at either time. Among early responders, final maintenance required the week-4 PUSH score to remain below baseline. Strict maintenance required all subsequent observed PUSH scores through the endpoint to remain below baseline. Temporary reversion was defined as at least one subsequent score equal to or higher than baseline. Visit-to-visit worsening was defined as an increase of at least 1 PUSH point between consecutive assessments; an increase of at least 2 points was analysed as a stricter definition.

To distinguish maintenance of benefit from the speed of subsequent improvement, incremental post-landmark change was calculated as landmark PUSH minus week-4 PUSH. In an additional trajectory analysis, a participant-specific post-landmark slope was estimated from all observed PUSH measurements strictly after the landmark and through day 35; at least two post-landmark observations were required. Slopes were expressed as PUSH points per week, with more negative values indicating faster subsequent improvement.

Statistical analysis

No separate sample-size calculation was

performed because this was an exploratory secondary analysis of a completed trial. Continuous variables were summarized using mean and standard deviation or median and interquartile range, as appropriate; categorical variables were summarized using frequencies and percentages. The primary landmark analysis included randomized participants with both the relevant landmark assessment and a week-4 outcome, including absorbing closure values.

Associations between binary early response and week-4 response were summarized using risk ratios and 95% confidence intervals; Fisher's exact test provided exact two-sided p values. Adjusted risk ratios were estimated using modified Poisson regression with an HC3 robust variance estimator (Zou, 2004), including treatment group, baseline PUSH score, and pressure-ulcer stage as covariates. Because subgroup cell counts were small, maintenance patterns by randomized group were treated as descriptive and no treatment-by-response interaction was tested.

Spearman correlation coefficients quantified associations between continuous early PUSH change and (a) total baseline-to-week-4 change and (b) incremental change occurring after the landmark. Percentile 95% confidence intervals were obtained from 10,000 patient-level bootstrap samples. The correlation with total change was interpreted descriptively because early change is a component of the total baseline-to-week-4 change. Post-landmark slopes were analysed using ordinary least-squares regression with HC3 robust standard errors, adjusting for treatment group, ulcer stage, and baseline PUSH score. Visit-to-visit worsening was summarized both as the proportion of participants with at least one episode and as the proportion of observed transitions. Between-group comparison used Fisher's exact test at the participant level and the Mann–Whitney U test for the number of worsening episodes per participant.

Missing non-closure outcomes were not imputed in the main analysis. Sensitivity analyses comprised: (1) analysis restricted to participants with an observed assessment in the week-4 window, without carrying closure forward; (2) conservative baseline observation carried forward for non-closure missing values; and (3) 2-point and 3-point response thresholds. No adjustment was made for multiple testing; effect estimates, confidence intervals, and exact p values are therefore emphasized over dichotomous significance testing. Analyses were conducted in Python 3.12.13 using pandas 2.2.3, NumPy 2.3.5, and SciPy 1.17.0.

Ethical considerations

The regional Ethics Committee for Clinical Research of Area Vasta Centro, Florence, Italy, approved the RISE_UP protocol on June 29, 2021 (reference 188813_spe) and a subsequent eligibility amendment in September 2021 (reference CEAVC Em. 2021-418_18813_spe). Written informed consent was obtained from participants or, when applicable, a relative or legal representative. The trial was registered before enrolment at ClinicalTrials.gov (NCT05130814). This secondary analysis used data collected under the approved protocol and did not introduce new interventions or participant contact.

Results

Participants and data availability

The source dataset contained 486 assessments from 48 randomized participants; 480 assessments occurred between baseline and day 35 and were retained. Participants contributed a median of 11 assessments (interquartile range [IQR], 9.75–12; range, 1–13). Forty-six participants had an observed day-7 assessment. Forty-three had an observed day-14 assessment, and two additional participants who had already achieved documented closure were assigned an absorbing score of 0 at day 14. Thirty-eight participants had an observed assessment during days 21–35; five additional participants had documented wound closure before this window and were assigned PUSH = 0, yielding 43 participants for both landmark analyses. The remaining five participants had no week-4 assessment and no documented closure; all had stage 2 ulcers, three were allocated to treatment and two to control.

The 43 participants in the main landmark analysis included 21 treated participants and 22 controls. Median age was 75.5 years (IQR, 69.3–81.2), 28 participants (65.1%) were male, 23 (53.5%) had stage 3 ulcers, and the median baseline PUSH score was 10 (IQR, 8–12). The selected assessments occurred at a median of

day 7 (range, 5–8), day 14 (range, 11–15), and day 26 (range, 21–29), excluding administratively assigned landmark values after confirmed closure.

Table 1. Availability of PUSH assessments for the secondary analysis.

Analysis point	Observed	Closure carried	Available	Used with week 4
Baseline	48	0	48	43
Day 7 (days 4–10)	46	0	46	43
Day 14 (days 11–17)	43	2	45	43
Week 4 (days 21–35)	38	5	43	43

Note. PUSH = Pressure Ulcer Scale for Healing. Closure-carried values were restricted to database records with PUSH = 0 and notes documenting closure of the original wound.

Early response and week-4 improvement

At day 7, 25 of 43 participants (58.1%) had an early PUSH reduction. Of these, 23 (92.0%) remained improved at week 4, compared with 9 of 18 participants (50.0%) without a day-7 response. The crude risk of week-4 improvement was 1.84 times higher among day-7 responders (95% CI, 1.14–2.96; Fisher's exact p = 0.004). After adjustment for treatment group, ulcer stage, and baseline PUSH score, the risk ratio was 1.86 (95% CI, 1.10–3.14; p = 0.022).

At day 14, 29 of 43 participants (67.4%) were early responders. Week-4 improvement was present in 25 of 29 responders (86.2%) and in 7 of 14 nonresponders (50.0%), corresponding to a crude risk ratio of 1.72 (95% CI, 1.001–2.970; Fisher's exact p = 0.022). The adjusted risk ratio was 1.89 (95% CI, 1.003–3.573; p = 0.049). Thus, early improvement identified participants more likely to be improved at week 4, but half of those without early improvement subsequently responded. The individual response pathways at both landmarks are displayed in Figure 1.

Table 2. Association between early PUSH response and week-4 response.

Landmark	Early response	Week-4 response among early responders	Week-4 response without early response	Crude RR (95% CI)	Adjusted RR (95% CI)	Fisher's exact p
Day 7	25/43 (58.1%)	23/25 (92.0%)	9/18 (50.0%)	1.84 (1.14–2.96)	1.86 (1.10–3.14)	0.004
Day 14	29/43 (67.4%)	25/29 (86.2%)	7/14 (50.0%)	1.72 (1.001–2.970)	1.89 (1.003–3.573)	0.022

Note. Early and week-4 response were defined as any PUSH reduction from baseline. Adjusted risk ratios were estimated using modified Poisson regression with HC3 robust standard errors and included treatment group, ulcer stage, and baseline PUSH. Exact p values are from Fisher's exact test for the crude 2 × 2 association. CI = confidence interval; RR = risk ratio.

Continuous early change and subsequent healing rate

Median PUSH improvement was 1 point (IQR, 0–2) at day 7, 2 points (IQR, 0–4) at day 14, and 3 points (IQR, 0.5–5) at week 4. Early continuous change correlated with total baseline-to-week-4 improvement at both day 7 (Spearman ρ = 0.58; bootstrap 95% CI, 0.31–0.78) and day 14 (ρ = 0.68; 95% CI, 0.44–0.84). However, these correlations partly reflect the arithmetic inclusion of early improvement in total improvement. When only the incremental change after each landmark was considered, the associations were close to zero: ρ = −0.04 (95% CI, −0.33 to 0.27) at day 7 and ρ = 0.00 (95% CI, −0.30 to 0.29) at day 14.

The analysis of post-landmark slopes used 41 participants after day 7 and 40 after day 14. After adjustment for treatment, ulcer stage, and baseline PUSH, early responders had an estimated additional reduction of 0.45 PUSH points per week after day 7 (slope difference, −0.45; 95% CI, −1.34 to 0.44; p = 0.314) and 0.57 points per week after day 14 (slope difference, −0.57; 95% CI, −1.42 to 0.28; p = 0.183). Although both point estimates favoured faster subsequent improvement among early responders, the confidence intervals were wide and included no

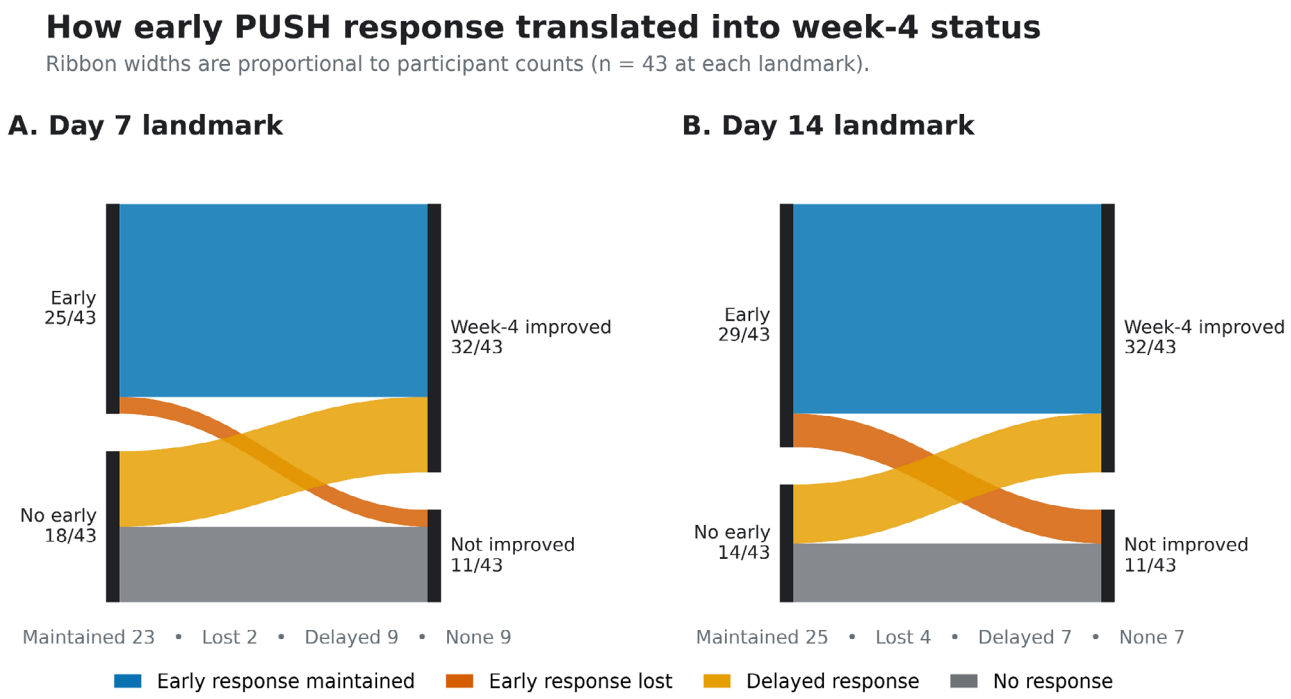

Figure 1. Early PUSH response and week-4 outcome at the day-7 and day-14 landmarks. Ribbon widths are proportional to participant counts. Maintained response indicates improvement at both the landmark and week 4; delayed response indicates no early improvement followed by improvement at week 4. PUSH = Pressure Ulcer Scale for Healing.

difference. The data therefore did not provide clear evidence that early response independently identified a faster subsequent healing rate.

Maintenance, loss, and delayed response

Using day 7 as the landmark, 23 participants (53.5% of the analysis cohort) had an early response that remained present at week 4, 2 (4.7%) lost their early response, 9 (20.9%) showed a delayed response, and 9 (20.9%) did not respond at either point. Of the 25 day-7 responders, 23 (92.0%) remained improved at week 4, but only 16 (64.0%) remained below baseline at every subsequent observation; 9 (36.0%) had at least one temporary return to baseline or worse.

Using day 14 as the landmark, 25 participants (58.1%) had a maintained early response, 4 (9.3%) lost the response, 7 (16.3%) responded later, and 7 (16.3%) remained nonresponders. Of the 29 day-14 responders, 25 (86.2%) remained improved at week 4, 22 (75.9%) met the strict maintenance definition, and 7 (24.1%) had a temporary reversion. In descriptive treatment-group analyses, final maintenance among day-7 responders was 100.0% in treated participants and 84.6% in controls; corresponding day-14 proportions were 93.3% and 78.6%. These arm-specific estimates were based on small denominators and were not subjected to formal interaction testing.

Visit-to-visit worsening

Across all 48 randomized participants, 432 consecutive-visit transitions were available. Thirty-eight participants (79.2%) had at least one increase of 1 or more PUSH points; 78 of 432 transitions (18.1%) met this definition. An increase of at least 2 points occurred in

Table 3. Temporal response patterns and maintenance.

Landmark	Maintained early response	Early response lost	Delayed response	No response	Strict maintenance among early responders	Temporary reversion among early responders
Day 7	23/43 (53.5%)	2/43 (4.7%)	9/43 (20.9%)	9/43 (20.9%)	16/25 (64.0%)	9/25 (36.0%)
Day 14	25/43 (58.1%)	4/43 (9.3%)	7/43 (16.3%)	7/43 (16.3%)	22/29 (75.9%)	7/29 (24.1%)

Note. Strict maintenance required all later observed PUSH values through the endpoint to remain below baseline. Temporary reversion required at least one later value equal to or greater than baseline.

28 participants (58.3%) and in 40 transitions (9.3%). The proportion with at least one 1-point worsening episode was 83.3% in the treatment group and 75.0% in the control group (Fisher's exact p = 0.724); the corresponding proportions for a 2-point increase were identical at 58.3% (p = 1.000). The number of 1-point worsening episodes per participant also did not differ between groups (Mann–Whitney U p = 0.750). These findings indicate that short-term PUSH oscillations were common in both randomized groups. The participant-level trajectories underlying these transitions are shown in Figure 2.

Table 4. Visit-to-visit worsening of the PUSH score.

Group	Participants	Visit pairs	Participants with ≥1-point worsening	≥1-point episodes	Participants with ≥2-point worsening	≥2-point episodes
Overall	48	432	38 (79.2%)	78/432 (18.1%)	28 (58.3%)	40/432 (9.3%)
Control	24	210	18 (75.0%)	37/210 (17.6%)	14 (58.3%)	18/210 (8.6%)
Treatment	24	222	20 (83.3%)	41/222 (18.5%)	14 (58.3%)	22/222 (9.9%)

Note. Transition percentages are descriptive because repeated transitions within a participant are not independent. Formal between-group testing was performed at the participant level.

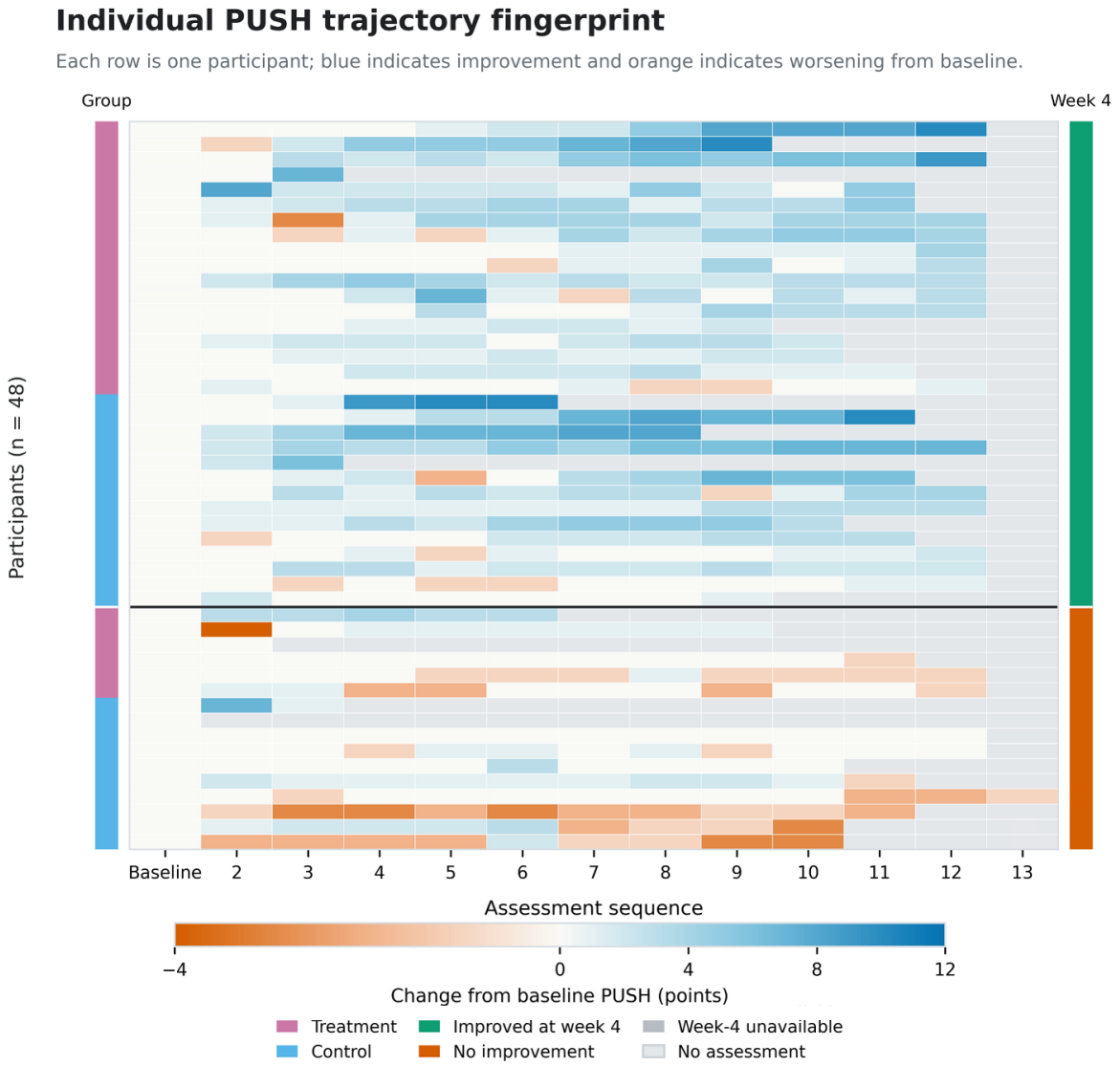

Figure 2. Patient-level PUSH trajectory fingerprint through day 35. Rows represent the 48 randomized participants and columns represent sequential recorded assessments. Cell colour indicates change from baseline PUSH: positive values denote improvement, negative values denote worsening, and grey denotes no recorded assessment. Side bars identify randomized group and week-4 outcome. Participants are ordered by week-4 status, randomized group, and magnitude of change. PUSH = Pressure Ulcer Scale for Healing.

Sensitivity analyses

The day-7 association remained evident when the analysis was restricted to the 38 participants with an observed week-4 assessment (RR, 1.80; 95% CI, 1.11–2.92; p = 0.011) and under conservative baseline observation carried forward for non-closure missing values (n = 48; RR, 1.83; 95% CI, 1.09–3.05; p = 0.012). For day 14, the complete-case estimate was less precise (RR, 1.67; 95% CI, 0.96–2.90; p = 0.061), whereas the conservative analysis of all 48 participants supported the association (RR, 1.96; 95% CI, 1.08–3.55; p = 0.010).

Using a more stringent definition of at least a 2-point reduction for both early and week-4 response, 15 of 17 day-7 responders (88.2%) and 13 of 26 nonresponders (50.0%) met the week-4 threshold (RR, 1.76; 95% CI, 1.16–2.69; p = 0.020). At day 14, the corresponding proportions were 19 of 22 (86.4%) and 9 of 21 (42.9%), respectively (RR, 2.02; 95% CI, 1.20–3.39; p = 0.004). Results using a 3-point threshold were directionally consistent. Across sensitivity analyses, early PUSH improvement was associated with the presence of improvement at week 4, whereas absence of early improvement did not exclude later response.

Table 5. Selected sensitivity analyses.

Landmark	Analysis	N	Response among early responders	Response without early response	RR (95% CI)	Fisher's exact p
Day 7	Observed week-4 cases only	38	18/20 (90.0%)	9/18 (50.0%)	1.80 (1.11–2.92)	0.011
Day 14	Observed week-4 cases only	38	20/24 (83.3%)	7/14 (50.0%)	1.67 (0.96–2.90)	0.061
Day 7	Conservative BOCF	48	23/28 (82.1%)	9/20 (45.0%)	1.83 (1.09–3.05)	0.012
Day 14	Conservative BOCF	48	25/31 (80.6%)	7/17 (41.2%)	1.96 (1.08–3.55)	0.010
Day 7	≥2-point early and final response	43	15/17 (88.2%)	13/26 (50.0%)	1.76 (1.16–2.69)	0.020
Day 14	≥2-point early and final response	43	19/22 (86.4%)	9/21 (42.9%)	2.02 (1.20–3.39)	0.004

Legend. BOCF = baseline observation carried forward; CI = confidence interval; RR = risk ratio.

Discussion

This exploratory secondary analysis produced four principal findings. First, participants with any PUSH reduction at day 7 or day 14 were more likely to remain improved at week 4 than participants without an early reduction. Second, early nonresponse did not imply subsequent failure: 50.0% of participants without improvement at either landmark showed improvement by week 4. Third, early change was correlated with total baseline-to-week-4 improvement but was not clearly associated with incremental post-landmark change or with a faster subsequent PUSH slope. Fourth, short-term reversals were common. Although most early responders remained improved at the final assessment, fewer maintained a score below baseline at every later visit, and almost four in five randomized participants experienced at least one 1-point visit-to-visit increase.

The day-7 and day-14 results support early PUSH response as a potential marker of short-term wound status. After adjustment for treatment group, ulcer stage, and baseline PUSH score, early responders had approximately 1.9 times the risk of week-4 improvement. These estimates were nevertheless derived from only 43 participants, and the confidence interval for the day-14 estimate only narrowly excluded the null. Early response was also a post-randomization characteristic, not a randomized exposure. The findings should therefore be interpreted as an association requiring external validation rather than as a causal effect or a ready-to-use clinical prediction rule.

The distinction between attained improvement and subsequent healing velocity is important. PUSH scores and wound-area trajectories have previously demonstrated prognostic value across pressure ulcers, diabetic foot ulcers, and venous leg ulcers (Cardinal et al., 2008; Gardner et al., 2005, 2011). In the present study, however, the correlation between early change and total week-4 change partly reflects mathematical coupling because early improvement is itself

included in the total change. When the analysis was restricted to change occurring after the landmark, correlations were close to zero. The adjusted post-landmark slope estimates favoured early responders but were imprecise and compatible with no difference. An early PUSH decrease may thus identify a wound that has already acquired an advantage by day 7 or day 14 without necessarily indicating that the wound will continue to improve at a persistently faster rate.

The delayed responses are equally relevant. Previous studies supporting early healing trajectories generally assessed area reduction over approximately 4 weeks, including work in venous and diabetic foot ulcers and in pressure ulcers among people with spinal cord injury (Cardinal et al., 2008; van Asbeck & Post, 2015). Those findings should not be translated directly into a rule for treatment failure after only 7 or 14 days, particularly when the outcome measure is a composite ordinal score rather than continuous planimetry. In this cohort, half of the early nonresponders improved later. Absence of an early PUSH reduction may justify a structured reassessment of the wound and care plan, but the present data do not support using it alone as a reason to discontinue an otherwise appropriate treatment.

The maintenance analyses show why serial observations matter. Final maintenance was high among early responders, reaching 92.0% after the day-7 landmark and 86.2% after the day-14 landmark, yet strict maintenance was lower because 36.0% and 24.1%, respectively, temporarily returned to baseline or worse. At the visit level, 18.1% of transitions worsened by at least 1 point and 9.3% worsened by at least 2 points. The high participant-level prevalence partly reflects the number of repeated opportunities to observe a fluctuation. PUSH remains a validated and responsive instrument (Choi et al., 2016; Gardner et al., 2005), but its components are recorded in discrete categories and can vary with wound condition and the timing of assessment. Moreover, the pressure-ulcer validation study evaluated the tool at weekly intervals, whereas RISE_UP assessments occurred approximately three times per week. The current analysis cannot determine whether individual reversals represented biological change, measurement variation, debridement-related changes, or shifts in exudate or tissue classification. It does show that a single 1-point increase should be interpreted within the preceding and subsequent trajectory.

The randomized treatment context should also be interpreted cautiously. Final maintenance was numerically more frequent among treated early responders than among controls at both landmarks, but these comparisons involved small denominators and were deliberately descriptive; no treatment-by-response interaction was tested. Consequently, this secondary analysis does not establish that blue-light photobiomodulation modifies the prognostic meaning of an early PUSH response. The parent randomized analysis remains the appropriate source for treatment-effect inference in this cohort (Dollaku et al., 2025). Reports of blue-light use in peristomal lesions and pediatric skin injuries broaden the clinical experience with the technology (Antonini & Gasperini, 2023; Nicolosi et al., 2025), but their uncontrolled designs, small samples, and different wound populations do not permit direct comparison with these older rehabilitation inpatients. The heterogeneity identified in the wider photobiomodulation literature reinforces the need for treatment-specific and wound-specific evidence (Petz et al., 2020).

Future studies should prospectively evaluate early PUSH change in larger, multicentre cohorts with standardized assessment timing and blinded outcome evaluation. External validation should report discrimination and calibration, compare total PUSH change with its individual components and continuous wound planimetry, and determine whether a single threshold or a repeated-confirmation rule better predicts clinically important outcomes such as closure, time to healing, or need for treatment escalation. Such work would clarify whether early PUSH dynamics can support individualized wound-care decisions without prematurely classifying delayed responders as failures.

Strengths and Limitations

This study used prospectively collected data from a randomized clinical trial and preserved the longitudinal structure of the dataset, allowing early response, delayed response, maintenance, and visit-to-visit worsening to be examined. All available repeated assessments within a defined 35-day period were used; their frequency captured short-term variations that could have been missed using only baseline

and final measurements. Landmark windows were specified around clinically interpretable time points, and documented closure was treated as an absorbing state. The main binary associations were supplemented by adjusted risk ratios, continuous-change analyses, post-landmark slopes, and sensitivity analyses for missing outcomes and more stringent response thresholds. Separating total improvement from incremental post-landmark change also reduced the risk of interpreting a part-whole correlation as evidence of continued acceleration.

This was an exploratory post hoc analysis of a small, single-centre, open-label trial that was not prospectively powered for prognostic analyses, maintenance patterns, or treatment-by-response interactions. Early PUSH response was a post-randomization characteristic; the observed associations cannot therefore be interpreted as causal and may be affected by residual confounding or regression to the mean. Five participants lacked a week-4 assessment without documented closure, and all had stage 2 ulcers; complete-case and conservative sensitivity analyses were broadly consistent with the main day-7 finding. Week-4 response was defined as any reduction from baseline rather than complete closure or a validated minimal clinically important difference. This definition is sensitive to 1-point changes, although analyses using 2-point and 3-point thresholds were directionally consistent.

Outcome assessors were not blinded, and the dataset did not permit attribution of temporary worsening to biological change, measurement conditions, debridement, or changes in exudate and tissue classification. Carrying a documented PUSH score of 0 forward assumes that closure of the original wound is an absorbing state within the short follow-up period. The 35-day follow-up did not permit evaluation of longer-term closure or recurrence, while the single-centre setting and inclusion of only stage 2 and stage 3 pressure ulcers limit generalizability. Finally, the same cohort was used to identify the association and estimate its magnitude, so predictive performance, calibration, and clinical utility remain unknown.

Clinical Implications

These exploratory findings favour a trend-based rather than a single-visit reading of PUSH. A day-7 or day-14 reduction can provide early evidence that the wound is moving in a favourable direction, but it should be confirmed with later assessments. Conversely, lack of early reduction should trigger review of pressure redistribution, perfusion, nutrition, infection or inflammation, moisture balance, dressing strategy, and adherence to the care plan rather than automatic classification as treatment failure. Plotting serial PUSH values alongside the component scores may help clinicians distinguish a sustained pattern from an isolated oscillation. These implications are hypothesis-generating and should not be interpreted as validated decision thresholds.

Conclusions

In this secondary analysis of RISE_UP, PUSH improvement at day 7 and day 14 was associated with a higher probability of improvement at approximately 4 weeks, but it did not clearly identify a faster rate of subsequent healing. Delayed response was common among early nonresponders, and temporary worsening occurred frequently between visits. Early PUSH change may therefore be useful as one element of serial clinical assessment, but neither a small early improvement nor its absence should be interpreted in isolation. Larger prospective studies are required before specific early-response thresholds can guide treatment decisions.

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