

# Engagement, Clinical Outcomes, and Derivation of a Weighted Composite Engagement Index (WCEI) in a Digital Therapeutic for Episodic Migraine

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## Introduction

Digital therapeutics (DTx) capture continuous usage data that serves as a window into patient behavior and remains largely underutilized. In two randomized controlled trials (RCTs) of a novel DTx for episodic migraine, CT-132<sup>1</sup>, clinical effectiveness was evaluated, with the treatment group achieving a significantly greater reduction in Monthly Migraine Days (MMDs) as compared to the digital control group. Accompanying these results was exceptionally high patient engagement.

While DTx engagement metrics are often analyzed and presented in isolation, this exploratory work leveraged high-frequency, digitally-derived usage data from the CT-132 RCTs in an attempt to bridge the gap between usage and outcomes. The analysis built upon existing composite score frameworks<sup>2,3</sup> to combine specific treatment component metrics and overall indicators into a single Weighted Composite Engagement Index (WCEI) by using elastic net to select the optimal set of predictor variables.

Establishing a standardized measure of engagement that correlates with clinical outcomes could optimize digital treatment and predict effectiveness in early-phase development in other indications.

## Methods

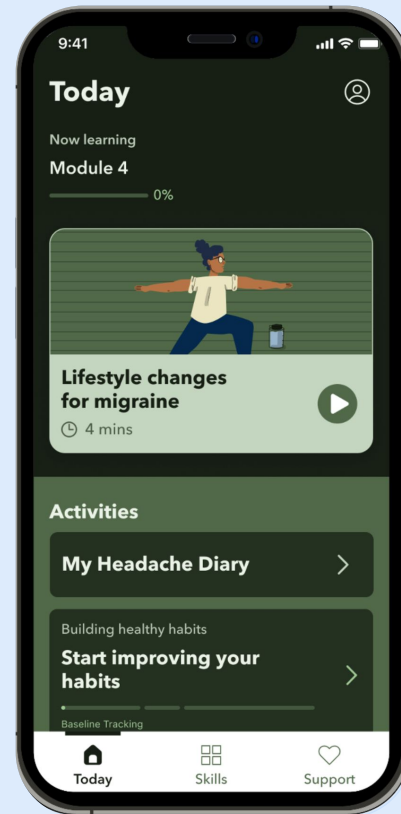
- An elastic net penalized linear regression model was applied to a 12-week Phase 3 RCT of the CT-132 DTx for the treatment of episodic migraine (NCT05853900)<sup>3</sup> to explore whether an optimal model could be derived from:
  - Predictor variables** included general and modality specific engagement metrics
  - Clinical outcome variable**: change from baseline in recorded values of Monthly Migraine Days (MMDs) without imputation
- The resultant non-zero coefficients were standardized and used as weights in the WCEI, which was applied to a Phase 3 bridging study of CT-132
- A linear regression incorporated general engagement metrics and change in baseline MMDs

## Demographics

| Demographics (mITT, n = 278)     | CT-132 n (%) | Demographics (mITT, n = 54)      | CT-132 n (%) |
|----------------------------------|--------------|----------------------------------|--------------|
| <b>Gender</b>                    |              | <b>Gender</b>                    |              |
| Female                           | 258 (92.8)   | Female                           | 51 (94.4)    |
| Male                             | 11 (4.0)     | Male                             | 3 (5.6)      |
| Other                            | 9 (3.2)      | Other                            | 0            |
| <b>Age (years)</b>               |              | <b>Age (years)</b>               |              |
| Mean                             | 38.4         | Mean                             | 38.2         |
| SD                               | 10.4         | SD                               | 10.74        |
| <b>Race</b>                      |              | <b>Race</b>                      |              |
| American Indian or Alaska Native | 1 (0.4)      | American Indian or Alaska Native | 0            |
| Asian                            | 1 (0.4)      | Asian                            | 1 (1.9)      |
| Black or African American        | 6 (2.1)      | Black or African American        | 2 (3.7)      |
| Multiple                         | 8 (2.9)      | Multiple                         | 0            |
| White or Caucasian               | 269 (96.4)   | White or Caucasian               | 51 (94.4)    |
| <b>Ethnicity</b>                 |              | <b>Ethnicity</b>                 |              |
| Hispanic or Latino origin        | 10 (3.5)     | Hispanic or Latino origin        | 5 (9.3)      |
| Non Hispanic or Latino origin    | 275 (96.5)   | Non Hispanic or Latino origin    | 49 (90.7)    |

\* Participants were representative across all geographic regions and household income brackets  
 \* Most participants had at least some college or above, with College Degree (60.9%) and Graduate or Professional Degree (35.4) comprising most participants' level of education  
 \* Participants were representative across all geographic regions and household income brackets  
 \* Most participants had at least some college or above, with College Degree (42.8%) and Graduate or Professional Degree (42.8) comprising most participants' level of education

## Conclusions



CT-132 is a 12-week smartphone application that treats migraine via brief daily lessons and exercises including an eDiary and just-in-time interventions via the Decision Support Tool.

Due to constraints of the data distribution (i.e., skew due to high engagement with CT-132), the initial, exploratory approach did not derive a model with high utility for understanding the full range of therapeutic interactions.

An additional linear regression was performed to demonstrate the overall relationship between engagement and clinical outcomes, with completion of therapeutic activities predicting episodic migraine reduction more than the number of times users opened CT-132 per day.

**Temporal Patterns:** Further work, such as a lag analysis, could examine the causal relationship between app usage and symptoms to examine a range of engagement patterns, such as “happy disengagement,” when users conclude treatment following early treatment benefits or symptom amelioration.

**Limitations:** Due to high overall engagement, the engagement variables were skewed; this may have affected model predictions. This analysis also used recorded eDiary reports of migraine symptoms without imputation, which may have further contributed to low variability in the data. Possible mediators, such as baseline severity, should also be investigated.

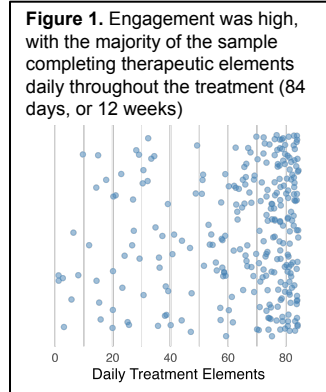
These results illustrate the challenges with developing a standardized composite score that can be applied across datasets and products. Future research can focus on enhancing understanding of how digital interactions lead to sustained behavior change.

## Results

### Engagement

Overall engagement and retention of participants in the trial was high. On average, participants opened the app 4.33 times per day and completed 87% of daily therapeutic elements. The majority (89.2%) completed treatment.

To characterize overall engagement patterns, we visualized the distribution of overall meaningful engagement with therapeutic elements (Figure 1). Additionally, we carried out a linear regression model which demonstrated that meaningful engagement - completing intended therapeutic components on a daily basis - had a stronger relationship to MMD reduction than simply opening the DTx app (Table 1).



**Figure 1.** Engagement was high, with the majority of the sample completing therapeutic elements daily throughout the treatment (84 days, or 12 weeks)

**Table 1.** Linear Regression of Engagement Predicting Change in MMDs

|                          | $\beta$ | Std. Error | t-value | p-value |
|--------------------------|---------|------------|---------|---------|
| <i>Intercept</i>         | -8.72   | 1.03       | -8.46   | 0.00    |
| Daily eDiary             | 0.09    | 0.02       | 4.04    | 0.00*** |
| Daily Treatment Elements | -0.02   | 0.02       | -1.45   | 0.15    |
| Daily App Opens          | 0.00    | 0.00       | 0.23    | 0.82    |

### Elastic Net & Weighted Composite Engagement Index (WCEI)

Limited data variability due to high engagement success prevented a full methodological exploration. The resulting lack of variance restricted the model's ability to identify predictive patterns.

The best fitting model retained all overall and modality specific engagement variables ( $\alpha = 0.2$ ). A standardized, composite engagement score - the WCEI - was calculated based on the initial model and applied to the bridging study dataset. Again, low variability in the key variables reduced interpretation of the model.

### References

- Snipes, et al. (2026). Effectiveness and safety of a first-in-class, prescription digital therapeutic for episodic migraine (CT-132): Phase 3 double-blind, randomized, controlled trial [Manuscript under review]
- Lakhan, S. E. (2025). The Composite Digital Therapeutic Index (cDTI): A Multidimensional Framework and Proof-of-Concept Application to FDA-Authorized Treatments. *Cureus*, 17(5).
- Boucher, E. M., & Raiker, J. S. (2024). Engagement and retention in digital mental health interventions: a narrative review. *BMC Digital Health*, 2(1), 52.