

Comparison of Daily vs Weekly Administration Formats of the Glycogen Storage Disease Functional Assessment Diary (GSD FAD)

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OBJECTIVES

The GSD FAD is a 31-item, disease-specific patient-reported outcome (PRO) that measures the signs/symptoms and impacts associated with Glycogen Storage Disease Type Ia (GSDIa).¹ It was developed as a daily eDiary in the DTX401-CL301 Phase 3, randomized, double-blind, placebo-controlled study investigating the efficacy and safety of DTX401 in individuals ≥8 years living with GSDIa (NCT05139316).

This analysis compared score equivalency between two administration formats of the GSD FAD, both administered at Week 48 and at Week 96:

- (1) a daily version that instructs subjects to report signs/symptoms and impacts "today", with scores calculated as daily total scores, averaged over a 7-day period; and
- (2) a once-weekly version that instructs subjects to report signs/symptoms and impacts experienced "over the past 7 days", with scores calculated as total scores.

Both forms of the GSD FAD yield three multi-item domain scores: GSD Daily Impacts Total Score, GSD Sleep Impacts Total Score, and GSD Symptoms Total Score; as well as four single-item scores (Disruptive to Plan Ahead, Felt Low Blood Sugar, Felt Stressed/Worried, Inconvenient to Follow Diet).

METHODS

Psychometric analyses were performed using Week 48 and Week 96 data from the Intent-to-Treat population, defined as all randomized subjects who received investigational DTX401 or Placebo. Analyses compared corresponding scores between the weekly and daily versions and included an evaluation of descriptives, internal consistency reliability (Cronbach's alpha (α) ≥ 0.70)², intra-rater reliability (ICC[C,1]) ≥ 0.70³, and convergent validity (Spearman correlations, r_s): weak 0.0 - 0.29, moderate 0.30 - 0.69, strong 0.70 - 0.89, very strong 0.90-1)⁴. All analyses were conducted using R version 4.4.0⁵ or higher, including *tidyverse*⁶, *psych*⁷, and *irr*⁸ packages.

RESULTS

Descriptive summaries of the scores at WK48 and WK96 showed slight differences, but overall, results were comparable between the two formats (Table 1).

The scores also exhibited acceptable internal consistency reliability (α ≥ 0.70) with similar estimates across formats (Tables 2). Most scores demonstrated acceptable intra-rater reliability (ICC[C,1] ≥ 0.70) across formats, though a few fell below the threshold (Table 3).

All scores showed adequate convergent validity (r_s ≥ 0.30) with moderate to very strong correlations, indicating that corresponding scores from each form measure concepts similarly (Table 4).

CONCLUSIONS

Results suggest that daily and weekly formats yield equivalent scores and provide initial evidence to support the use of the Weekly GSD FAD version in research settings where the administration of a daily eDiary is not feasible. Because sample size for these analyses was limited, estimates just under the performance threshold would likely result in higher estimates in a larger sample. Future research should evaluate equivalence in a larger, more heterogeneous sample.

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Table 1. Descriptive Summaries of GSD FAD Scores from the Weekly and Daily Forms

Week 48										
Score	Form	N	Mean (SD)	Median	Q1 - Q3	Min - Max	Percent with lowest score	Percent with highest score	Statistical binning at lowest score	Statistical binning at highest score
GSD Daily Impacts Total Score	Weekly	13	5.69 (7.63)	4.00	2.0 - 6.0	0.0 - 29.0	23.1%	7.7%	Yes	No
	Daily	13	4.45 (6.06)	2.25	0.8 - 6.4	0.0 - 22.5	23.1%	7.7%	Yes	No
GSD Sleep Impacts Total Score	Weekly	15	3.53 (2.88)	3.00	1.0 - 6.0	0.0 - 9.0	20.0%	6.7%	No	No
	Daily	15	2.72 (2.24)	2.50	0.7 - 4.0	0.0 - 6.4	20.0%	6.7%	No	No
GSD Symptoms Total Score	Weekly	15	8.20 (6.34)	5.00	4.0 - 13.0	0.0 - 20.0	13.3%	6.7%	No	No
	Daily	15	4.19 (4.19)	2.71	0.9 - 6.5	0.0 - 14.0	13.3%	6.7%	Yes	No
Disruptive to Plan Ahead Due to GSD1a Diet Score	Weekly	15	0.53 (0.92)	0.00	0.0 - 1.0	0.0 - 3.0	66.7%	6.7%	Yes	No
	Daily	15	0.51 (0.92)	0.00	0.0 - 0.5	0.0 - 2.5	66.7%	6.7%	Yes	No
Felt Low Blood Sugar Score	Weekly	15	0.80 (0.94)	1.00	0.0 - 1.0	0.0 - 3.0	46.7%	6.7%	Yes	No
	Daily	15	0.48 (0.43)	0.40	0.0 - 0.7	0.0 - 1.2	26.7%	6.7%	No	No
Felt Stressed/Worried Score	Weekly	15	0.40 (1.12)	0.00	0.0 - 0.0	0.0 - 4.0	86.7%	6.7%	Yes	No
	Daily	15	0.39 (0.71)	0.00	0.0 - 0.3	0.0 - 2.0	66.7%	6.7%	Yes	No
Inconvenient to Follow Diet Score	Weekly	15	0.53 (0.92)	0.00	0.0 - 1.0	0.0 - 3.0	66.7%	6.7%	Yes	No
	Daily	15	0.41 (0.73)	0.00	0.0 - 0.5	0.0 - 2.4	66.7%	6.7%	Yes	No

Week 96										
Score	Form	N	Mean (SD)	Median	Q1 - Q3	Min - Max	Percent with lowest score	Percent with highest score	Statistical binning at lowest score	Statistical binning at highest score
GSD Daily Impacts Total Score	Weekly	10	11.60 (9.72)	9.50	5.2 - 18.2	0.0 - 28.0	10.0%	10.0%	No	No
	Daily	10	10.68 (11.29)	5.54	3.0 - 20.5	0.0 - 28.7	10.0%	10.0%	Yes	No
GSD Sleep Impacts Total score	Weekly	13	4.69 (2.81)	4.00	3.0 - 7.0	0.0 - 10.0	7.7%	7.7%	No	No
	Daily	13	4.16 (2.82)	3.80	2.2 - 5.8	0.0 - 10.0	7.7%	7.7%	No	No
GSD Symptoms Total Score	Weekly	12	8.83 (6.22)	8.50	4.5 - 11.2	0.0 - 21.0	8.3%	8.3%	No	No
	Daily	12	5.82 (3.71)	5.40	3.9 - 8.1	0.0 - 12.2	8.3%	8.3%	No	No
Disruptive to Plan Ahead Due to GSD1a Diet Score	Weekly	13	1.62 (1.39)	1.00	1.0 - 2.0	0.0 - 4.0	23.1%	15.4%	No	No
	Daily	13	1.14 (1.23)	0.83	0.1 - 1.8	0.0 - 4.0	23.1%	7.7%	Yes	No
Felt Low Blood Sugar Score	Weekly	12	1.00 (0.85)	1.00	0.0 - 2.0	0.0 - 2.0	33.3%	33.3%	No	No
	Daily	12	0.76 (0.63)	0.78	0.2 - 1.2	0.0 - 1.6	25.0%	8.3%	No	No
Felt Stressed/Worried Score	Weekly	13	0.85 (0.90)	1.00	0.0 - 2.0	0.0 - 2.0	46.2%	30.8%	Yes	No
	Daily	13	0.86 (1.05)	0.50	0.0 - 1.2	0.0 - 3.5	38.5%	7.7%	Yes	No
Inconvenient to Follow Diet Score	Weekly	13	1.54 (1.27)	1.00	1.0 - 2.0	0.0 - 4.0	15.4%	15.4%	No	No
	Daily	13	1.23 (1.23)	1.00	0.1 - 1.6	0.0 - 4.0	23.1%	7.7%	Yes	No

Key: N, count of observations; SD, standard deviation; Q1, first quartile; Q3, third quartile. Note: Percent with the lowest or highest score is calculated as the frequency of observed scores equal to the minimum or maximum score observed divided by N (the count of observations). Low GSD FAD scores indicate lower levels of GSDIa symptoms and impacts, whereas high GSD FAD scores indicate higher levels of GSDIa symptoms and impacts. Statistical binning at the lowest score or highest score indicates the level of score level ceiling or floor effects. Created on: 2025-04-28 23:14:17

Table 2. Internal Consistency Reliability of GSD FAD Scores from Weekly and Daily Forms

Score	Form	Alpha
Week 48		
GSD Daily Impacts Total Score	Weekly	0.90
	Daily	0.92
GSD Sleep Impacts Total Score	Weekly	0.93
	Daily	0.90
GSD Symptoms Total Score	Weekly	0.84
	Daily	0.89
Week 96		
GSD Daily Impacts Total Score	Weekly	0.91
	Daily	0.93
GSD Sleep Impacts Total Score	Weekly	0.86
	Daily	0.90
GSD Symptoms Total Score	Weekly	0.88
	Daily	0.83

Key: Alpha, Cronbach's Alpha
Note: Alpha estimates for eDiary scores are estimated daily and averaged across seven-day time periods leading up to either Week 48 or Week 96. Alpha estimates for scores from the Weekly form are estimated conventionally using Week 48 and Week 96 item responses. Created on: 2025-04-29 11:44:21

Table 3. Intra-Rater Reliability Between GSD FAD Scores from the Daily and Weekly Forms

Score	N	ICC(C,1)	L95	U95
Week 48				
GSD Daily Impacts Total Score	13	0.88	0.66	0.96
GSD Sleep Impacts Total score	15	0.74	0.38	0.90
GSD Symptoms Total Score	15	0.57	0.10	0.83
Disruptive to Plan Ahead Due to GSD1a Diet Score	15	0.84	0.59	0.94
Felt Low Blood Sugar Score	15	0.45	-0.07	0.77
Felt Stressed/Worried Score	15	0.59	0.12	0.84
Inconvenient to Follow Diet Score	15	0.71	0.33	0.89
Week 96				
GSD Daily Impacts Total Score	10	0.96	0.84	0.99
GSD Sleep Impacts Total score	13	0.96	0.87	0.99
GSD Symptoms Total Score	12	0.66	0.16	0.89
Disruptive to Plan Ahead Due to GSD1a Diet Score	13	0.75	0.36	0.92
Felt Low Blood Sugar Score	12	0.85	0.55	0.95
Felt Stressed/Worried Score	13	0.25	-0.32	0.69
Inconvenient to Follow Diet Score	13	0.91	0.73	0.97

Key: ICC(C,1), Intraclass correlation coefficient for the consistency of single ratings
Note: The ICC(C,1) was estimated from the variance components of a two-way mixed effects model. Created on: 2025-04-28 23:14:21

Table 4. Convergent Validity of GSD FAD Scores from the Weekly and Daily Forms

Scores	Estimate
Week 48	
GSD Daily Impacts Total Score	0.56
GSD Sleep Impacts Total score	0.71
GSD Symptoms Total Score	0.59
Disruptive to Plan Ahead Due to GSD1a Diet Score	0.79
Felt Low Blood Sugar Score	0.72
Felt Stressed/Worried Score	0.60
Inconvenient to Follow Diet Score	0.52
Week 96	
GSD Daily Impacts Total Score	0.89
GSD Sleep Impacts Total score	0.97
GSD Symptoms Total Score	0.78
Disruptive to Plan Ahead Due to GSD1a Diet Score	0.77
Felt Low Blood Sugar Score	0.90
Felt Stressed/Worried Score	0.57
Inconvenient to Follow Diet Score	0.82

Note: Correlations were calculated using pairwise complete observations and Spearman correlations. Created on: 2025-04-28 23:14:16