

Meaningful Within-Patient Change of the IWQOL-Lite-CT Physical Function Composite in Adults With Obesity

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Introduction

The Impact of Weight on Quality of Life–Lite Clinical Trials Version (IWQOL-Lite-CT) is a patient-reported outcome measure (PRO) used to assess effects of weight management therapy on physical function (PF) among clinical trial participants.

To ensure treatment benefits are meaningful to patients when using PROs, the FDA recommends defining meaningful score differences (MSDs), which are usually based on what patients would consider meaningful within-patient change (MWPC).

Although one MWPC threshold for the IWQOL-Lite-CT PF Composite has been established previously, the FDA recommends using a range of MWPC thresholds to aid with the interpretation of change in a PRO score.

Objective

To provide additional MWPC threshold to refine and calibrate a range of MWPC thresholds to aid in the interpretation of change of the IWQOL-Lite-CT PF Composite in adults with obesity.

Method

This analysis used blinded patient data from the randomized, double-blind, phase 2 trial of lotiglipron (NCT05579977) in adults with obesity without diabetes.

PF MWPC thresholds were estimated using anchor-based regression analyses using the Patient Global Impression of Severity (PGI-S) for physical limitation as the primary anchor, and the Patient Global Impression of Change (PGI-C) for physical limitation was the secondary anchor. PGI-S asked participants to choose the response that best describes the limitations in their ability to do daily activities over the past 7 days and used a 5-point scale: 0 none, 1 mild, 2 moderate, 3 severe, 4 very severe.

PGI-C asked participants to choose the response that best describes the overall change in their ability to do daily activities since they started taking the study medication. A 5-point scale was used for PGI-C: 1 much better, 2 a little better, 3 no change, 4 a little worse, 5 much worse.

Results

Demographic baseline characteristics of patients from the study outlined in Table 1 are comparable to those of STEP 1 trial which is the base for the previously published MWPC threshold of 14.6.

Table 1. Baseline Demographics and IWQOL-Lite-CT Scores

	NCT05579977 ^a	STEP-1
N	389	1945
Age, mean (SD), years	49.1 (±12.4)	46.5 (12.71)
Sex, n (%)		
Female	237 (60.9)	1440 (74.0)
Male	152 (39.1)	505 (26.0)
Race, n (%)		
Asian	23 (5.9)	260 (13.8)
Black or African American	40 (10.3)	111 (5.9)
White	318 (81.7)	973 (74.5)
Other	8 (2.1)	NA
Ethnicity, n (%)		
Hispanic or Latino	59 (15.2)	229 (12.1)
Body mass index (kg/m ²)		
Mean (SD)	37.8 (6.2)	37.9 (6.66)
Median, range	36.6, 30.0-75.0	36.6, 26.5-83.0
IWQOL-Lite-CT Physical Function Composite		
Baseline Mean (SD)	64.10 (22.51)	65.4 (24.0)

^a Data for stratum 2 only.

Using PGI-S change as the primary anchor, the MWPC threshold was 12.16 using a 2-category change and 6.08 using a 1-category change (Table 2). The MWPC value of 12.16 was interpreted as a medium effect (effect size: 0.54).

Table 2. MWPC estimations for IWQOL-Lite-CT Physical Function Composite

Anchor	MWPC of Physical Function Composite	
	Based on 1-category change in anchor MWPC/Effect Size	Based on 2-category change in anchor MWPC/Effect Size
PGI-S based	6.08/0.27	12.16/0.54
PGI-C based	3.96/0.18	7.91/0.35

Data from week 20.

The MWPC estimations are based on change in PGI-S and PGI-C as continuous predictors. Standardized effect sizes were calculated by dividing the difference in means by the standard deviation (SD) value at baseline.

Standardized Effect sizes with values of 0.2 standard deviation units are generally regarded as "small," 0.5 as "medium," and 0.8 as "large."

The correlation between the change in the PF Composite and the change in PGI-S (primary anchor) was also numerically larger (-0.31) compared with the correlation between the change in the PF Composite and PGI-C (-0.18) (both $P < 0.05$) (Table 3). This correlation is above the recommended threshold (0.30) for defining an acceptable association between an anchor and a change in a PRO score.

Table 3. Correlations between changes in IWQOL-Lite-CT Physical Function Composite and anchors

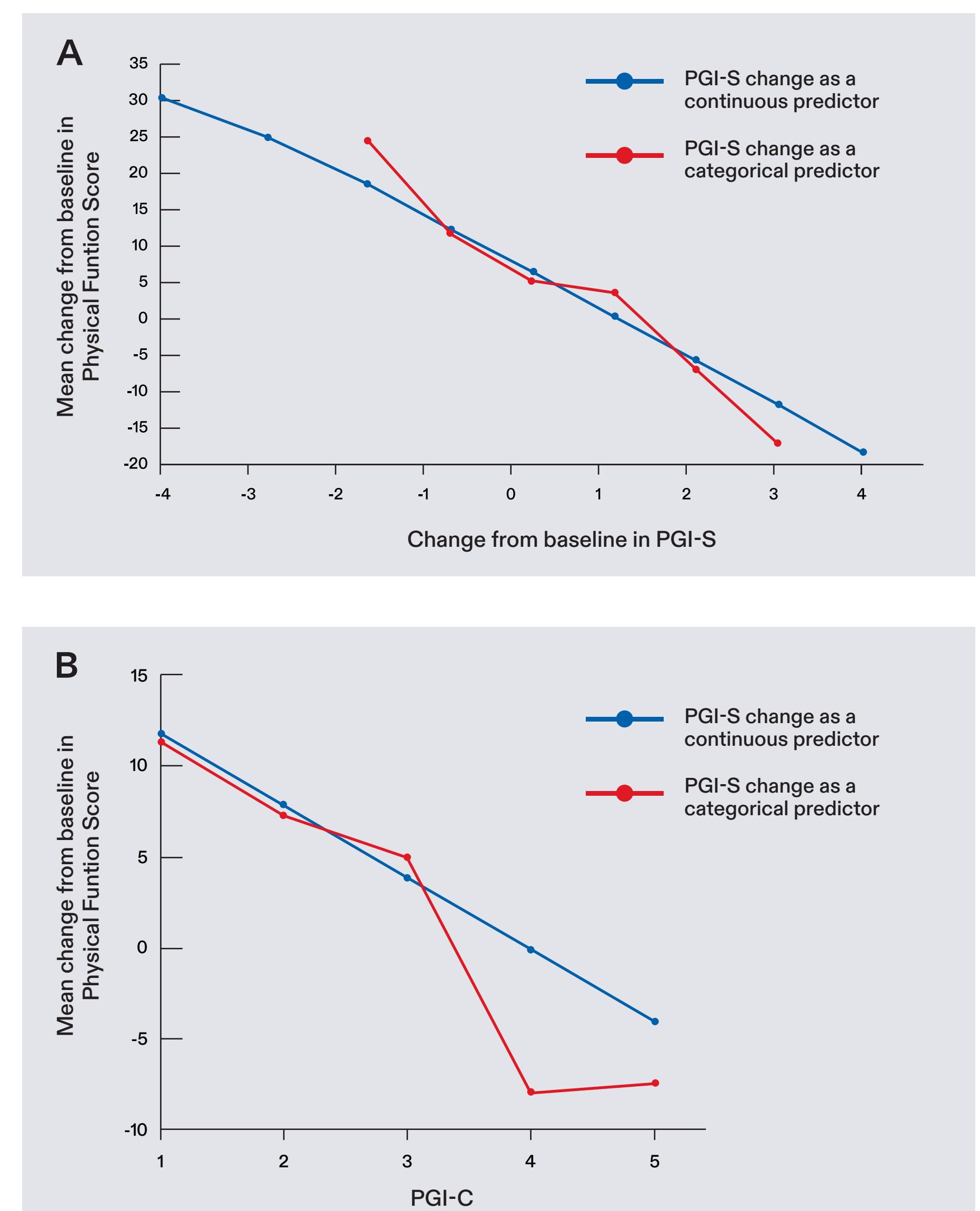
Week	Correlation between change in Physical Function Score and change in PGI-S	Correlation between change in Physical Function Score and PGI-C
20	-0.31	-0.18

Note: both correlations are significant ($p < 0.05$).

When PGI-S change or PGI-C was used as a categorical variable, the functional relationship between these anchors and the change in the PF Composite from baseline was the same as compared with the functional relationship when P-GIS change or PGI-C was used as a continuous variable, respectively, supporting the linearity assumption for the relationship.

The departure from linearity for large changes and small changes in an anchor corresponds to the small number of available observations for those categories.

Figure 1. Relationship of the Change in IWQOL-Lite-CT Physical Function Composite With the Change in PGI-S and With PGI-C



IWQOL-Lite-CT = Impact of Weight on Quality of Life – Lite Clinical Trials; MWPC = meaningful within-patient change; PGI-C = Patient Global Impression of Change; PGI-S = Patient Global Impression of Severity.

Data from week 20.

Conclusions

A threshold of 12.16 can be considered as MWPC for the IWQOL-Lite-CT PF Composite. This threshold complements a published responder threshold of 14.16, and these thresholds can be used together to determine clinical meaningfulness of the change in IWQOL-Lite-CT PF Composite.

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Conflict of Interest

AGB, NLP, JCC, JTS, and XL are employees of Pfizer Inc. and may hold shares and/or stock options in the company. SM is a full-time employee of RTI Health Solutions, an independent nonprofit research organization. RLK receives royalties for the IWQOL-Lite-CT from Duke University and has previously received consulting fees from Pfizer Inc.