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Fatigue Improvement Correlates With Reductions in Work Productivity Impairment and Related Indirect Cost in Patients With Crohn's Disease: Post Hoc Analysis of Phase 3 Risankizumab Induction Trials

Edouard Louis,[1] Julian Panes,[2] Subrata Ghosh,[3] Britta Siegmund,[4] Wan-Ju Lee,[5] Huiwen Deng,[5,6] Kristina Kligys,[5] Jasmina Kalabic,[7] Edward V. Loftus, Jr[8]

[1]University Hospital CHU of Liège, Liège, Belgium; [2]Hospital Clínic Barcelona, IDIBAPS, CIBERehd, Barcelona, Spain; [3]APC Microbiome Ireland, University College Cork, Ireland; [4]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin. Department of Gastroenterology, Infectious Diseases and Rheumatology (including Nutrition Medicine); [5]AbbVie Inc., North Chicago, IL, USA; [6]Department of Pharmacy Systems Outcomes and Policy, University of Illinois at Chicago, Chicago, IL, USA; [7]AbbVie Deutschland GmbH & Co. KG, Ludwigshafen, Germany; [8]Mayo Clinic College of Medicine and Science, Rochester, MN, USA

OBJECTIVE

To assess (1) the correlation between fatigue and other key clinical and patient reported outcomes, and (2) indirect cost burden associated with fatigue in patients with CD using clinical trial data from Phase 3 risankizumab induction trials ADVANCE and MOTIVATE

CONCLUSIONS

Clinically meaningful improvement in fatigue had moderate to strong correlations with improvement in disease symptoms, quality of life, work productivity, and daily activity

Patients achieving normative levels of fatigue had 29% reduction in overall work impairment, resulting in 11.6 hours gained per week and $18,726/€17,199 saved per person per year

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INTRODUCTION

- Patients with Crohn's disease (CD) frequently report fatigue, which may reduce health-related quality of life and work productivity, thereby contributing to higher patient and societal costs[1]
- The impact of fatigue on the economic burden of CD has not been characterised

METHODS

Study cohort:

- Patients with moderate to severe CD who received risankizumab (RZB; 600 mg or 1200 mg IV) or placebo (PBO) in the Phase 3 clinical trials ADVANCE and MOTIVATE were pooled and analysed
- All patients with non-missing values, regardless of RZB or PBO IV treatment, were included in the analysis

Key Covariates:

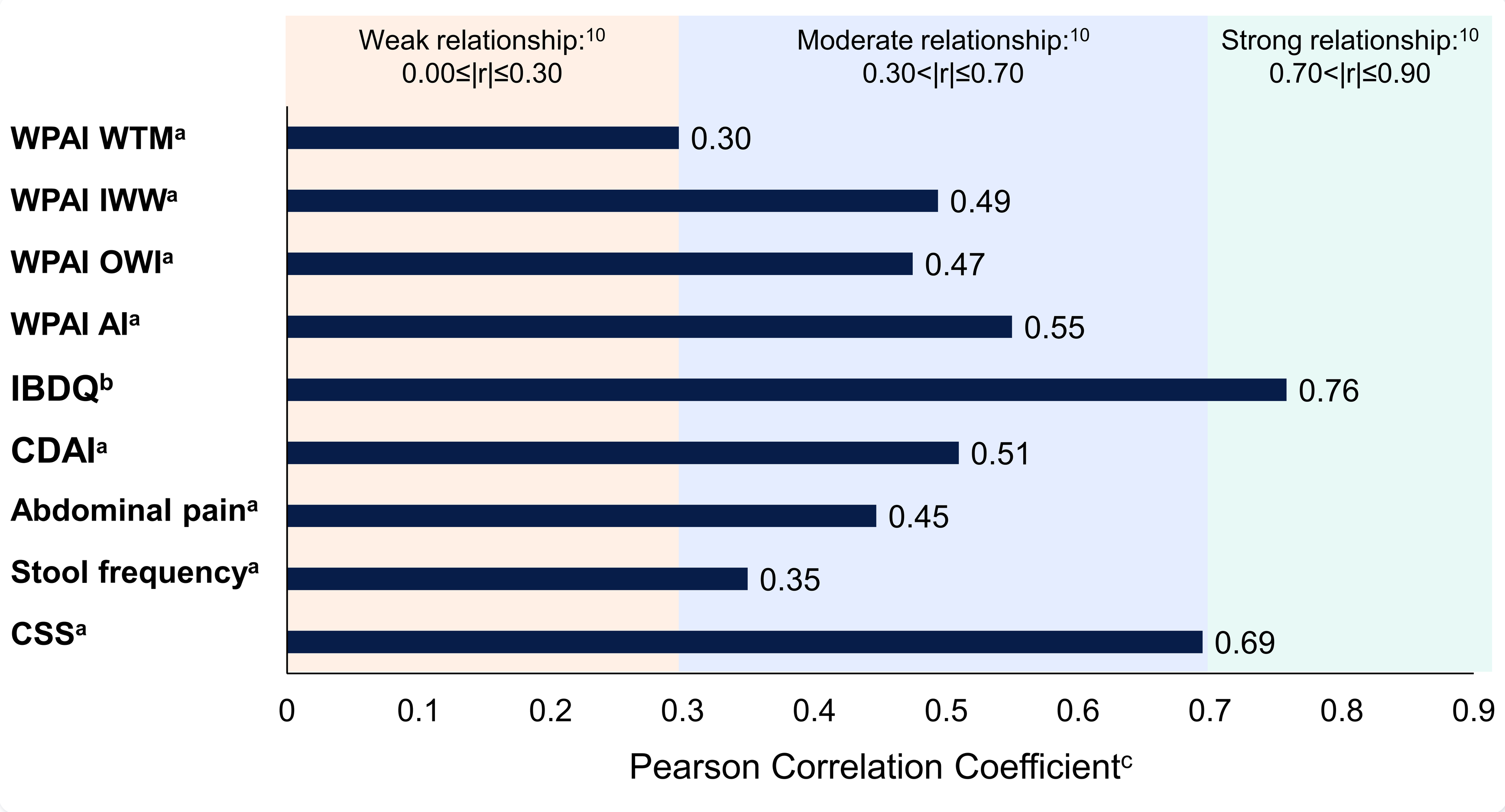
- Key clinical outcomes and patient-reported quality of life were assessed and listed below. The corresponding meaningful within-person change (MWPC) of each measure was also provided
  - Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F)
    - MWPC = ≥9-point increase; Normative value = ≥40.1 points[2]
  - Work Productivity and Activity Index (WPAI) questionnaire[3]
    - Work Time Missed (WTM) MWPC = 6.5% reduction
    - Impairment While Working (IWW) MWPC = 6.1% reduction
    - Overall Work Impairment (OWI) MWPC = 7.3% reduction
    - Activity Impairment (AI) MWPC = 8.5% reduction
  - Inflammatory Bowel Disease Questionnaire Total Score (IBDQ)[4,5]
    - MWPC = ≥16-point increase
  - Clinical disease activity index (CDAI)[5]
    - MWPC = ≥100-point decrease
  - Patient-reported abdominal pain and stool frequency[6]
    - MWPC = ≥30% reduction
  - Crohn's symptom severity (CSS) questionnaire[7]
    - MWPC = ≥9-point increase

Outcomes and Analytical Approach:

- The Pearson correlation between changes from baseline to week 12 in FACIT-F vs all other assessments
- Mean change from baseline to week 12 in all assessments stratified by the mean change from baseline in FACIT-F scores based on quartile in 4 groups: mean change in FACIT-F<2, 2≤FACIT-F<9, 9≤FACIT-F<17, and FACIT-F≥17
- Regression analyses used to assess the relationship between improvements from baseline in FACIT-F and WPAI OWI
  - Results of regression analysis were used to calculate cost savings based on WPAI scores and average hourly wages (US and EU)[8,9]
- Annualised cost savings were determined in patients who achieved a clinically meaningful improvement (≥9-unit increase) or normative values (total score >40) in FACIT-F at week 12

RESULTS

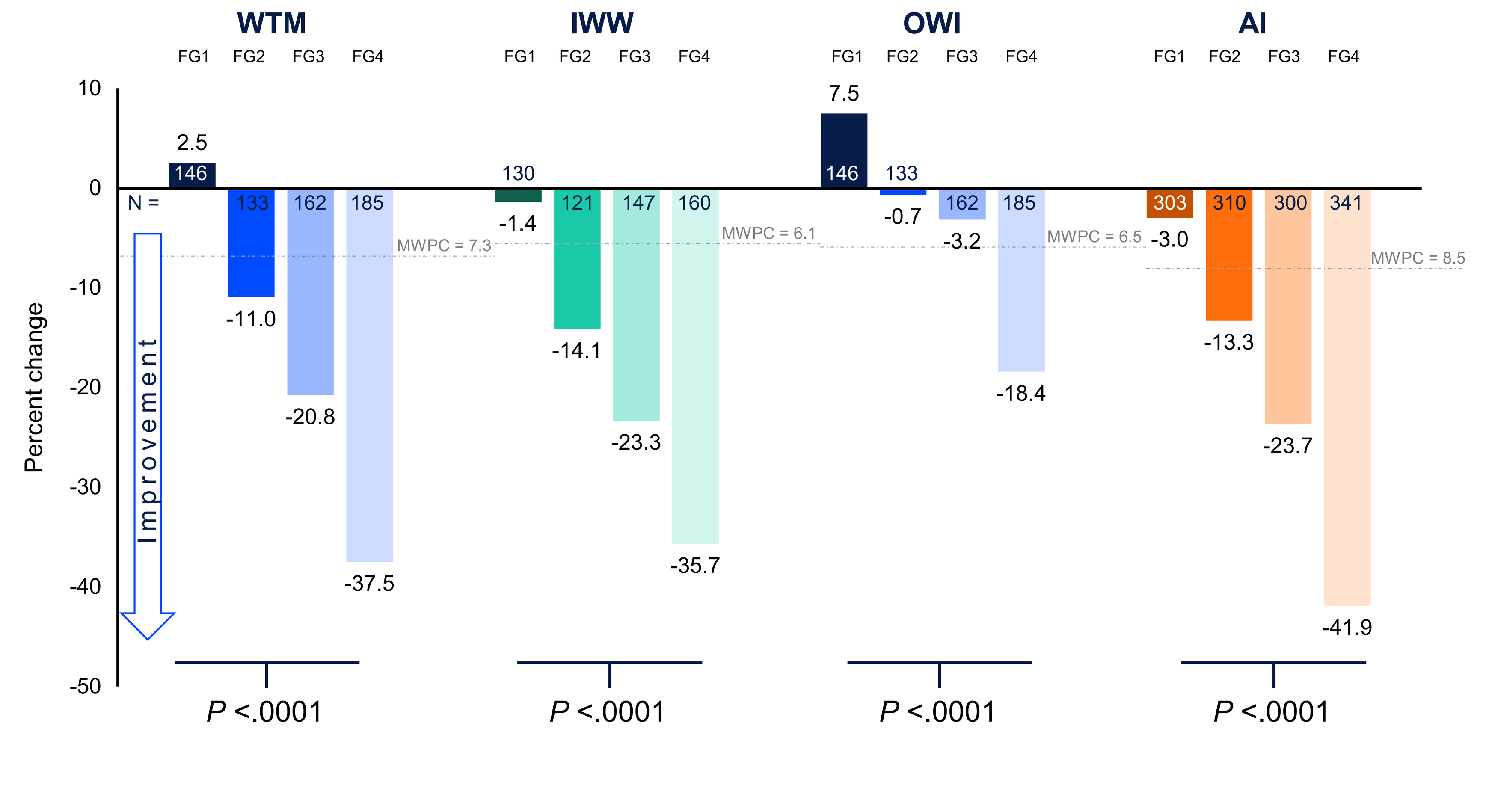
Figure 1. FACIT-F has Moderate to Strong Correlation With Key CD Symptoms, Quality of Life Measures, and Work Productivity Based on Change Score From Baseline to Week 12



AI, activity impairment; CD, Crohn disease; CDAI, clinical disease activity index; CSS, Crohn's symptom severity; IBDQ, Inflammatory Bowel Disease Questionnaire; IWW, impairment while working; OWI, overall work impairment; WPAI, Work Productivity and Activity Impairment questionnaire; WTM, work time missed.

[a]A reduction in score denotes symptom/disease improvement. [b]An increase in score denotes symptom/disease improvement. [c]Absolute correlation values are shown. All correlations with FACIT-F were negative except for IBDQ, which had a strong positive correlation.

Figure 2. Patients Experience Less Work and Activity Impairment With Improving FACIT-F Scores From Baseline to Week 12

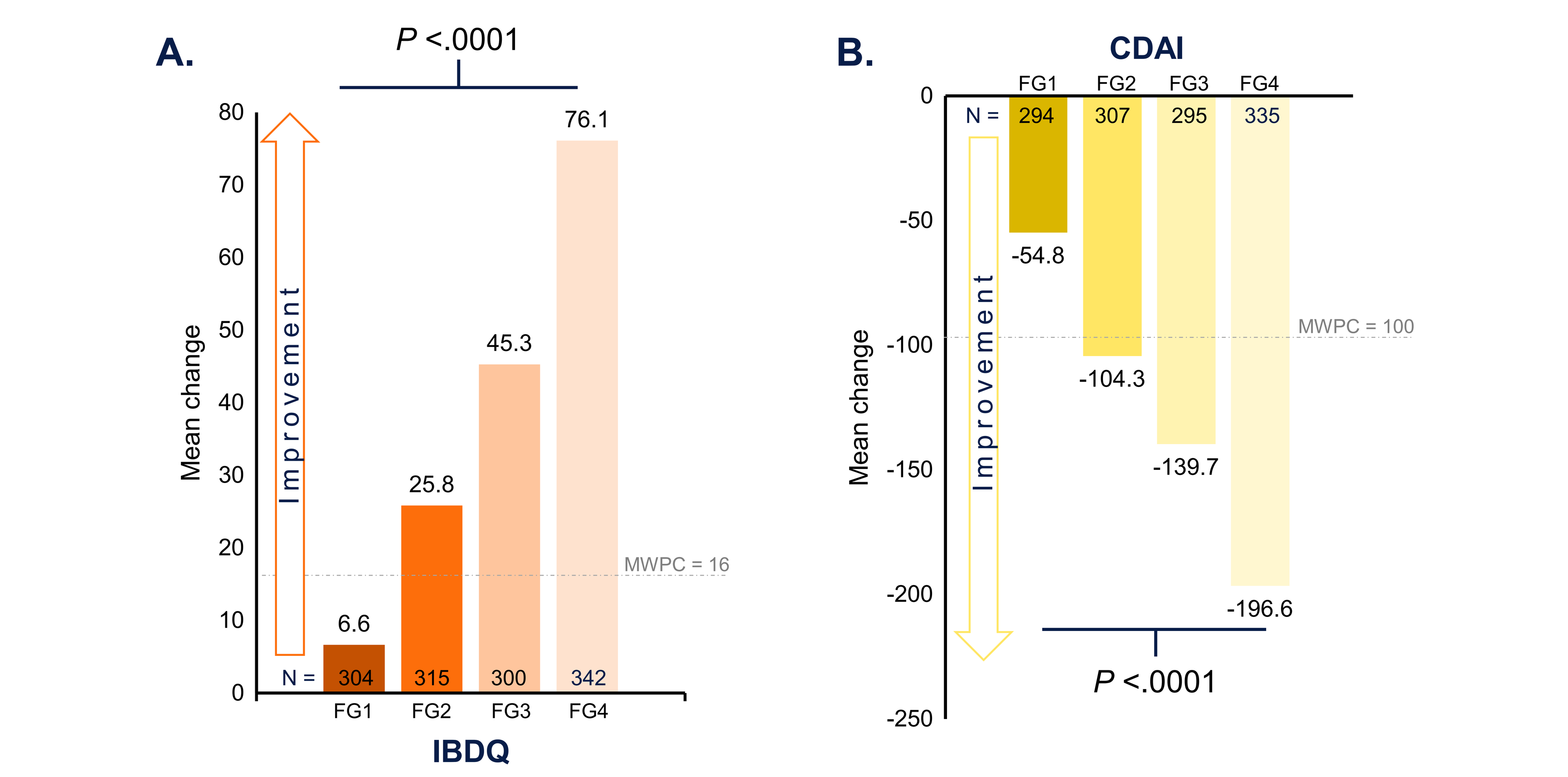


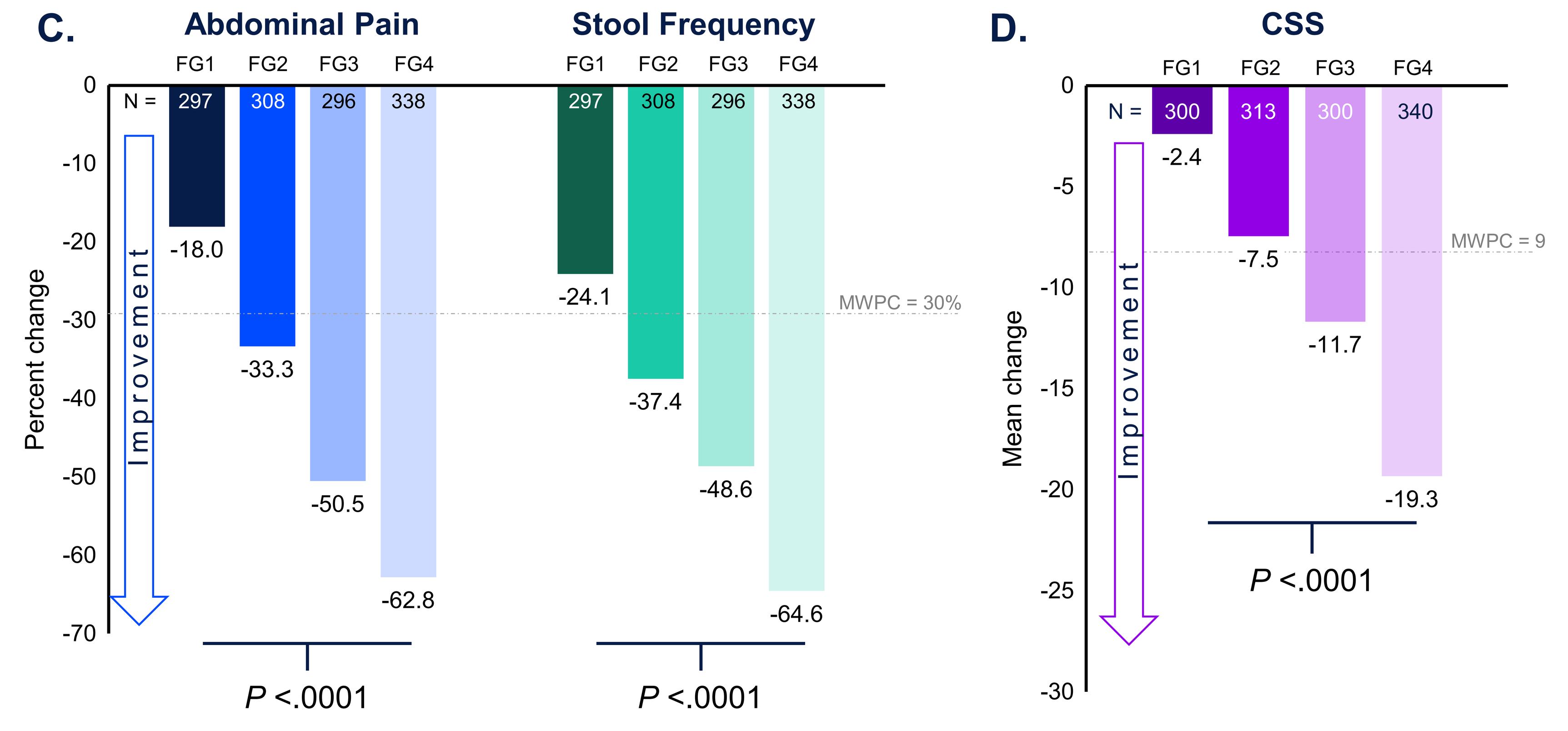
FG1 = mean change <2 | FG2 = 2≤FACIT-F<9 | FG3 = 9≤FACIT-F<17 | FG4 = FACIT-F≥17

AI, activity impairment; FG, fatigue group; IWW, impairment while working; MWPC, meaningful within-person change; OWI, overall work impairment; WPAI, Work Productivity and Activity Impairment questionnaire; WTM, work time missed.

Dotted line indicates the MWPC for the given outcome (ie, WPAI AI [8.5% reduction], WPAI IWW [6.1% reduction], WPAI OWI [7.3% reduction], and WPAI WTM [6.5% reduction]). All data stratified by change in FACIT-F.

Figure 3. Disease Symptoms and Severity Improve With Improving FACIT-F From Baseline to Week 12





FG1 = mean change <2 | FG2 = 2≤FACIT-F<9 | FG3 = 9≤FACIT-F<17 | FG4 = FACIT-F≥17

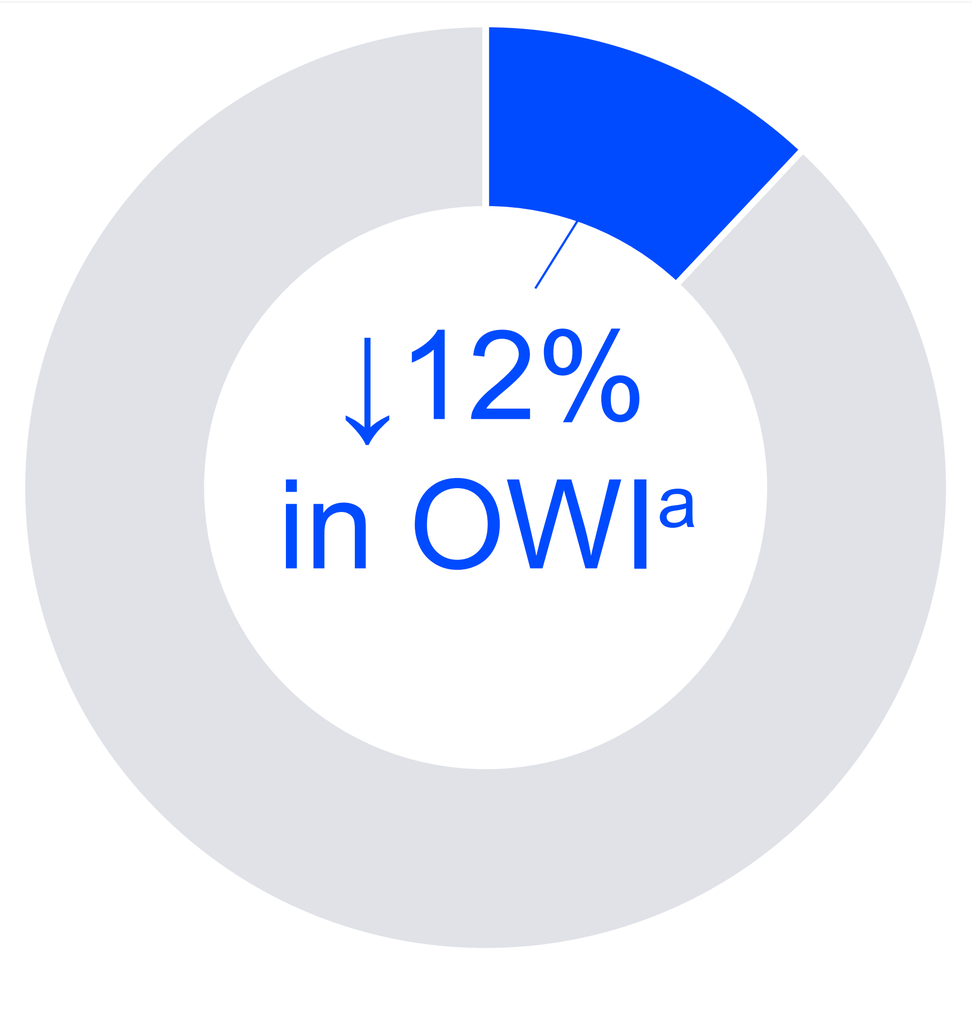
CDAI, clinical disease activity index; CSS, Crohn's symptom severity; FG, fatigue group; IBDQ, Inflammatory Bowel Disease Questionnaire; MWPC, meaningful within-person change.

Dotted line indicates the MWPC for the given outcome (ie, abdominal pain [30% decrease], stool frequency [30% reduction], CSS [9-point reduction], IBDQ [≥16-point increase], and CDAI [≥100-point decrease]).

All data stratified by change in FACIT-F.

Figure 4. Improvement in FACIT-F Was Associated With an Up to 29% Reduction in Overall Work Impairment, Resulting in Cost Savings

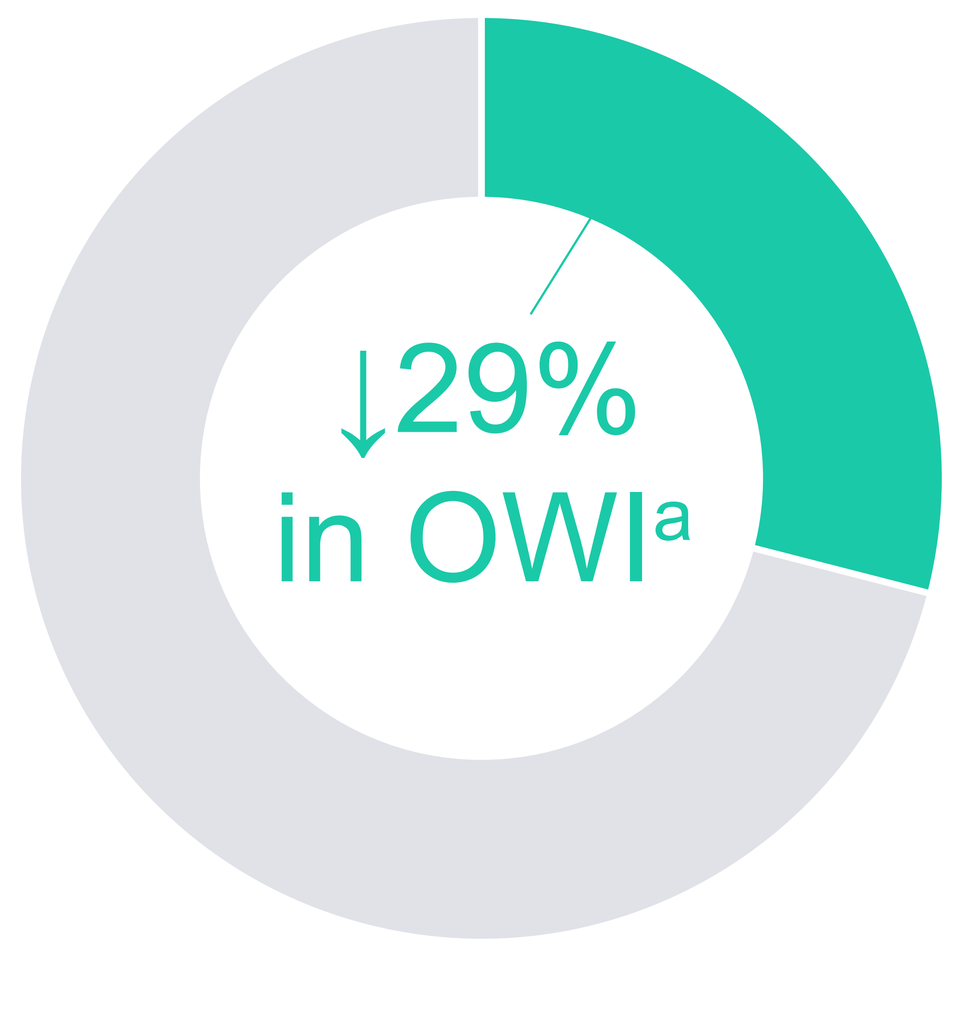
A. Achieving *Clinically Meaningful Improvement* in FACIT-F



Indirect Cost Savings:

- **+4.8** working hr/week
- **$7749**/year[b]
- **€7117**/year[c]

B. Achieving *normative value* in FACIT-F



Indirect Cost Savings:

- **+11.6** working hr/week
- **$18,726**/year[b]
- **€17,199**/year[c]

FACIT-F, Functional Assessment of Chronic Illness Therapy–Fatigue; OWI, overall work impairment.

[a]A decrease in OWI indicates improved work abilities. [b]Based on average USA hourly wage of $31.03. [c]Based on average European hourly wage of €28.50.