

CORRESPONDENCE OF MULTIPLE HEALTH OUTCOMES MEASURES IN RESPONSIVENESS TO MMX® MESALAMINE TREATMENT FOR PATIENTS WITH ULCERATIVE COLITIS

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Background

- Few clinical trials examining treatments for mild to moderate ulcerative colitis (UC) have assessed its impact on patients' health-related quality of life (HRQoL) or on patients' work-related outcomes (WRO), such as productivity or absenteeism
- No clinical trials or outcomes studies of UC patients have simultaneously included SF-36 (generic HRQoL), SIBDQ (disease-specific HRQoL), and WPAI (WRO) instruments
- Thus, within this patient population, the responsiveness of all three instruments to the same treatment, the degree of association among the instruments, and the degree to which each of these measures corresponds to changes in disease activity, is unknown

Objectives

- To examine changes in both HRQoL and WRO in patients with mild-to-moderate active UC following 8 weeks of daily treatment with 2.4-4.8 g/day of MMX® mesalamine
- To examine the association between changes in generic HRQoL, disease-specific HRQoL, and WRO
- To examine the correspondence between changes in these measures of HRQoL and WRO with changes in disease activity

Methods

Study Population and Design

- Data were collected from the Strategies in Maintenance for Patients Receiving Long-term Therapy (SIMPLE) trial, a phase IV, multi-center, single-arm, open-label trial that consisted of an 8 week acute phase and a 12 month maintenance phase
- The data presented here are from the acute phase, during which adult patients diagnosed with active mild-to-moderate UC at baseline received MMX mesalamine 2.4-4.8g/day treatment for 8 weeks (dose titrated based on physician decision)
- Study outcome measures were assessed at baseline and 8-week endpoint

Outcomes Measures

Generic HRQoL: SF12v2 (SF-12v2® Health Survey)

- 12 item self-report, generic HRQoL survey (using a four-week recall period)
 - Contains 8 domains that measure functional health and well-being
 - Physical functioning (PF) – Vitality (VT)
 - Role physical (RP) – Social functioning (SF)
 - Bodily pain (BP) – Role emotional (RE)
 - General health (GH) – Mental health (MH)
- Each domain and summary measure is standardized into a T-score (Mean=50; SD=10)
- Higher scores indicate better HRQoL in that domain

Disease-specific HRQoL: SIBDQ (Short Inflammatory Bowel Disease Questionnaire)

- 10 item self-report, HRQoL survey specific to patients with irritable bowel disease (IBD) (using a two-week recall period)
 - Affords calculation of 4 scales to measure the impact of IBD on different domains of functional health and well-being:
 - Bowel symptoms
 - Systemic symptoms
 - Emotional function
 - Social function
- Higher scores indicate better HRQoL

Work-related outcomes: WPAI:SHP (Work Productivity and Activity Impairment Questionnaire: Specific Health Problem)

- 6 item self-report work related outcomes survey (using a one-week recall period)
 - Affords calculation of 4 scales to measure the impact of IBD on different domains of impairment in work or other activities:
 - Absenteeism
 - Presenteeism (impairment at work)
 - Work productivity loss (overall work impairment)
 - Activity Impairment
- WPAI scale scores are impairment percentages, with higher numbers indicating greater impairment /less productivity

Disease activity: Stool frequency (SF) & Rectal bleeding severity (RBS)

- Both were single item patient-reported measures (using a daily recall period)
 - Stool frequency:** score of 0: ≤1 more than usual; score of 1: 2-3 more than usual; score of 2: ≥4 more than usual
 - Rectal bleeding severity:** score of 0: no blood ; score of 1: streaks of blood; score of 2: obvious blood; score of 3: mostly blood
 - Each was recorded daily via phone-based interactive voice response system
 - The mean of responses from the three days prior to assessment point was used
 - Higher scores indicate more active disease

Analysis

Impact of MMX mesalamine treatment on UC patients' HRQoL and WRO

- Paired-sample t-tests were used to test for differences between baseline and endpoint SF-12v2, SIBDQ, and WPAI scale and summary scores

Associations among changes in HRQoL and WRO scores following treatment

- Pearson correlation coefficients assessed the strength and direction of associations between baseline-endpoint change in SF-12v2, SIBDQ, and WPAI scale scores

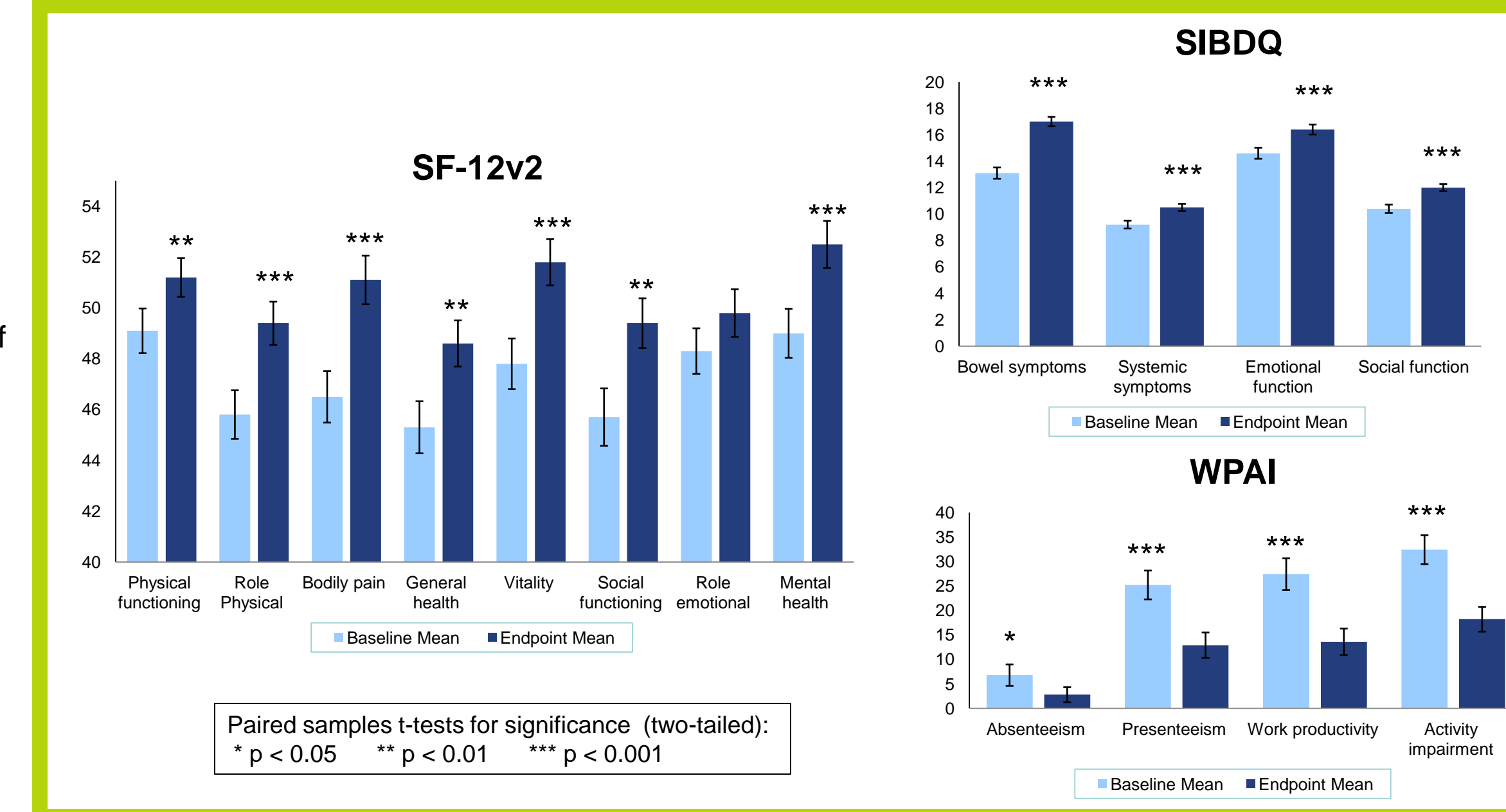
Associations among changes in HRQoL and WRO with changes in disease activity

- Pearson correlation coefficients assessed the strength and direction of associations between baseline-endpoint change in SF-12v2, SIBDQ, and WPAI scale scores with change in stool frequency and rectal bleeding severity

Results

Mean HRQoL and Work-related Outcomes of Active Mild-to-moderate UC Patients Before and After Daily MMX Mesalamine Treatment

Figure 1. Mean SF-12v2, SIBDQ, and WPAI scale scores at baseline and 8-week endpoint. Error bars indicate standard error of means.



Associations Among Changes in HRQoL & WRO Following Daily MMX Mesalamine Treatment

Table 1. Pearson coefficients for correlations among SF-12v2, SIBDQ, and WPAI change scores.

		SF-12v2							SIBDQ				
		PF	RP	BP	GH	VT	SF	RE	MH	Bowel	Systemic	Emotional	Social
SIBDQ	Bowel	0.29	0.51	0.57	0.40	0.49	0.42	0.39	0.26	---	---	---	---
	Systemic	0.29	0.43	0.47	0.39	0.60	0.53	0.56	0.40	---	---	---	---
	Emotional	0.30	0.42	0.46	0.37	0.48	0.58	0.46	0.67	---	---	---	---
	Social	0.42	0.63	0.61	0.35	0.52	0.67	0.56	0.38	---	---	---	---
WPAI	Absent	0.00	-0.34	-0.39	-0.06	-0.30	-0.29	-0.28	-0.13	-0.40	-0.07	-0.12	-0.22
	Present	-0.31	-0.61	-0.56	-0.20	-0.42	-0.40	-0.52	-0.28	-0.68	-0.32	-0.52	-0.62
	Productivity	-0.29	-0.62	-0.58	-0.17	-0.43	-0.45	-0.53	-0.29	-0.70	-0.32	-0.50	-0.63
	Impairment	-0.38	-0.60	-0.57	-0.38	-0.51	-0.51	-0.51	-0.36	-0.59	-0.48	-0.55	-0.69

Note: correlation coefficients printed in blue ink are statistically significant at $p < 0.05$ (two-tailed)

Correspondence among Changes in HRQoL, WRO, and Disease Activity Following Daily MMX Mesalamine Treatment

Table 2. Pearson coefficients for correlations between change in HRQoL & WRO scales and changes in disease activity measures

	Stool frequency	Rectal bleeding severity
SF-12v2		
Physical functioning	-0.26**	-0.29**
Role Physical	-0.32**	-0.38***
Bodily pain	-0.35***	-0.38***
General health	-0.32**	-0.28**
Vitality	-0.36***	-0.47***
Social functioning	-0.33***	-0.40***
Role emotional	-0.25*	-0.35***
Mental health	-0.12	-0.23*
Average correlation	-0.29	-0.35
SIBDQ		
Bowel symptoms	-0.45***	-0.55***
Systemic symptoms	-0.35***	-0.38***
Emotional function	-0.29**	-0.42***
Social function	-0.40***	-0.52***
Average correlation	-0.37	-0.47
WPAI		
Absenteeism	0.17	0.29*
Presenteeism	0.39***	0.47***
Work productivity	0.35**	0.47***
Activity impairment	0.47**	0.54***
Average correlation	0.35	0.45

Note: Average correlation coefficients were computed using Fisher's r-to-z transformation
 Two-tailed test for significance: * $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$

Main Findings

- With the exception of the SF-12v2 RE scale, significant improvement in health outcomes was found for all scale and summary scores of the SF-12v2, SIBDQ, and WPAI (Figure 1)
- Mostly moderate and significant intercorrelations were found among changes in scale scores for the 3 outcomes measures (Table 1); the average correlation was 0.47 between SF-12v2 and SIBDQ, -0.39 between SF-12v2 and WPAI, and -0.48 between SIBDQ and WPAI
- Mostly moderate and significant intercorrelations were found between changes in scores for the 3 outcomes measures and decreases in stool frequency and rectal bleeding)

Conclusions

- Consistent moderate correlations among three outcomes measures, and between each of these outcomes and clinical symptoms, indicated coherence of these three instruments in measuring UC patients' response to treatment
- Baseline-endpoint changes across all scales, along with links to changes in disease activity, indicates that each of the instruments were responsive to treatment, and may be valuable tools in measuring treatment benefits above and beyond clinical symptoms



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