

Disease-specific, Health-related Quality of Life in Patients With Quiescent Ulcerative Colitis: Effects of One Year Maintenance Treatment With MMX^{®†} Mesalazine

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INTRODUCTION

- Ulcerative colitis (UC) is a chronic disease characterized by inflammation of the large intestine, with typical symptoms including abdominal pain, diarrhoea, and rectal bleeding
- Several studies have identified disease activity (ie, symptom frequency/severity) as a key predictor of health-related quality of life (HRQL) in UC patients¹⁻³
- Thus, a treatment regimen that produces maintenance of disease remission in patients with quiescent UC should also prevent decreases in patients' HRQL

OBJECTIVES

- To examine changes in HRQL in patients with mild-to-moderate quiescent UC who receive daily MMX[®] mesalazine 2.4 g/day for 6 and 12 months
- To examine the correspondence between changes in HRQL and changes in disease activity over the 12-month treatment regimen
- To compare HRQL of clinically recurrent and non-recurrent patients at 12 months

METHODS

Study Population and Design

UC patient sample

- Data were collected from the Strategies in Maintenance for Patients Receiving Long-term Therapy (SIMPLE) trial, a US-based, multicenter, single-arm, open-label trial that consisted of an 8-week acute phase (n = 132) and a 12-month maintenance phase (n = 206)
- The data presented in the current analyses are from the 12-month maintenance phase, during which adult patients with mild-to-moderate quiescent UC received MMX mesalazine 2.4 g/day QD
- Quiescence of UC in the current study was defined as a patient obtaining a score of 0 on UC symptom measures of stool frequency (≤ 1 more bowel movement than normal) and rectal bleeding (no bleeding)
- HRQL and disease activity were assessed at baseline and 6- and 12-month visits; clinical recurrence of disease was assessed at the 12-month visit
- No imputation methods were used to replace missing data due to early withdrawal

Study Outcomes

HRQL measure: SIBDQ (Shortened version of the Inflammatory Bowel Disease Questionnaire)⁴

- 10-item, self-report, inflammatory bowel disease (IBD)-specific health survey with a 2-week recall period
- Includes 4 domains measuring impact of IBD on functional health and well-being
 - Bowel symptoms
 - Systemic symptoms
 - Emotional function
 - Social function
- A total score that measures overall impact of IBD on HRQL can also be computed
- Each domain score is the sum of responses to 2 or 3 items; the total score is the sum of responses to all items
- Higher scores indicate better HRQL

Disease activity measures: stool frequency and rectal bleeding severity

- Both were single-item, patient-reported measures
 - Stool frequency (SF): 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 (RBS): score of 0, no blood; score of 1, streaks of blood; score of 2, obvious blood; score of 3, mostly blood
- Each was measured daily throughout the trial (reported via interactive voice response)
- Average score from the 3 days prior to assessment point was used
- Lower scores indicate less disease activity

Clinical recurrence of UC

- Patients were classified as clinically recurrent if meeting both of the following criteria:
 - Self-report of ≥ 4 bowel movements per day above their normal frequency
 - Self-report of any rectal bleeding, urgency, or abdominal pain
- Classification of clinical recurrence took place at the 12-month visit

Statistical Analyses

HRQL of patients with quiescent UC at baseline and following 6 and 12 months of daily MMX mesalazine treatment

- Repeated-measures analysis of variance (ANOVA) models were used to test for differences in patients' SIBDQ scale and summary scores across baseline and 6- and 12-month visits

Correspondence between changes in patients' HRQL and changes in disease activity following 12 months of daily MMX mesalazine treatment

- Pearson correlation coefficients assessed the strength and direction of associations between changes from baseline to Month 12 in SIBDQ, SF, and RBS scores

HRQL in clinically recurrent and non-recurrent patients following 12 months of daily MMX mesalazine treatment

- A multivariate analysis of covariance (MANCOVA) model, with recurrence status as a between-subjects factor and with patient age, gender, and body mass index (BMI) as covariates, tested for differences between recurrent and non-recurrent patients for each SIBDQ domain and total score at Month 12

RESULTS

HRQL of patients with quiescent UC at baseline and following 6 and 12 months of daily MMX mesalazine treatment (Figure 1)

- No statistically significant (all $P > 0.10$) change in scores across baseline and 6- and 12-month visits were observed for any SIBDQ domain or for the total SIBDQ score
- The absolute magnitude of differences across time were extremely small; no change in mean for each domain and total score across the 3 assessments exceeded 3%

Correspondence between changes in patients' HRQL and changes in disease activity following 12 months of daily MMX mesalazine treatment (Table 1)

- With the exception of the systemic symptoms domain, moderate correlations (all statistically significant at $P < 0.01$) were observed between changes in SIBDQ scores and changes in both SF and RBS measures, indicating that decreases in disease activity were associated with increases in HRQL

HRQL in clinically recurrent and non-recurrent patients following 12 months of daily MMX mesalazine treatment (Figure 2)

- Clinically recurrent patients scored significantly lower than non-recurrent patients on all domains and total score ($P < 0.05$) except for the systemic symptoms domain

HRQL of Patients With Quiescent UC at Baseline and Following 6 and 12 Months of Daily MMX Mesalazine Treatment

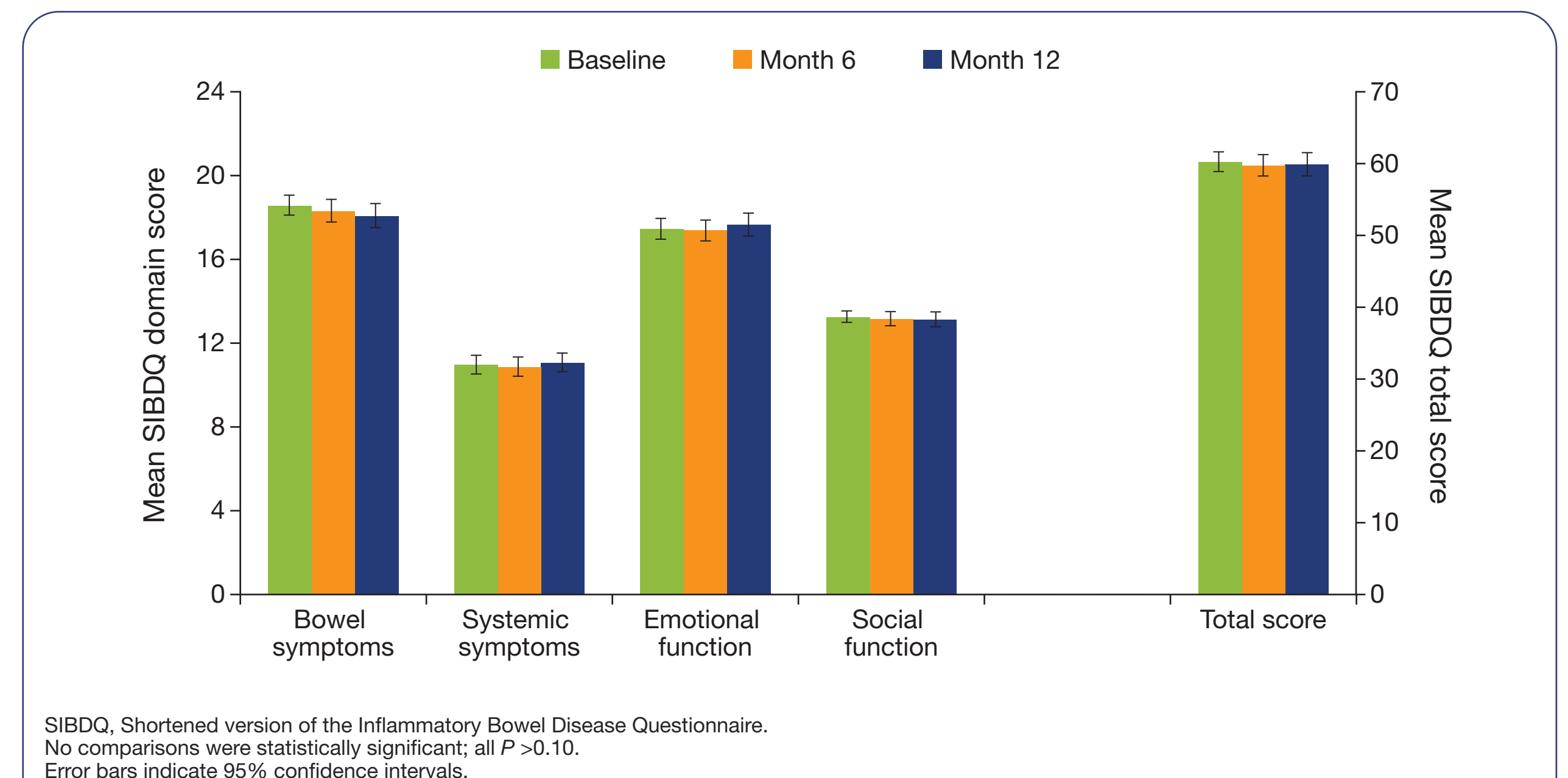


Figure 1. Mean SIBDQ scores for patients with responses at baseline and 6- and 12-month visits (n = 128).

Correspondence Between Changes in Patients' HRQL and Changes in Disease Activity Following 12 Months of Daily MMX Mesalazine Treatment

Table 1. Pearson Correlations Between Changes From Baseline to Month 12 in SIBDQ Scores and Measures of Disease Activity (n = 130)

	SF	RBS
Bowel symptoms	-0.28**	-0.36***
Systemic symptoms	-0.12	-0.12
Emotional function	-0.27**	-0.29**
Social function	-0.38***	-0.34***
Total score	-0.33***	-0.36***

SIBDQ, Shortened version of the Inflammatory Bowel Disease Questionnaire; SF, stool frequency; RBS, rectal bleeding severity. ** $P < 0.01$. *** $P < 0.001$.

Sensitivity of SIBDQ Scores to Clinical Recurrence Status

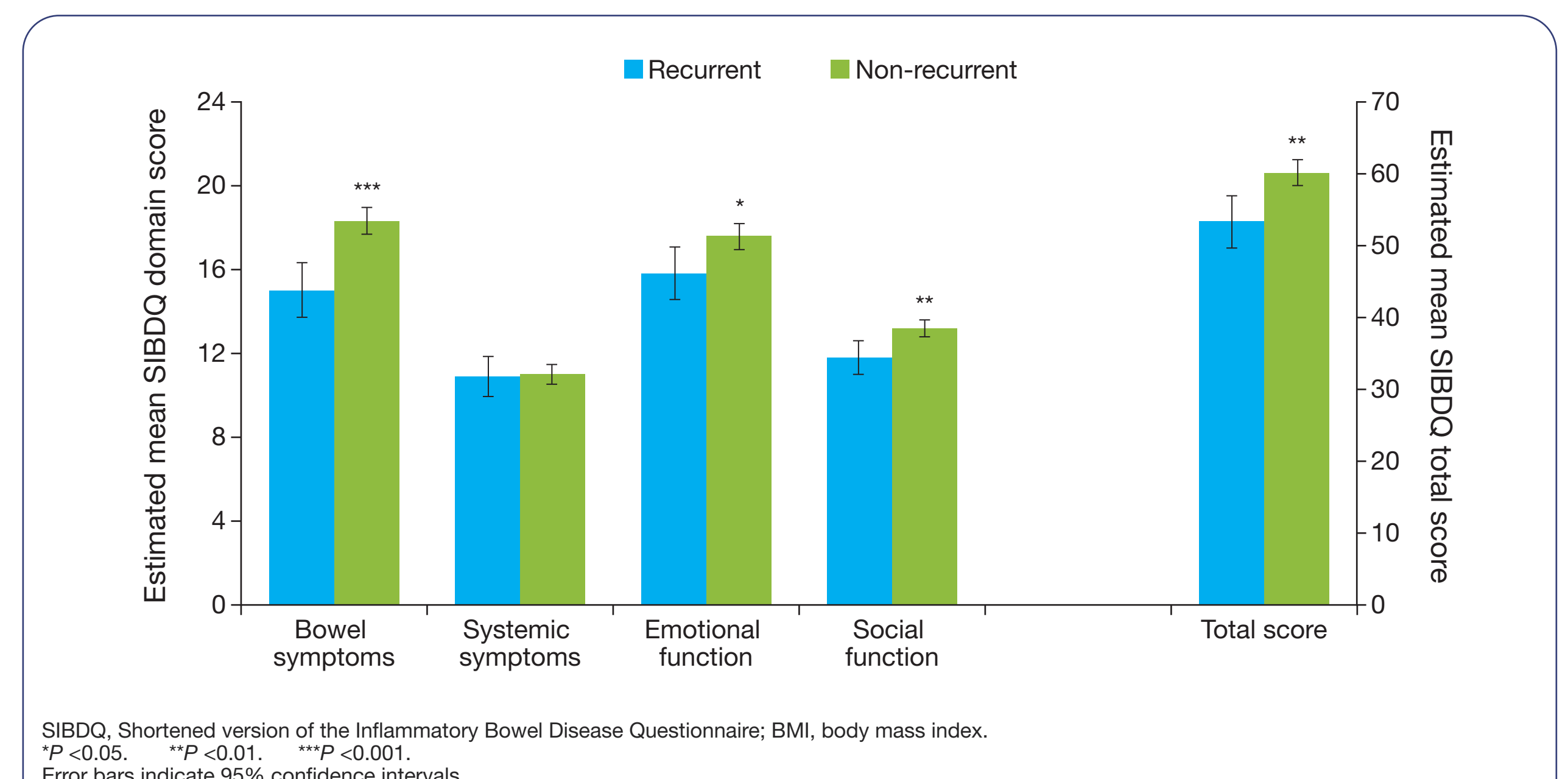


Figure 2. Estimated mean SIBDQ scores (adjusted by age, gender, and BMI) at the 12-month visit of the maintenance phase for clinically recurrent (n = 29) and non-recurrent (n = 117) patients.

Safety and Tolerability

- At least 1 treatment-emergent adverse event was reported by 123 of the 208 patients (59.1%) in the maintenance phase safety population, with the majority of events reported as mild or moderate in severity

LIMITATIONS

- The open-label design used in this study may have led to biases in patients' responses due to expected changes from treatment; a randomized controlled trial will be needed to confirm these results
- The lack of data imputation for early withdrawal patients may have biased results, since patients who dropped out early may have had worse health outcomes than those who stayed in the trial

CONCLUSIONS

- Patients receiving maintenance treatment with daily MMX mesalazine exhibited highly stable HRQL over the course of the trial; no drop-off was observed in any dimension of HRQL at the midpoint or end of the 12-month treatment period
- Consistent with findings from previous research,¹⁻³ HRQL was associated with disease activity; decreases in disease activity over the course of the trial were generally accompanied by improved HRQL
- Further, patients in the study whose disease remained in remission demonstrated significantly better average HRQL than patients with clinically recurrent disease

References

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[†]MMX[®] is a registered trademark of Cosmo Technologies, Ltd., Ireland.

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