

HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH MILD-TO-MODERATE ULCERATIVE COLITIS BEFORE AND AFTER 8 WEEKS' TREATMENT WITH MMX MESALAMINE: COMPARISON WITH 2009 US GENERAL POPULATION NORMS

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Introduction

- Ulcerative colitis (UC) is a chronic inflammatory disease of the large intestine and rectum with associated symptoms including abdominal pain, diarrhea, rectal bleeding, and the persistent urge to defecate
- The presence and severity of these symptoms have a significant negative impact on a UC patient's physical, social, and psychological functioning and well-being: studies examining the burden of UC on health-related quality of life (HRQL) through comparison of UC patients and general population samples have found deficits on virtually all aspects of UC patients' HRQL¹⁻³
- Several clinical and observational studies have identified symptom severity/degree of disease activity as a strong (and typically the strongest) predictor of UC patient's generic HRQL^{1,4,5}
- Assuming that disease activity impacts HRQL directly, we hypothesized that patients with active mild-to-moderate UC who receive the MMX Multi Matrix System[®] (MMX[®])* formulation of mesalamine, which has been shown to significantly reduce UC activity,^{6,7} should show a reduction in disease burden on HRQL

Objectives

- To assess the burden of disease on HRQL for patients with mild-to-moderate active UC relative to an age- and gender-matched 2009 United States (US) general population normative sample using the 12-item Short Form health outcomes measure, version 2 (SF-12v2[®]†)
- To measure the change in the burden of disease following 8 weeks of daily treatment with MMX mesalamine in a clinical trial setting

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 phase IV, multicenter, single-arm, open-label trial that consisted of an 8-week acute phase (n = 138) and a 12-month maintenance phase (n = 207)
- The data presented in the current analyses are from the acute phase, during which patients received MMX mesalamine 2.4-4.8 g/day QD for 8 weeks (initial dosage and any subsequent titration was determined by the clinician)
- Enrollment in the acute phase was restricted to adults of both genders who were diagnosed with currently active UC of mild-to-moderate severity
- HRQL was assessed at baseline and week 8 (endpoint) visits; the subsample of patients with HRQL scores at both times (n = 107) will be referred to as 'completers'

US general population normative sample

- This sample was derived from responses to a 2009 Internet-based norming survey
- Respondents were drawn from a national probability sample of US non-institutionalized adults from the Knowledge Panel^{®‡} maintained by Knowledge Networks (<http://www.knowledgenetworks.com/knpanel/index.html>)
- A total of 8,719 individuals participated in the survey; 6,045 of these individuals completed the SF-12v2

Patient-Reported Outcomes Measure

SF12v2[®] Health Survey⁸

- 12-item self-report survey of generic HRQL that uses a 4-week recall period
- Contains 8 domains that measure functional health and well-being
 - Physical functioning (PF)
 - Role physical (RP)
 - Bodily pain (BP)
 - General health (GH)
 - Vitality (VT)
 - Social functioning (SF)
 - Role emotional (RE)
 - Mental health (MH)
- From these 8 domains, 2 summary scores can be calculated
 - Physical component summary (PCS)
 - Mental component summary (MCS)
- Each domain and summary score is standardized into a T-score, with a mean of 50 and a standard deviation of 10
- Minimally important differences (MIDs) for PCS and MCS, which reflect the smallest group difference that would be considered clinically significant, have been empirically estimated at 3 points⁹
- Higher domain and summary scores indicate better HRQL

Analysis Plan

Assessment of Initial Disease Burden: Comparison of HRQL Between UC Patients at Baseline With US General Population Normative Sample

- SF-12v2 scores from the US normative sample were estimated based on weighted adjustments to match the age and gender distributions of the baseline UC patient trial sample using least squares multiple regression models for each domain and summary measure
- Univariate analysis of variance (ANOVA) models were used to test for significant differences between UC patients' baseline domain and summary scores and estimated scores from the matched US normative sample; mean differences relative to MIDs for PCS and MCS measures were used to interpret the clinical meaningfulness of group differences in mental and physical HRQL

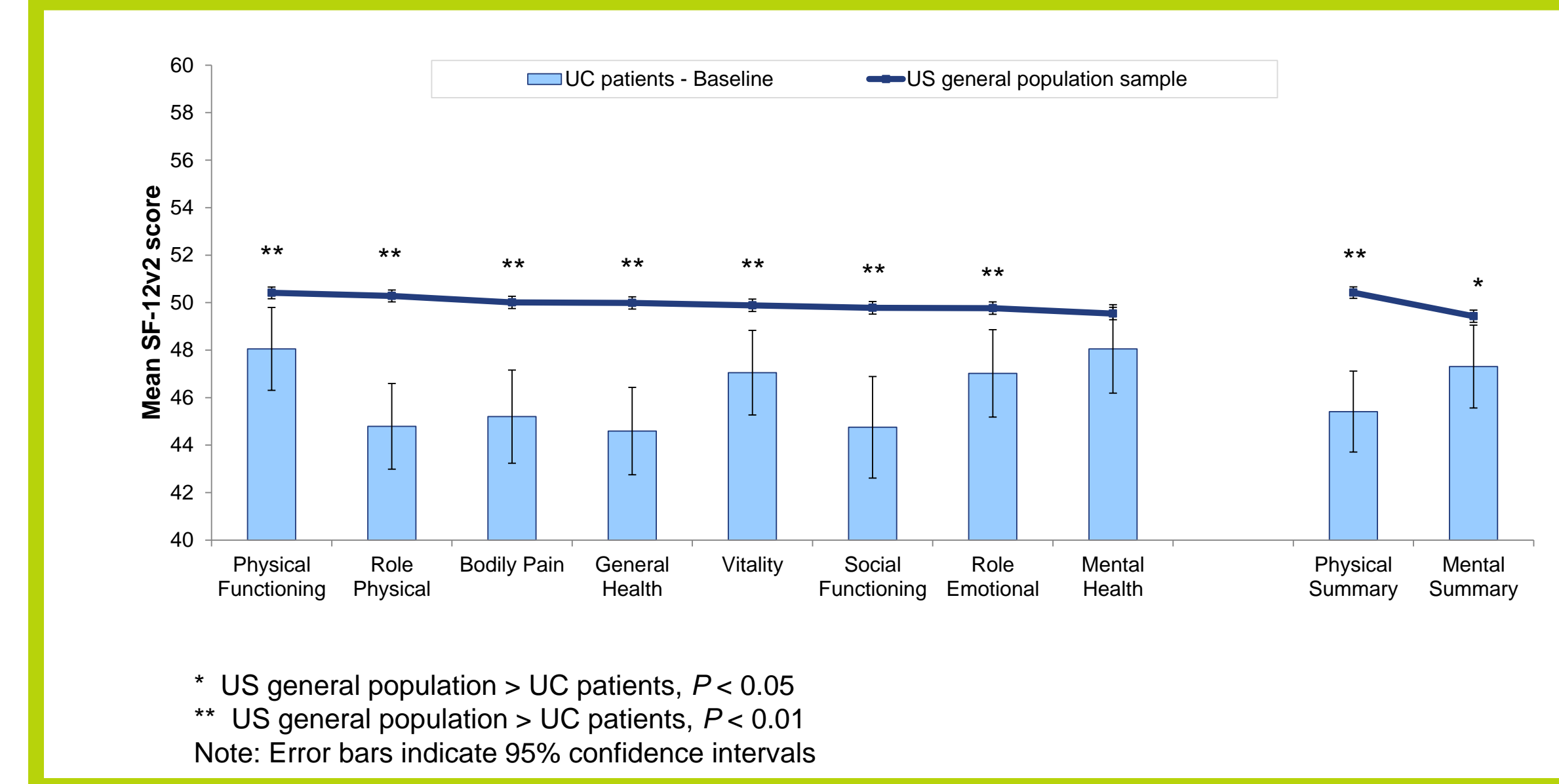
Assessment of Post-treatment Disease Burden: Comparison of HRQL Between Completers at Baseline and Endpoint With US General Population Normative Sample

- SF-12v2 scores from the US normative sample were estimated based on weighted adjustments to match the age and gender distributions of the 'completer' subgroup in the trial sample using least squares multiple regression models for each domain and summary measure
- Given the possibility that patients with a larger initial burden were more likely to withdraw from the study prior to the 8-week visit, which could lead to an overestimation in the interpretation of change in patient burden from baseline to endpoint, we analyzed both baseline and endpoint burden for the 'completers' subgroup
- Using similar techniques as those described above, univariate ANOVA models tested for significant differences between completers' baseline and endpoint domain and summary scores with estimated scores from the general population sample, while mean differences relative to MIDs for PCS and MCS measures were used to interpret the clinical meaningfulness of group differences in HRQL

Results

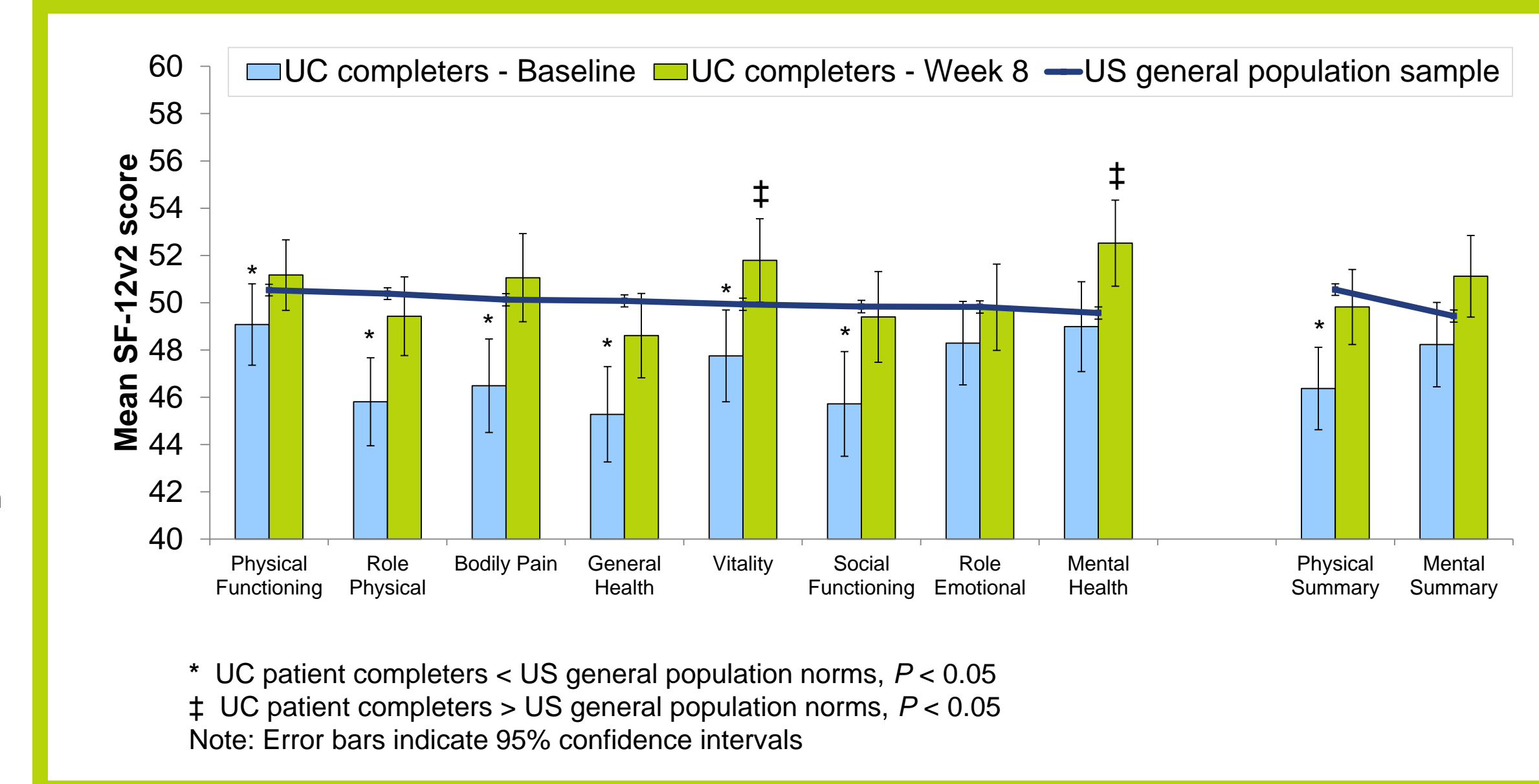
Initial Disease Burden: Comparison of HRQL Between UC Patients at Baseline with 2009 US General Population Normative Sample

Figure 1. Mean SF-12v2 Scores for UC Sample at Baseline (n = 130) and the US General Population Normative Sample (n = 6,045)



Post-treatment Disease Burden: Comparison of HRQL Between Completers at Baseline and Endpoint with 2009 US General Population Normative Sample

Figure 2. Mean SF-12v2 Scores for UC Completers at Baseline and Endpoint (n = 107) and the US General Population Normative Sample (n = 6,045)



Main Findings: Initial Disease Burden (Figure 1)

- Mean SF-12v2 scores for UC patients at baseline were significantly below those of the matched general population scores on all domains with the exception of MH (P = 0.12 for MH; P < 0.01 for all other domains)
- Means for both summary measures for UC patients at baseline were statistically lower than for the general population; however, only differences in PCS scores exceeded the established MID of 3 points (PCS: 45.4 vs. 50.4, P < 0.001; MCS: 47.3 vs. 49.4, P < 0.05)

Main Findings: Post-treatment Disease Burden (Figure 2)

- While UC patient completers scored significantly below the matched population for the majority of scales and for the PCS at baseline, SF-12v2 scores for these patients following 8 weeks of treatment were either statistically equivalent to, or even exceeded (VT and MH; P < 0.05 for both), scores from the matched general population sample
- Mean differences between UC patients at endpoints and the matched general sample were < 2 points for both PCS and MCS scores, indicating that UC patients were clinically equivalent with the general population in both mental and physical HRQL following 8 weeks of treatment

Limitations

- While the open-label design used here provides a more naturalistic, real-world setting in which to examine the effectiveness of MMX treatment, it 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

Conclusions

- The burden of mild-to-moderate UC on HRQL is broad, negatively impacting most dimensions of mental and physical functioning and well-being
- After receiving an 8-week regimen of daily treatment with MMX mesalamine, these patients showed normal levels on all dimensions of HRQL, with SF-12v2 domain and summary scores both statistically and clinically at least equivalent to a demographically matched general population sample

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