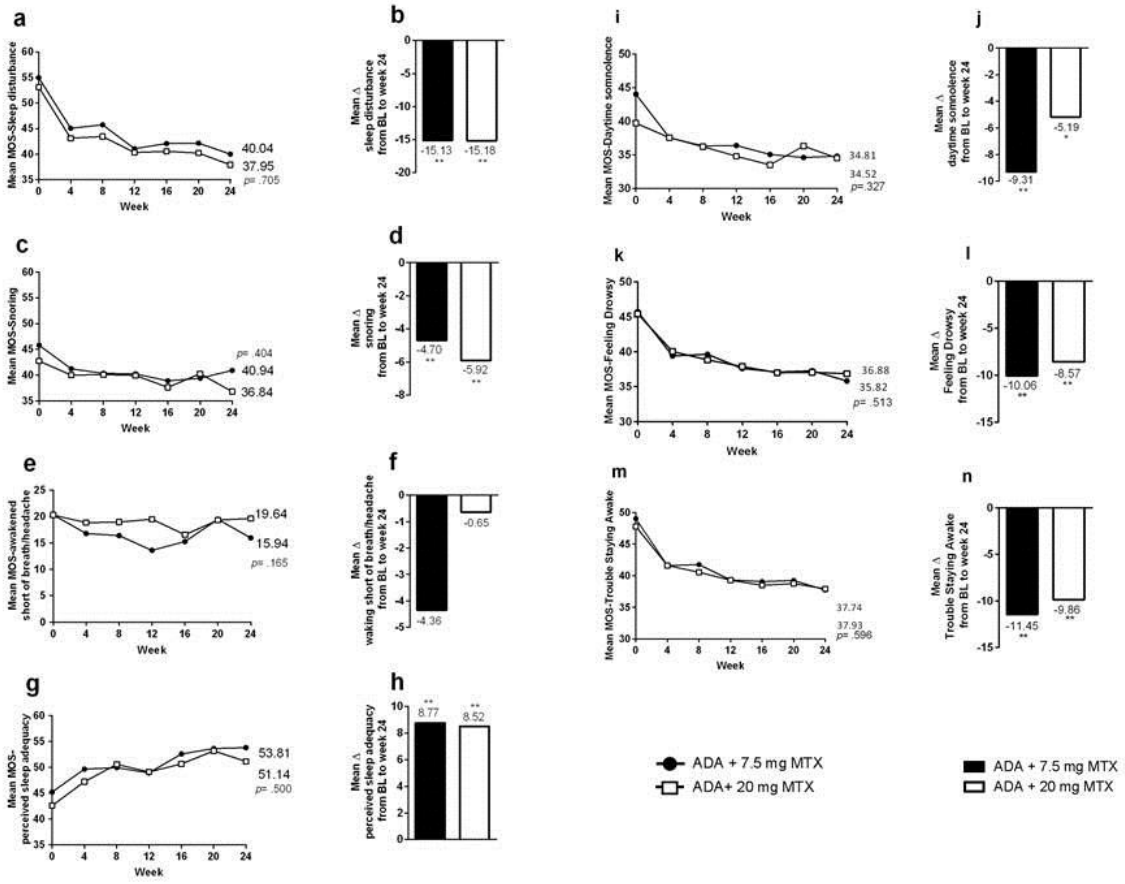
SUPPLEMENTARY METHODS:

Sleep quality was measured using the Medical Outcomes Sleep (MOS) Index II which is composed of 6 subdomains: sleep disturbance, daytime somnolence, perceived sleep, awakened short of breath or with headache, snoring and sleep quantity. For each of these, with the exception of sleep adequacy, a higher score indicates poorer quality of sleep.

Sexual impairment due to RA was measured using a global question of “how much did your RA affect sexual functioning over the past 7 days?”. The patients chose a score from 0 to 10 with 0 representing no effect and 10 representing RA completely preventing sexual functioning.

SUPPLEMENTARY FIGURES:

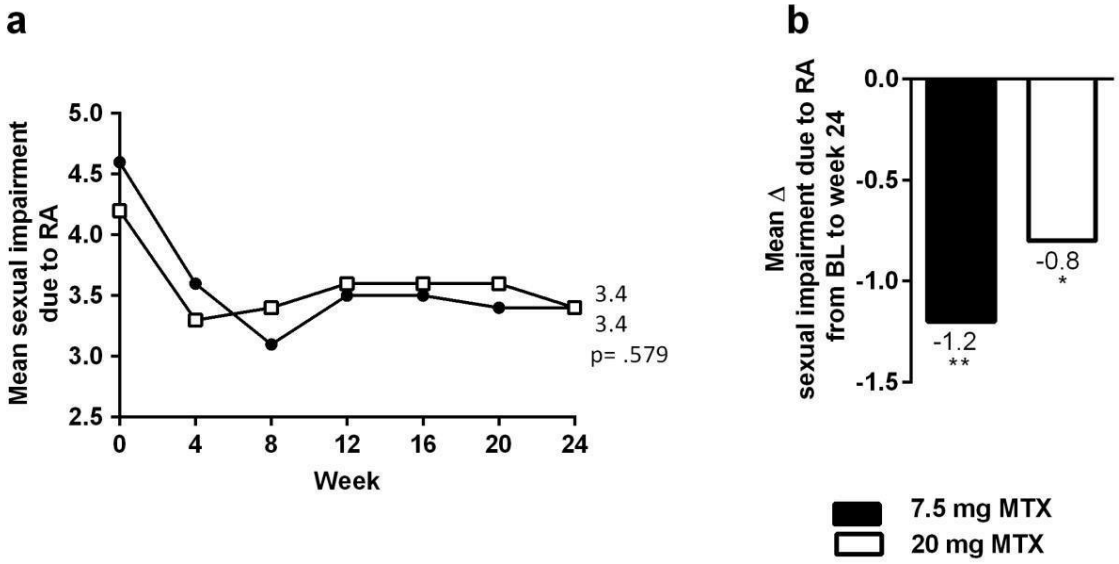
Supplemental figure 1. (a) Sleep Disturbance over time (b) Mean change in Sleep Disturbance from baseline to Week 24
(c) Snoring over time (d) Mean change in Snoring from baseline to Week 24
(e) Awakened Short of Breath over time (f) Mean change in Awakened Short of Breath from baseline to Week 24
g) Perceived Sleep Adequacy over time (h) Mean change in Perceived Sleep Adequacy from baseline to Week 24
(i) Daytime Somnolence over time (j) Mean change in Daytime Somnolence from baseline to Week 24
(k) Feeling Drowsy over time (l) Mean change in Feeling Drowsy from baseline to Week 24
(m) Trouble Staying Awake over time (n) Mean change in Trouble Staying Awake from baseline to Week 24
P-values of comparison between MTX dosage groups at Week 24 (ANCOVA) in a, c, e, g, i, k, m. ***p* <.001, comparison between scores at baseline and at Week 24(t-test) for each MTX dosage group in b, d, f, h, j, l and n.



Supplemental figure 2. (a) Sexual impairment due to RA over time. *P*-values of comparison between MTX dosage groups at Week 24 (ANCOVA).

(b) Mean change in sexual impairment due to RA from baseline to Week 24

***p* <.001, comparison between scores at baseline and at Week 24(t-test) for each MTX dosage group.



SUPPLEMENTARY TABLES:

Table S1: Patient demographics, disease characteristics and PROs at Baseline

	Low dosage MTX+ADA (N=154)	High dosage MTX+ADA (N=155)	Total (N=309)
Age, years	55.1 ± 13.1	54.5 ± 11.1	54.8 ± 12.1
Female, n (%)	120 (77.9)	111 (71.6)	231 (74.8)
RA duration, years	5.9 ± 8.5	4.7 ± 6.5	5.3 ± 7.6
TJC68	31.1 ± 16.8	31.4 ± 17.3	31.2 ± 17.0
SJC66	17.8 ± 10.1	18.9 ± 11.6	18.3 ± 10.9
PhGA (VAS, 0-100mm)	61.6 ± 20.6	61.1 ± 19.7	61.3 ± 20.1
PGA (VAS, 0-100mm)	62.6 ± 22.3	65.0 ± 23.4	63.8 ± 22.8
PGA pain (VAS, 0-100mm)	65.3 ± 21.0	68.3 ± 20.8	66.8 ± 20.9
DAS28(CRP)	5.8 ± 0.9	5.8 ± 1.0	5.8 ± 0.9
HAQ-DI	1.5 ± 0.6[a]	1.5 ± 0.7[b]	1.5 ± 0.6
Prior biologic DMARD, n (%)	10 (6.5)	7 (4.5)	17 (5.5)
WPAI			
- % time in absenteeism	9.0 ± 17.6[c]	11.5 ± 21.5[d]	10.3 ± 19.6
- % time in presenteeism	44.5 ± 30.5[c]	47.8 ± 26.6[d]	46.1 ± 28.6
- Overall work impairment	47.6 ± 30.6[c]	51.0 ± 28.5[d]	49.3 ± 29.5
- activity impairment (%)	57.0 ± 27.3[e]	61.9 ± 25.8[f]	59.5 ± 26.6
SF-36			
- PCS	31.6 ± 8.5[a]	31.5 ± 8.5[h]	31.5 ± 8.5
- MCS	44.7 ± 13.2[a]	41.9 ± 12.4[h]	43.3 ± 12.8
MOS Index II			

Sleep disturbance	55.0 ± 26.0[g]	53.1 ± 26.6[b]	54.0 ± 26.3
Snoring	45.8 ± 31.9[i]	42.8 ± 30.0[h]	44.3 ± 30.9
Awakened short of breath	20.3 ± 27.1[i]	20.3 ± 26.9[h]	20.3 ± 27.0
Daytime somnolence	44.0 ± 25.2[g]	39.7 ± 21.4[b]	41.9 ± 23.4
Perceived sleep adequacy	45.2± 24.9[a]	42.6 ± 23.1[b]	43.9 ± 24.0
Sleep Problems Index 6 (Feeling drowsy)	45.8 ± 20.9[g]	45.4 ±18.3[b]	45.6 ± 19.6
Sleep Problems Index 9 (Trouble staying awake)	49.0 ± 20.7[i]	47.8 ±18.8[b]	48.4 ±19.8
TSQM			
- Effectiveness	46.1 ± 19.0[j]	42.6 ± 20.1[k]	44.4 ± 19.6
- Side-effects	88.9 ± 21.0[l]	86.1 ± 24.2[q]	87.5 ± 22.6
- Convenience	72.3 ± 17.5[j]	74.1 ± 19.4[r]	73.2 ± 18.4
- Global satisfaction	59.9 ± 21.1[j]	54.4 ± 22.3[s]	57.2 ± 21.8
Sexual Impairment due to RA	4.6 ± 3.7[o]	4.2 ± 3.6[p]	4.4 ± 3.6

All values are mean ± standard deviation unless otherwise indicated. There were no statistical differences between the dosage groups at baseline. [a]N=151, [b]N=154,[c]N=64, [d]N=62, [e]N=137, [f]N=143, [g]N=150, [h]N=152. [i]N=149. [j]N=101, [k]N=97, [l]N=99, [o]N=144, [p]N=141, [q]N=100, [r]N=95, [s]N=96. RA, rheumatoid arthritis; DMARD, disease modifying anti-rheumatic drug; TJC, tender joint count; SJC, swollen joint count; PGA, patient's global assessment of disease activity; PhGA, physician's global assessment of disease activity; PRO, patient reported outcome; MTX, methotrexate; ADA, adalimumab; DAS28(CRP), 28 joint disease activity score based on C-reactive protein; HAQ-DI, health assessment questionnaire-disability index; WPAI, work productivity and activity index; SF-36, short form- 36; P/MCS, physical/mental component summary; MOS Index II, Medical Outcomes Sleep Index II; TSQM, Treatment Satisfaction Questionnaire for Medication

Table S2: Correlation between improvements from baseline to week 24, in WPAI-presenteeism and improvements in fatigue[a], pain and physical function, Pearson's coefficient (r)

	ADA +7.5 mg/week MTX	ADA +20 mg/week MTX
Improvement in SF-36 (vitality)	0.51	0.50
Improvement in PGA-pain	0.59	0.66
Improvement in HAQ-DI	0.59	0.77

[a]Fatigue is represented by SF-36(vitality). WPAI, work productivity and activity impairment, ADA, adalimumab; MTX. Methotrexate; SF-36, short form 36; PGA-pain, patient pain; HAQ-DI, health assessment questionnaire-disability index