Appendix: Supplementary tables A-E [posted as supplied by author]

Table A: Details Of Imputation For Missing Data

Issue	Imputation Methods
Outcomes assessed every 6 months	In subjects who had missing outcomes at 6 months, under the monotone assumption, baseline outcomes and explanatory covariates was used to impute the missing values at 6 months. For patients who had missing outcomes at 12 months, baseline and 6 months outcomes with explanatory covariates were used to impute the missing values at 12 months. If outcome variables were missing at 6 and 12 months then the outcome variables at 6 months was imputed first followed by the outcomes at 12 months.
Outcomes assessed every month	The disease activity score for 28 joints and its components were imputed using multivariate sequential imputation using chained equations. Firstly, all missing values were filled in by simple random sampling with replacement from the observed values. The first variable with missing values, say tender joint count at month one, was regressed on all other variables tender joint count-0, tender joint count-2,………..tender joint count-12, restricted to individuals with the observed tender joint count-1. Missing values in tender joint count-1 were replaced by simulated data points drawn from the corresponding posterior predictive distribution of tender joint count-1. Then, the next variable with missing was replaced by the same cycle
Number of cycles	The imputation was 20 cycles. At the end of the cycle one imputed dataset was created. The process was repeated to create 20 imputed datasets. The 20 datasets were combined using Rubin's rules [1,2], therefore, the estimates and standard errors presented here are the combined ones. As an additional check of the robustness of the analyses performed to the missing at random assumption we further analysed the individual outcomes using the linear increments method of Diggle et al [3] to handle the missingness. As the results obtained using this approach were qualitatively the same as that of the multiple imputation approach adopted, we report only the findings from the standard multiple imputation analyses.

1. Little RJA, Rubin DB. Statistical Analysis with Missing Data. 2nd ed. Hoboken, NJ: John Wiley and Sons, Inc; 2002
2. Schafer JL. Analysis of Incomplete Multivariate Data. 1st ed. London, United Kingdom: Chapman and Hall Ltd; 1997.
3. Diggle P, Farewell D, Henderson R. Analysis of longitudinal data with drop-out: objectives, assumptions and a proposal. J R Stat Soc C-Appl 2007; 56: 499-550.

Table B. Trial Treatments In The Two Treatment Strategies

	Therapies	Patients
Combination Disease Modifying Drugs Strategy		
Disease Modifying Drug Treatments (n=104)	One	0
	Two	46
	Three	48
	Four	8
	Five	2
Main Disease Modifying Drug Combinations (n=104)	Methotrexate/Leflunomide	62
	Methotrexate/Ciclosporin	17
	Methotrexate/Sulfasalazine/Hydroxychloroquine	13
	Methotrexate/Gold	10
	Other	2
Switched To Tumour Necrosis Factor Inhibitors (n=46)	Adalimumab	25
	Etanercept	14
	Infliximab	4
	Withdrew Before Starting	3
Steroids (n=27)	Oral Prednisolone	24
	Depomedrone injections	3
Tumour Necrosis Factor Inhibitor Strategy		
Initial Tumour Necrosis Factor Inhibitors (n=101)	Adalimumab	58
	Etanercept	34
	Infliximab	9
Second Tumour Necrosis Factor Inhibitors (n=16)	Adalimumab	7
	Etanercept	9
	Infliximab	0
Steroids (n=19)	Oral Prednisolone	19
	Depomedrone injections	0

Table C: Changes In Primary Outcome (Health Assessment Questionnaire Score) In Intention To Treat And Complete Case Populations

Population	Strategy	Number	Initial	Final	Difference	Regression Coefficient (95%CI)	
			Mean (95% CI)	*Mean (95% CI)*	*Mean (95% CI)*	*Unadjusted*	*Adjusted*
Intention to treat	*Disease Modifying Drugs*	104	1.80 (1.68, 1.91)	1.35 (1.20, 1.50)	-0.45 (-0.55,-0.34)	-0.14 (-0.29, 0.01)	-0.15 (-0.31, -0.003)
	Tumour Necrosis Factor Inhibitors	101	1.90 (1.77, 2.03)	1.59 (1.43, 1.76)	-0.30 (-0.42,-0.19)		
Complete cases	*Disease Modifying Drugs*	72	1.85 (1.71, 1.99)	1.33 (1.16, 1.51)	-0.52 (-0.63, -0.41)	-0.14 (-0.32, 0.03)	-0.15 (-0.32, 0.03)
	Tumour Necrosis Factor Inhibitors	75	1.84 (1.68, 2.00)	1.47 (1.27, 1.66)	-0.38 (-0.51, -0.24)		

Combination disease modifying drugs are favoured by negative values for regression coefficients; the tumour necrosis factor inhibitor strategy was the reference group

Table D: Changes In Secondary Outcomes For Quality Of Life And Erosive Progression In Intention To Treat Population

Outcome	Strategy	Number	Initial	12 months	Difference 12-0	Regression Coefficient (95%CI)	
			Mean (95% CI)	*Mean (95% CI)*	*Mean (95% CI)*	*Unadjusted*	*Adjusted*
EQ5D-3L	*Disease Modifying Drugs*	104	0.39 (0.33, 0.45)	0.59 (0.53, 0.65)	0.20 (0.13,0.27)	0.06 (-0.04, 0.15)	0.11 (0.03, 0.18)
	Tumour Necrosis Factor Inhibitors	101	0.35 (0.28, 0.41)	0.49 (0.43, 0.55)	0.14 (0.08,0.21)		
SF-36 Physical Component Summary Score	*Disease Modifying Drugs*	104	28.4 (27.1, 29.7)	34.4 (32.2, 36.5)	6.0 (3.8, 8.1)	0.23 (-2.79, 3.26)	1.40 (-1.41, 4.22)
	Tumour Necrosis Factor Inhibitors	101	27.3 (25.9, 28.7)	33.0 (31.1, 35.0)	5.8 (3.7, 7.9)		
SF-36 Physical Component Summary Score	*Disease Modifying Drugs*	104	43.4 (41.0, 45.8)	48.4 (46.0, 50.8)	5.0 (2.2, 7.8)	-0.42 (-4.35, 3.51)	1.73 (-1.61, 5.07)
	Tumour Necrosis Factor Inhibitors	101	40.7 (38.3, 43.1)	46.1 (43.7, 48.6)	5.4 (2.7 8.2)		
Larsen Score	*Disease Modifying Drugs*	104	45.1 (37.0, 53.2)	46.3 (38.1, 54.5)	1.26 (0.19,2.34)	-0.11 (-1.67, 1.41)	-0.35 (-2.06, 1.37)
	Tumour Necrosis Factor Inhibitors	101	37.9 (30.2, 45.6)	39.3 (31.2, 47.4)	1.37 (0.26,2.48)		

Combination disease modifying drug strategy is favoured by positive differences with EQ5D-3L and SF-36 scores, and negative differences with Larsen scores; the tumour necrosis factor inhibitor strategy was the reference group

Table E Treatment Effects On Disease Activity In Intention To Treat Population Changes In Disease Activity Score For 28 Joints And Its Components Using Generalised Estimating Equations

Variable	Regression Coefficient (95%CI)	
	Unadjusted	*Adjusted*
Disease Activity Score For 28 Joints	0.48 (0.17, 0.79)	0.40 (0.10, 0.69)
Tender Joint Count	1.69 (-0.11, 3.50)	0.93 (-0.51,2.36)
Swollen Joint Count	0.86 (-0.55, 2.27)	0.63 (-0.31, 1.57)
Erythrocyte Sedimentation Rate	4.04 (0.40, 7.67)	4.62 (1.47, 7.77)
Patients Global Assessment	2.83 (-3.20, 8.85)	1.96 (-3.11, 7.04)

The tumour necrosis factor inhibitor strategy is favoured by positive differences; the tumour necrosis factor inhibitor strategy was the reference group