MOTILITY Results

Figure 1. Study flow

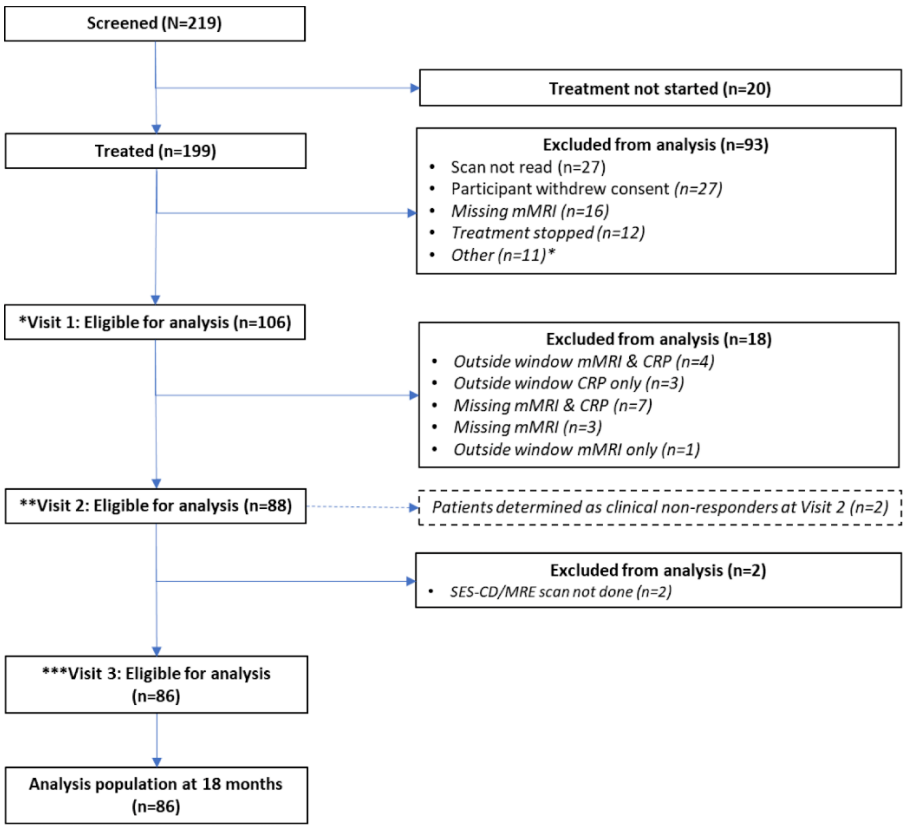

Table 1. Baseline characteristics

Baseline Characteristics	Trial population					
	Primary analysis population N = 86		Population not analysed N = 113		Total N = 199	
	Mean	(sd)	Mean	(sd)	Mean	(sd)
Age (years)	39.0	(13.8)	36.8	(14.3)	37.8	(14.1)
SES-CD score	6.0	(4.9)	4.9	(3.4)	5.5	(4.3)
MRE score	6.4	(1.7)	5.9	(2.2)	6.3	(1.8)
C-reactive protein (mg/l)	10.9	(13.0)	12.2	(14.8)	11.6	(14.0)
EQ-5D-5L	0.8	(0.2)	0.8	(0.2)	0.8	(0.2)
CUCQ-8	32.5	(22.1)	37.2	(24.2)	35.1	(23.4)
IBD-Control-8	8.3	(3.3)	8.5	(3.3)	8.4	(3.3)
Faecal calprotectin (µg/g)	140.9	(164.1)	209.9	(355.4)	166.6	(253.0)
	n	(%)	n	(%)	n	(%)
Smoking Status						
Non-smoker	39	(45.35)	59	(52.21)	98	(49.25)
Current smoker	13	(15.12)	17	(15.04)	30	(15.08)
Ex-smoker	13	(15.12)	18	(15.93)	31	(15.58)
Missing	21	(24.42)	19	(16.81)	40	(20.10)
Previous bowel surgery						
No surgery	57	(66.28)	69	(61.06)	126	(63.32)
Single surgery	17	(19.77)	26	(23.01)	43	(21.61)
Multiple surgeries	12	(13.95)	18	(15.93)	30	(15.08)
History of biological therapy						
No	70	(81.40)	105	(92.92)	175	(87.94)
Yes	16	(18.60)	8	(7.08)	24	(12.06)
Age at diagnosis (years)						
A1 (<= 16)	6	(6.98)	16	(14.16)	22	(11.06)
A2 (17 - 40)	65	(75.58)	77	(68.14)	142	(71.36)
A3 (> 40)	15	(17.44)	18	(15.93)	33	(16.58)
Missing	0	(0)	2	(1.77)	2	(1.01)
L1 (ileal)						
No	22	(25.58)	27	(23.89)	49	(24.62)
Yes	59	(68.60)	70	(61.95)	129	(64.82)
Missing	5	(5.81)	16	(14.16)	21	(10.55)
L2 (colonic)						
No	61	(70.93)	70	(61.95)	131	(65.83)
Yes*	1	(1.16)	1	(0.88)	2	(1.01)
Missing	24	(27.91)	42	(37.17)	66	(33.17)

L3 (ileocolonic)						
No	39	(45.35)	44	(38.94)	83	(41.71)
Yes	28	(32.56)	40	(35.40)	68	(34.17)
Missing	19	(22.09)	29	(25.66)	48	(24.12)
L4 (upper digestive modifier)						
No	61	(70.93)	69	(61.06)	130	(65.33)
Yes	0	(0)	2	(1.77)	2	(1.01)
Missing	25	(29.07)	42	(37.17)	67	(33.67)
Behaviour						
B1 (non-stricturing, non-penetration)	45	(52.33)	55	(48.67)	100	(50.25)
B2 (stricturing)	29	(33.72)	39	(34.51)	68	(34.17)
B3 (penetrating)	11	(12.79)	10	(8.85)	21	(10.55)
Missing	1	(1.16)	9	(7.96)	10	(5.03)
Perianal disease modifier (p)						
No	79	(91.86)	95	(84.07)	174	(87.44)
Yes	6	(6.98)	6	(5.31)	12	(6.03)
Missing	1	(1.16)	12	(10.62)	13	(6.53)

SES-CD (Simple Endoscopic Score for Crohn's Disease)

MRE (Magnetic Resonance Enterography)

EQ-5D-5L (European Quality of life score, 5 Dimension, 5 Level)
CUCQ-8 (Crohn's and Ulcerative Colitis Questionnaire, 8 item)

IBD-Control-8 (Inflammatory Bowel Disease-Control-8)
sd (standard deviation)

Primary and Secondary Outcome Measures

Primary and Secondary outcome #1 and #2

Table 2. 2x2 contingency table for the primary outcome (sensitivity) and first secondary outcome (specificity) of both stable or improved mMRI and CRP normalisation for response or remission (RoR) at 1 year.

	mMRI				
	Response	**No response**	**Total**	**Sensitivity (%) (95% CI)**	**Specificity (%) (95% CI)**
RoR at 1 year	**22**	**9**	**31**	**71.0 (52.0 - 85.8)**	**30.9 (19.1 - 44.8)**
No RoR at 1 year	**38**	**17**	**55**		
Total	**60**	**26**	**86**		
	CRP				
RoR at 1 year	**14**	**17**	**31**	**45.2 (27.3 - 64)**	**67.3 (53.3 - 79.3)**
No RoR at 1 year	**18**	**37**	**55**		
Total	**32**	**54**	**86**		
McNemar's test p-value				**0.0078**	**0.0005**

Difference in area under the receiver operating characteristic curve (ROC AUC) between changes from baseline to the week 12-30 in continuous small bowel motility MR (mMRI) score and in C-reactive protein levels (CRP) to predict RoR at 12 months.

Figure 2. ROC AUC for mMRI percentage change versus CRP change from baseline

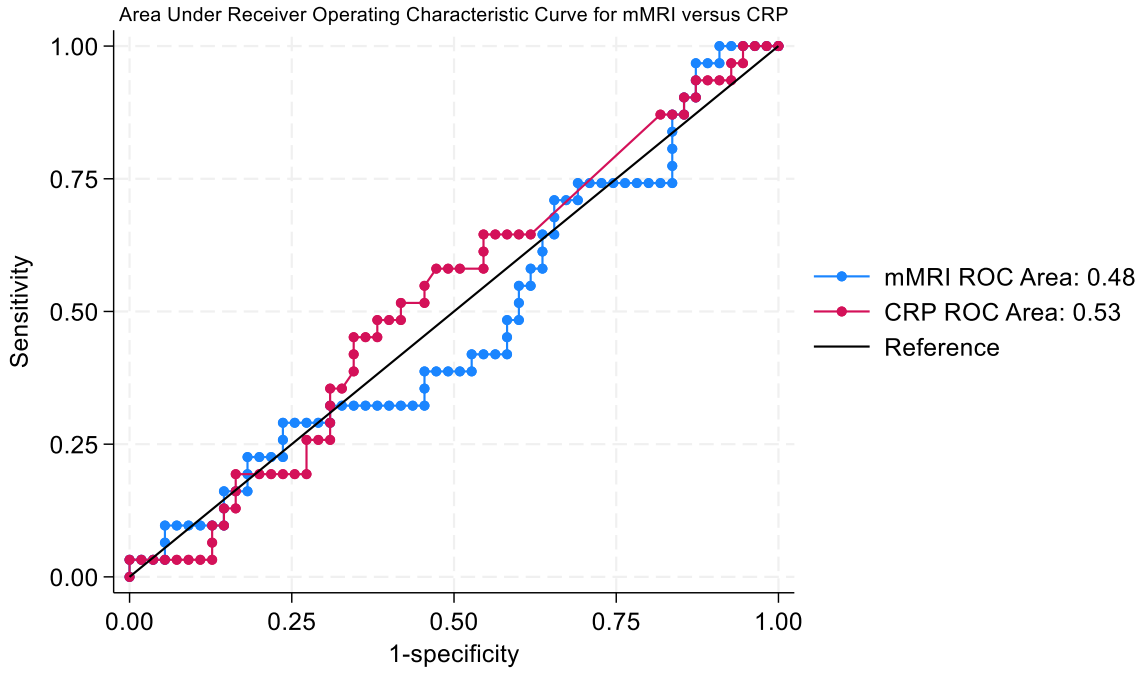

Table 3. ROC AUC Statistics mMRI and CRP

	AUC ROC	Optimal cut point	Sensitivity at optimal cut point	Specificity at optimal cut point
mMRI	0.48	0.58	0.58	0.58
CRP	0.53	0.55	0.97	0.13

mMRI: mMRI percentage change from baseline to week 12-30

CRP: change from baseline to week 12 -30

The optimal cut-point for mMRI is a change of 0.58% from baseline. This value has been derived using the Youden method which defines the optimal cut-point as the point maximising the Youden function, which is the difference between true positive rate and false positive rate over all possible cut-point values.

Secondary Outcome #3

Difference in prognostic accuracy between changes in the continuous small bowel motility MR score *versus* changes in C-reactive protein levels at week 12-30 to predict clinically significant improvements from baseline to one year in each quality-of-life measure (EQ-5D-5L, CUCQ-8 and IBD-Control 8).

Multivariable regression models were constructed using the change in the relevant QoL score as the outcome variable, and percentage change in the MRI-measured small bowel motility as well as change in CRP between baseline and week 12-30 as continuous explanatory variables. The motility MRI-based model was compared to the CRP-based model, for each QoL measurement method using Akaike information criterion (AIC) to see which test better predicts changes in patient QoL. The best-fit model according to AIC is the one that explains the greatest amount of variation using the fewest possible independent variables.

Clinically significant improvements in quality of life: from baseline to one year.

- European Quality of Life 5 dimension, 5 level (EQ-5D-5L) score: defined as a 0.076 point improvement
- Crohn's and Ulcerative Colitis Questionnaire 8 item (CUCQ-8) score, defined as 9 points
- IBD-Control-8 defined as 4 points

Table 4. Effect of change in mMRI and change in CRP on change in QoL measures

Quality of Life measure	N	mMRI			CRP		
		Coefficient (95% CI)	p-value	AIC*	Coefficient (95% CI)	p-value	AIC**
***EQ-5D-5L**	72	0.0001 (-0.0003, 0.001)	0.52	-58	-0.001 (-0.004, 0.001)	0.16	-60
***CUCQ-8**	76	0.04 (-0.002, 0.08)	0.07	642	0.13 (-0.07, 0.33)	0.18	644
***IBD-Control 8**	65	0.004 (-0.01, 0.01)	0.39	361	0.05 (0.01, 0.10)	0.03	357

*Model adjusted for age at diagnosis, sex, history of previous surgery, presence of perianal disease and presence of a stoma.

**AIC (Akaike information criterion) – Smaller values indicate better model fit.

Secondary Outcome #4

Difference in (i) sensitivity and (ii) specificity between stable or improved MRI-measured small bowel motility and normalisation of faecal calprotectin (FC) at week 12-30 for predicting RoR. Difference in (iii) ROC AUC between changes from baseline to week 12-30 in small bowel motility and in faecal calprotectin for predicting RoR.

Table 5: Sensitivity and Specificity between mMRI versus normalisation of FC at week 12-30 to predict RoR at 12 months

	mMRI				
12 months	**Response**	**No response**	**Total**	**Sensitivity (%) (95% CI)**	**Specificity (%) (95% CI)**
Response or Remission	10	6	16	62.5 (35.4 - 84.8)	30.0 (14.7 - 49.4)
No response	21	9	30		
Total	31	15	46		
	FC				
Response or Remission	2	14	16	12.5 (1.6 - 38.3)	80.0 (61.4 – 92.3)
No response	6	24	30		
Total	8	38	46		
McNemar's test p-value				0.04	0.0007

Figure 3. ROC AUC for FC change versus mMRI percentage change from baseline

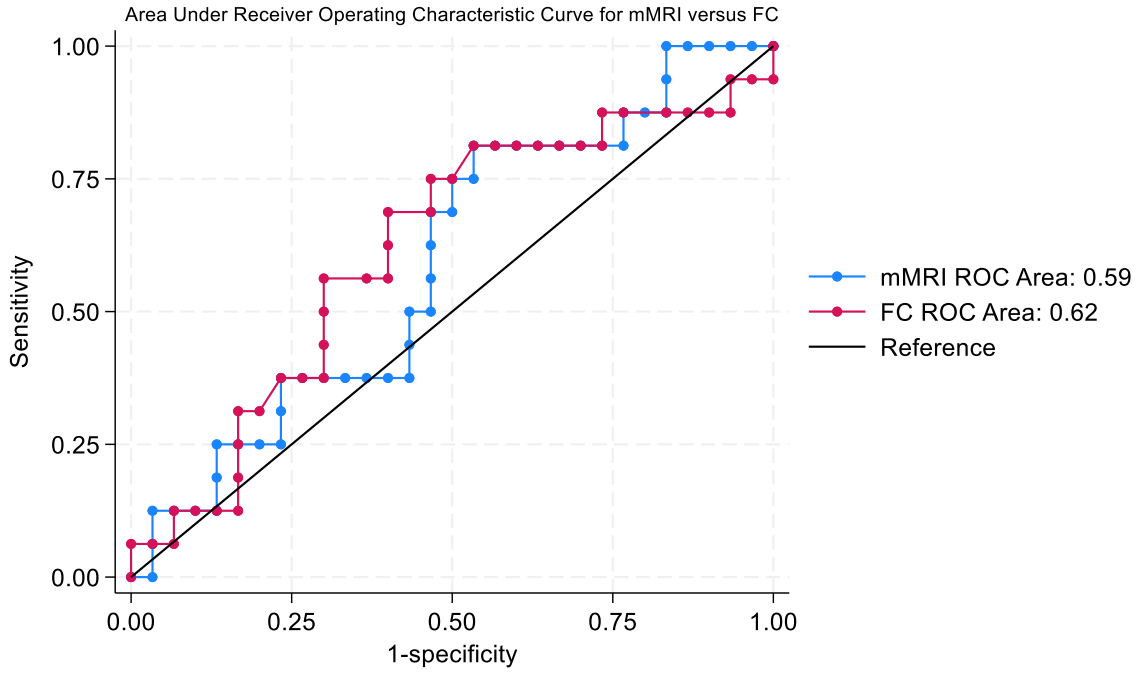

Table 6. ROC AUC Statistics mMRI and FC

	AUC ROC	*Optimal cut point	Sensitivity at optimal cut point	Specificity optimal cut point
***mMRI**	0.59	0.53	0.62	0.43
***FC**	0.62	0.64	0.69	0.60

mMRI: mMRI percentage change from baseline to week 12-30

FC: change from baseline to week 12 -30

The optimal cut-point for mMRI is a change of 0.53% from baseline. This value has been derived using the Youden method which defines the optimal cut-point as the point maximising the Youden function, which is the difference between true positive rate and false positive rate over all possible cut-point values.

Secondary Outcome #5

Difference in prognostic accuracy between changes in the continuous MRI-measured small bowel motility score *versus* changes in faecal calprotectin levels at week 12-30 to predict clinically significant improvements from baseline to one year in each Quality of Life (QoL) measure.

Clinically significant improvements in quality of life: from baseline to one year.

- European Quality of Life 5 dimension, 5 level (EQ-5D-5L) score: defined as a 0.076 point improvement
- Crohn's and Ulcerative Colitis Questionnaire 8 item (CUCQ-8) score, defined as 9 points
- IBD-Control-8 defined as 4 points

Table 7. Effect of change in mMRI versus change in FC on change in QoL measures

		mMRI			**FC**		
Quality of Life measure	**N**	**mMRI (95% CI)**	**p-value**	**AIC****	**FC (95% CI)**	**p-value**	**AIC****
***EQ-5D-5L**	44	0.0001 (-0.0004, 0.0006)	0.68	-31.9	0.00003 (-0.0002, 0.0002)	0.76	-31.8
***CUCQ-8**	44	0.000097 (-0.05, 0.05)	0.99	366.5	-0.0076 (-0.025, 0.0096)	0.38	365.5
***IBD-Control 8**	38	0.0007 (-0.014, 0.015)	0.92	240.5	-0.005 (-0.01, -0.0001)	0.05	220.5

*Model adjusted for age at diagnosis, sex, history of previous surgery, presence of perianal disease and presence of a stoma.

**AIC (Akaike information criterion) – Smaller values indicate better model fit.

Secondary Outcome #6

Difference in prognostic accuracy and incremental prognostic value of multivariate prognostic models including MRI-measured small bowel motility *versus* those including (i) C-reactive protein and (ii) faecal calprotectin for response to biologic therapy at one year. Additional predictor covariates of non-response to biological therapy including age at diagnosis, Montreal subtype of disease, current use of tobacco and presence of perianal disease have been used in the models.

Table 8. Effect of change in mMRI versus change in change in C-Reactive protein (CRP) and chance in Faecal calprotectin (FC)

	N	Odds Ratio (95% CI)	p-value	AIC*
mMRI	39	0.99 (0.99 – 1.00)	0.43	60.9
CRP	39	1.05 (0.96 – 1.16)	0.29	60.1
FC	39	1.00 (0.99 – 1.00)	0.43	60.9

*AIC (Akaike information criterion) – Smaller values indicate better model fit.