

Supplementary 3: Attrition Analysis, Secondary Outcomes and Multivariate Regression Forest Plot.

Introduction

Below are extended analyses accompanying the main manuscript including full attrition analysis, specific values for symptom count, HADS score and SF12 scores over the study period and an illustrative forest plot of predictors of poor outcome.

Table 1: Marginally more patients from the not at all/somewhat (functional) group were lost to follow up.

	Total	Symptoms Explained by Disease	
		Not at All/Somewhat	Largely/Completely
Recruited	3781	1144	2637
12 Month Outcome Data	2581 (68%)	716 (63%)	1865 (71%)

Table 2: Lost-to follow up groups differ in several baseline characteristics.

	12-Months		p Chi2	Effect Size OR
	No Follow Up N (%)	Follow Up N (%)		
Total	1200	2581		
Symptoms 'Somewhat/Not at All' Explained by Disease	428 (36%)	716 (28%)	<0.001	1.44
Female Gender	644 (54%)	1517 (59%)	0.004	1.23
Negative Expectation of Recovery	479 (40%)	1118 (43%)	0.06	1.15
Psychological Attribution of Symptoms	563 (47%)	1046 (41%)	<0.001	0.76
Receipt of Incapacity or DLA	286 (24%)	594 (23%)	0.6	0.95
SIMD 2004 Most Deprived Quintile	316 (26%)	409 (16%)	<0.001	0.53
	Mean \pm SD		Student's t	Cohen's d
Age	41.0 \pm 15.8	48.8 \pm 16.0	<0.001	-0.49
PHQ13	5.0 \pm 3.2	4.5 \pm 3.0	<0.001	0.19
SF12 Physical Function	67.5 \pm 37.3	65.3 \pm 37.2	0.09	0.06
HADS Total	13.3 \pm 8.8	11.3 \pm 7.9	<0.001	0.24
Illness Worry	0.9 \pm 1.0	0.7 \pm 0.9	<0.001	0.17

Table 3: Age, gender and deprivation quintile all predict study retention in both groups.

Multivariate Logistic Regression				
	Pathophysiological		Functional	
	OR (CI) for Retention	p	OR (CI) for Retention	p
Gender		0.001		0.001
Male	1		1	
Female	1.37 (1.14-1.65)		1.80 (1.30-2.49)	
Age		0.000		0.000
≤35	1		1	
36-45	1.63 (1.27-2.09)		1.80 (1.30-2.49)	
46-55	2.38 (1.83-3.09)		2.91 (1.98-4.26)	
≥56	3.39 (2.62-4.37)		3.24 (2.18-4.80)	
Diagnosis		0.078		0.606
Not at All			1	
Somewhat			0.93 (0.72-1.22)	
Largely	1			
Completely	1.18 (0.98-1.43)			
PHQ13 Symptom Count		0.314		0.391
0-2	1		1	
3-5	0.89 (0.71-1.12)		0.74 (0.50-1.10)	
6-8	0.82 (0.62-1.09)		0.74 (0.48-1.15)	
9-13	0.71 (0.48-1.03)		0.65 (0.39-1.10)	
SF12 Physical Functioning		0.534		0.839
0	0.96 (0.68-1.36)		0.91 (0.56-1.48)	
25	1.19 (0.82-1.72)		1.00 (0.60-1.68)	
50	1.11 (0.84-1.48)		1.22 (0.79-1.87)	
75	1.20 (0.91-1.57)		1.01 (0.69-1.50)	
100	1		1	
HADS Total		0.138		0.141
0-7	1		1	
8-14	0.93 (0.74-1.17)		1.01 (0.71-1.46)	
15-21	0.78 (0.58-1.05)		0.76 (0.50-1.15)	
≥22	0.66 (0.46-0.96)		0.62 (0.38-1.03)	
Illness Worry		0.853		0.218
0	1		1	
1	0.93 (0.74-1.17)		0.82 (0.59-1.13)	
2	0.96 (0.73-1.26)		0.95 (0.65-1.41)	
3	0.85 (0.56-1.30)		1.38 (0.83-2.29)	
Negative Expectation of Recovery		0.168		0.952
No	1		1	
Yes	1.14 (0.95-1.38)		1.01 (0.76-1.33)	
Psychological Attribution		0.279		0.049
Yes	1		1	
No	1.12 (0.91-1.37)		0.75 (0.56-1.00)	
Receipt of Benefits		0.859		0.176
No	1		1	
Yes	0.98 (0.75-1.26)		1.29 (0.89-1.86)	
SIMD 2004 Quintile		0.000		0.009
1 (Least Deprived) - 4	1		1	
5 (Most Deprived)	0.61 (0.49-0.76)		0.65 (0.47-0.90)	

Table 4: Baseline disease burden differs between functional groups and the disparity remains across the study period.

		Baseline Mean (CI)	3 Month Mean (CI)	12 Month Mean (CI)	Baseline - 3 Month Change	3 Month - 12 Month Change
HADS Score Total	Unexplained	13.83 (13.31-14.35)	13.65 (13.02-14.27)	13.45 (12.77-14.13)	0.48 (0.06-0.90)	-0.08 (-0.49-0.33)
	Explained	11.10 (10.81-11.41)	11.43 (11.05-11.81)	11.28 (10.90-11.66)	0.70 (0.46-0.95)	0.07 (-0.18-0.32)
	t-Test p	<0.001	<0.001	<0.001	0.36	0.54
	Cohen's d	0.33	0.26	0.26	-0.041	-0.030
Symptom Count	Unexplained	8.40 (8.12-8.68)	7.77 (7.40-8.14)	8.47 (8.09-8.86)	-0.27 (-0.54--0.01)	0.74 (0.49-1.00)
	Explained	6.66(6.49-6.82)	6.10 (5.89-6.31)	6.67 (6.45-6.89)	-0.26 (-0.41--0.11)	0.66 (0.50-0.82)
	t-Test p	<0.001	<0.001	<0.001	0.93	0.60
	Cohen's d	0.39	0.37	0.38	-0.0043	0.028
Normalised SF12 MCS	Unexplained	19.19 (18.14-20.25)	17.96 (16.64-19.28)	18.70 (17.32-20.09)	-2.01 (-3.27--0.74)	0.77 (-0.55-2.09)
	Explained	23.42 (22.70-24.14)	22.11 (21.25-22.97)	23.27 (22.37-24.16)	-2.11 (-2.91--1.32)	0.66 (-0.13-1.46)
	t-Test p	<0.001	<0.001	<0.001	0.89	0.89
	Cohen's d	-0.23	-0.22	-0.24	0.0062	0.0068
Normalised SF12 PCS	Unexplained	30.61 (29.72-31.52)	30.57 (28.76-32.37)	29.86 (28.67-31.06)	-0.56 (-1.94-0.82)	-0.89 (-2.36-0.59)
	Explained	33.37 (32.78-33.96)	32.86 (31.69-34.03)	31.71 (30.95-32.48)	-0.44 (-1.30-0.43)	-0.39 (-1.33-0.54)
	t-Test p	<0.001	0.036	0.012	0.88	0.58
	Cohen's d	-0.18	-0.138	-0.11	-0.010	-0.040

Figure 1: Forest Plot of Multivariate Regression Coefficients by Functional Group

