Telehealth in motor neuron disease to increase access to specialist multidisciplinary care: a pilot, feasibility study.

Supplementary data tables

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Table 1 Patient outcome measures collected.[1]

	Baseline	3 months	6 months	12 months	18 months	Clinic visits
Patient characteristics						
Age, gender	X					
Frequency of technology use	X					
Broadband/mobile internet access	X					
Difficulties using TiM	X					
Need for help using TiM	X					
Medical history						
Diagnosis	X					
Disease duration	X					
Comorbidities	X					
Drug history	X					
Quality of life						
ALSAQ-40 (218)	X	X	X	X	X	
SF-36 v1 (219)	X	X	X	X	X	
EQ-5D+D	X	X	X	X	X	
Clinical measures						
ALS-FRS-R (205)	X	X	X	X	X	
Pain score (current and worst)**	X	X	X	X	X	
CSS-MND saliva scale (220)	X	X	X	X	X	
Hospital Anxiety and Depression score (221)	X	X	X	X	X	
Survival						X
Adverse events		X	X	X	X	X
Health resource use						
Clinician encounters**	X	X	X	X	X	X
Hospital admissions**	X	X	X	X	X	X
Informal care use**	X	X	X	X	X	
Formal care use**	X	X	X	X	X	
Satisfaction						
MND care satisfaction**	X	X	X	X	X	
TiM satisfaction**		X*	X*	X*	X*	

[1] *intervention arm only ** questionnaires designed for the trial

Table 2 Carer outcome measures collected.

	Baseline	3 months	6 months	12 months	18 months	Clinic visits
Carer characteristics						
Age, gender	X					
Relationship to patient	X					
Frequency of technology use	X					
Difficulties using TiM	X					
Quality of life						
SF-36 v1 (219)	X	X	X	X	X	
Clinical measures						
Hospital Anxiety and Depression score (221)	X	X	X	X	X	
Zarit Burden Interview (222)	X	X	X	X	X	
Adverse events		X	X	X	X	X
Satisfaction						
MND care satisfaction**	X	X	X	X	X	
TiM satisfaction**		X*	X*	X*	X*	

*intervention arm only, ** questionnaires designed for the trial

Figure 1 Detailed description of the semi-structured interviews.

Month 1 interviews
Total interviews=20 Patients=18 Carers=13
Patient and carer interviewed together (Interviews=12) Patients interviewed alone (Interviews=6) Carer interviewed alone (Interviews = 1) Patient and carer not interviewed due to illness (Interviews=2) Carer not interviewed unavailable (n=3)

Baseline interviews
Total interviews=17 Patients=16 Carers=15
Patient and carer interviewed together (Interviews=12) Patients interviewed alone (Interviews=2) Carer interviewed alone (Interviews=0) Patient interviewed by email (Interviews=1) Carer interviewed by email (Interviews=1) Patient and carer interviewed together and patient provided supplemental email answers (Interviews=1) Patients and carer not interviewed due to time constraints (Interviews = 4) Carers not interviewed unavailable (n=1)

Month 6 interviews
Total interviews=19 Patients=17 Carers=13
Patient and carer interviewed together (Interviews=11) Patients interviewed alone (n=6) Carer interviewed alone (Interviews= 3) Patient and carer not interviewed as had withdrawn or died (Interviews=3) Carer not interviewed unavailable (n=2)

In one case a patient was interviewed with his carer, who was not participating in the study. In one case a community nurse was present during the interview. She later was interviewed as part of the study. Telephone interviews were conducted when the patient lived at a distance from the study centre and email interviews were used when the patient had significant dysarthria. All interviews took place in the patients' home except one which took place in a café at the request of the carer. The transcripts were not returned to participants to avoid over burdening them but they were checked by EH who transcribed interviews where participants had speech disturbance. The results were presented to the trial management group which included a member of the Sheffield MND Research Advisory Group who was an experienced volunteer visitor to families with MND and she provided context and confirmed validity of the findings.

Figure 2 Mean ALSAQ-40 sub-scores and standard errors at baseline, three, six, and twelve months.

Scores range from 0 (best possible QoL) to 100 (worse possible QoL). An * indicates scores where the mean change from baseline differs significantly from baseline ($p < 0.05$).
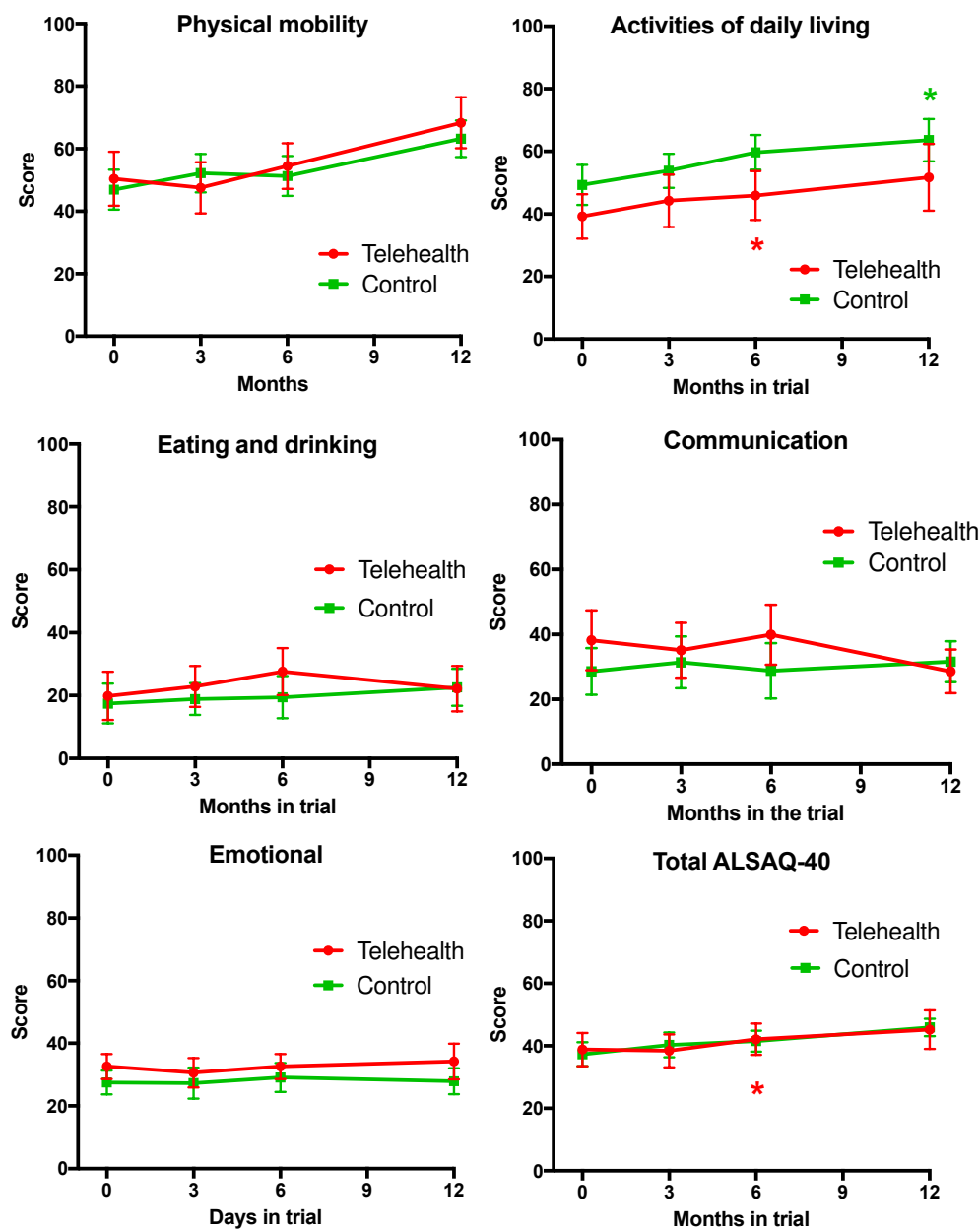
Table 3 Patient ALSAQ-40 index scores

Mean, standard deviation (SD), mean change from the baseline and 95% confidence intervals. Scores range from 0 (best possible QoL) to 100 (worse possible QoL). Cells highlighted in bold indicate where scores are significantly different to baseline.

Patient ALSAQ-40	Base-line	3 months			6 months		12 months	
	ALSAQ-40 Mean (SD)	ALSAQ-40 Mean (SD)	Mean change from baseline (CI)		ALSAQ-40 Mean (SD)	Mean change from baseline (CI)	ALSAQ-40 Mean (SD)	Mean change from baseline (CI)
Telehealth	n=18	n=16	n=15		n=16	n=16	n=6	n=6
Physical mobility	50.4 (36.6)	47.5 (34.6)	-4.7 (-15.4, 6.1)		54.5 (30.9)	5.8 (-3.8, 15.4)	68.3 (26.8)	10.4 (-3.6, 24.4)
Activities of daily living	39.2 (30.2)	44.2 (35.6)	5.8 (-0.1, 11.8)		45.9 (33.1)	**8.4 (1.6, 15.3)**	51.7 (45.2)	15.8 (-1.5, 33.1)
Eating and drinking	19.9 (32.5)	22.9 (27.6)	6.1 (-1.4, 13.6)		27.6 (31.7)	**11.5 (2.6, 20.3)**	22.2 (30.6)	13.9 (-16.7, 44.5)
Communic-ation	38.3 (39.0)	35.1 (35.9)	0.5 (-5.0, 5.9)		39.9 (39.1)	3.6 (-2.1, 9.3)	28.6 (45.2)	13.1 (-12.1, 38.3)
Emotional	32.6 (16.8)	30.6 (20.0)	0 (-6.4, 6.4)		32.6 (16.9)	1.4 (-4.6, 7.5)	34.2 (24.3)	3.8 (-13.0, 20.5)
Total	38.8 (22.5)	38.4 (22.2)	0.83 (-2.6, 4.3)		42.1 (21.2)	**5.4 (0.2, 10.6)**	45.2 (26.3)	10.8 (-1.5, 23.2)
Control	n=20	n=15	n=15		n=12	n=12	n=7	n=6
Physical mobility	46.9 (28.7)	52.2 (27.6)	1.6 (-12.9, 16.1)		51.3 (28.6)	8.3 (-8.2, 24.9)	63.2 (26.1)	15.0 (-17.6, 47.6)
Activities of daily living	49.3 (28.7)	53.8 (24.2)	2.3 (-7.0, 11.6)		59.7 (24.6)	9.0 (-9.6, 18.9)	63.6 (30.4)	**15.8 (1.9, 30.0)**
Eating and drinking	17.5 (28.2)	18.9 (22.6)	0.6 (-7.1, 8.3)		19.5 (30.1)	8.3 (-10.7, 27.4)	22.6 (26.2)	2.8 (-6.3, 11.8)
Communic-ation	28.6 (32.2)	31.4 (35.8)	1.5 (-5.9, 8.9)		28.8 (38.1)	8.0 (-20.5, 36.6)	31.6 (28.2)	9.5 (-9.8, 28.9)
Emotional	27.5 (17.0)	27.3 (22.0)	-1.4 (-9.2, 6.3)		29.1 (20.5)	-2.3 (-16.4, 11.8)	27.9 (18.6)	-3.8 (-23.6, 16.1)
Total	37.3 (17.2)	40.3 (17.7)	0.8 (-2.6, 4.3)		41.5 (14.9)	5.8 (-3.7, 15.3)	45.9 (12.5)	10.8 (-1.5, 23.2)
Total	n=38	n=31	n=30		n=28	n=28	n=13	n=12
Physical mobility	48.6 (32.3)	49.8 (31.0)	0.9 (-6.7, 8.6)		53.1 (29.4)	6.9 (-1.4, 15.2)	65.6 (25.5)	12.7 (-1.8, 27.3)
Activities of daily living	44.5 (29.5)	48.9 (30.5)	1.6 (-12,9, 16.1)		51.8 (30.0)	**8.7 (3.3, 14.0)**	58.1 (29.0)	**15.8 (6.8, 24.9)**
Eating and drinking	18.6 (28.4)	21.0 (25.0)	2.3 (-7.0, 8.3)		24.1 (30.8)	**10.1 (1.3, 19.0)**	22.4 (27.1)	8.3 (-5.2, 21.9)
Communic-ation	33.3 (35.4)	33.3 (35.3)	01.5 (-5.9, 8.9)		35.2 (38.3)	5.5 (-6.1, 17.1)	30.2 (35.3)	11.3 (-1.7, 24.3)
Emotional	29.9 (16.9)	29.0 (20.7)	-1.4 (-9.2, 6.3)		31.1 (18.2)	-0.2 (-6.6, 6.3)	30.8 (20.8)	0 (-10.9, 10.9)
Total	38.0 (19.6)	39.3 (19.9)	0.88 (-2.9, 4.7)		41.8 (18.5)	**5.6 (0.9, 10.2)**	45.6 (19.1)	8.6 (-0.4, 17.6)

Table 4 RAND-36 physical (PCS) and mental (MCS) sub-scores.
The mean and standard deviation (SD) of the mean scores, the mean change from baseline and the 95% confidence interval of the mean change from baseline. These are standardised to a normative reference population in which the mean is 50 and Standard deviation is 10.

Patient SF-36	Base-line Mean (SD)	3 months Mean (SD)	Change from baseline Mean (CI)	6 months Mean (SD)	Change from baseline Mean (CI)	12 months Mean (SD)	Change from baseline Mean (CI)
Telehealth							
PCS	n=18	n=16	n=15	n=16	n=16	n=6	n=6
Mean (SD/CI)	30.1 (9.1)	30.7 (7.7)	-0.7 (-3.3, 1.9)	28.2 (8.6)	-3.1 (-7.1, 0.9)	22.6 (4.1)	-5.8 (-15.0, 3.4)
MCS	n=18	n=16	n=15	n=16	n=16	n=6	n=6
Mean (SD/CI)	52.3 (10.0)	50.7 (11.7)	-1.4 (-5.4, 2.6)	52.3 (12.3)	-0.2 (-4.2, 3.8)	48.8 (15.8)	-5.7 (-18.8, 7.2)
Control							
PCS	n=20	n=14	n=14	n=12	n=12	n=6	n=6
Mean (SD/CI)	28.0 (8.7)	26.6 (5.8)	-0.6 (-5.4, 4.3)	27.0 (7.9)	-0.1 (-7.8, 7.6)	23.7 (3.0)	-6.6 (-13.8, 0.5)
MCS	n=20	n=14	n=14	n=12	n=12	n=6	n=6
Mean (SD/CI)	54.3 (9.5)	55.1 (13.5)	0.9 (-5.4, 7.3)	50.8 (12.1)	-3.6 (-10.7,3.6)	54.7 (9.2)	-1.3 (-17.8,15.3)
Total							
PCS	n=38	n=30	n=29	n=28	n=28	n=12	n=12
Mean (SD/CI)	29.0 (8.8)	28.3 (7.2)	-0.7 (-3.2, 1.9)	27.7 (8.2)	-1.8 (-5.5, 1.9)	23.2 (3.5)	**-6.2 (-11.0,-1.4)**
MCS	n=38	n=30	n=29	n=28	n=28	n=12	n=12
Mean (SD/CI)	53.3 (9.7)	52.7 (12.6)	-0.3 (-3.8, 3.2)	51.7 (12.0)	-1.7 (-5.2, 1.9)	51.8 (12.7)	-3.5 (-12.2, 5.2)

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Figure 3 RAND-36 scores

Physical component scores (PCS) and mental component scores (MCS) mean and standard errors. RAND-36 scores are standardised to a normative reference population (mean is 50 and SD is 10.) An * indicates scores where the mean change from baseline differs significantly different from baseline ($p < 0.05$).
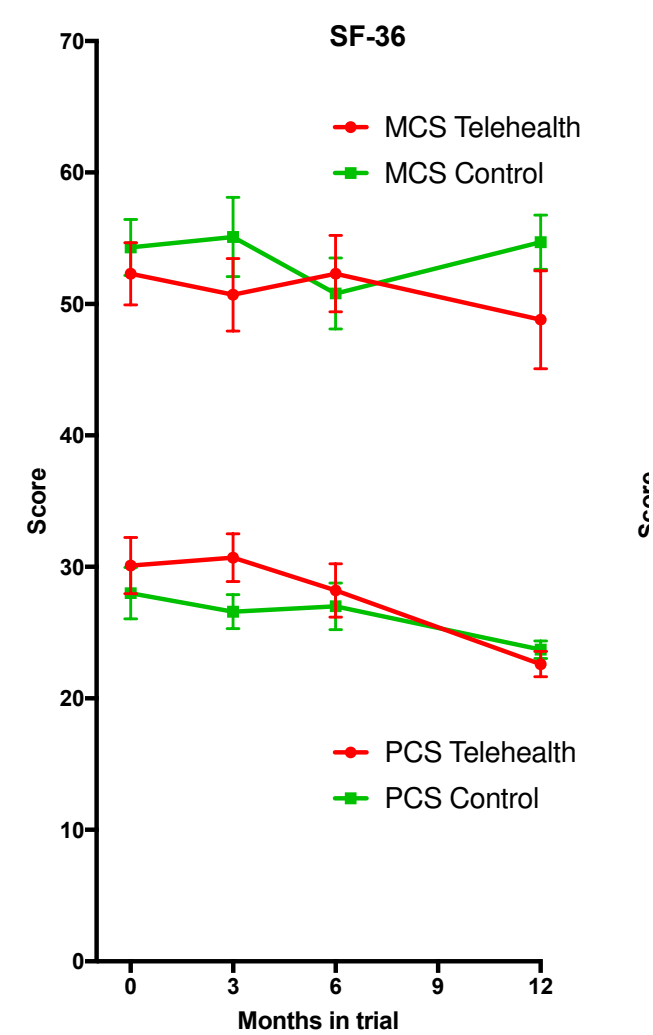
Table 5 EQ-5D-3L and EQ-5D plus dignity bolt-on and the EQ5D thermometer.

Patient EQ-5D	Baseline Mean (SD)	3 months Mean (SD)	3 months Change from baseline Mean (CI)	6 months Mean (SD)	6 months Change from baseline Mean (CI)	12 months Mean (SD)	12 months Change from baseline Mean (CI)
Telehealth	n=17	n=16	n=14	n=16	n=15	n=6	n=6
EQ5D-3L	0.52 (0.31)	0.49 (0.27)	-0.04 (-0.13, 0.05)	0.49 (0.30)	-0.07 (-0.20, 0.06)	0.39 (0.36)	-0.09 (-0.38, 0.21)
EQ5D-3L+D	0.46 (0.40)	0.48 (0.30)	-0.02 (-0.18, 0.14)	0.47 (0.35)	-0.04 (-0.24, 0.16)	0.26 (0.54)	-0.15 (-0.63, 0.33)
Thermometer	61.1 (22.5)	63.8 (25.0)	-2.1 (-8.7, 4.6)	61.6 (20.5)	-3.7 (-9.6, 2.3)	57.5 (22.3)	-5.8 (-12.8, 1,1)
Control	n=20	n=15	n=15	n=12	n=12	n=6[2]	n=6[3]
EQ5D-3L	0.53 (0.27)	0.50 (0.29)	0.02 (-0.10, 0.14)	0.46 (0.25)	-0.11 (-0.22, 0.01)	0.37 (0.33)	-0.25 (-0.50, 0.0)
EQ5D-3L+D	0.49 (0.37)	0.44 (0.41)	0.01 (-0.10, 0.14)	0.44 (0.29)	-0.10 (-0.21, 0.01)	0.26 (0.48)	-0.27 (-0.59, 0.04)
Thermometer	64.5 (20.6)	64.6 (26.8)	0.9 (-13.5, 15.4)	61.7 (25.3)	-6.7 (-19.8, 6.5)	60.9 (21.6)	-7.0 (-37.2, 23.2)
Total	n= 37	n=31	n=29	n=28	n=27	n=12[3]	n=12[3]
EQ5D-3L	0.53 (0.29)	0.50 (0.27)	-0.01 (-0.01, 0.06)	0.47 (0.27)	**-0.09 (-0.17, -0.01)**	0.38 (0.33)	-0.17 (-0.33, 0.00)
EQ5D-3L+D	0.48 (0.37)	0.46 (0.35)	-0.01 (-0.10, 0.08)	0.46 (0.32)	-0.07 (-0.18, 0.05)	0.26 (0.49)	-0.21 (-0.45, 0.03)
Thermometer	63.0 (21.3)	64.2 (25.5)	-0.5 (-8.2, 7.1)	61.6 (23.0)	-5.0 (-11.2, 1.2)	59.3 (21.1)	-6.4 (-20.7, 7.7)

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[2] Control group n=6 in EQ5D calculations and n=7 in thermometer calculations at both 6 and 12 months.

Table 6 EQ-5D-3L and EQ-5D plus dignity bolt-on and the EQ5D thermometer.

In these calculations, patients who had died were included in the scoring and were assigned a score of 0. Thermometer scores are unchanged.

Patient EQ-5D	Base-line Mean (SD)	3 months Mean (SD)	3 months Change from baseline Mean (CI)	6 months Mean (SD)	6 months Change from baseline Mean (CI)	12 months Mean (SD)	12 months Change from baseline Mean (CI)
Telehealth							
n= *	17	17	15	17	16	8	8
EQ5D-3L Mean (SD/CI)	0.52 (0.31)	0.46 (0.29)	-0.05 (-0.14, 0.03)	0.46 (0.31)	-0.08 (-0.20, 0.04)	0.35 (0.37)	-0.12 (-0.33, 0.08)
EQ5D-3L+D Mean (SD/CI)	0.46 (0.40)	0.44 (0.41)	-0.03 (-0.18, 0.12)	0.44 (0.35)	-0.05 (-0.23,0.14)	0.20 (0.47)	-0.17 (-0.50, 0.15)
Thermometer n=	17	16	14	16	15	6	6
Mean (SD/CI)	61.1 (22.5)	63.8 (25.0)	-2.1 (-8.7, 4.6)	61.6 (20.5)	-3.7 (-9.6, 2.3)	57.5 (22.3)	-5.8 (-12.8, 1,1)
Control							
n=*	20	15	15	14	14	8	7
EQ5D-3L Mean (SD/CI)	0.53 (0.28)	0.50 (0.28)	0.02 (-0.10, 0.14)	0.39 (0.28)	-0.12 (-0.26, 0.01)	0.28 (0.33)	-0.28 (-0.48, -0.08)
EQ5D-3L+D Mean (SD/CI)	0.49 (0.37)	0.44 (0.41)	0.00 (-0.12, 0.12)	0.38 (0.31)	-0.08 (-0.23, 0.07)	0.19 (0.43)	-0.28 (-0.51, 0.10)
Thermometer n=	20	15	15	12	12	7	7
Mean (SD/CI)	64.5 (20.6)	64.6 (26.8)	0.9 (-13.5, 15.4)	61.7 (25.3)	-6.7 (-19.8, 6.5)	60.9 (21.6)	-7.0 (32.6)
Total							
n= *	37	32	30	31	30	16	15
EQ5D-3L Mean (SD/CI)	0.53 (0.29)	0.49 (0.28)	-0.02 (-0.09, 0.05)	0.43 (0.29)	-0.10 (-0.19, -0.02)	0.29 (0.33)	-0.20 (-0.33, 0.08)
EQ5D-3L+D Mean (SD/CI)	0.48 (0.37)	0.44 (0.41)	-0.02 (-0.10, 0.07)	0.41 (0.33)	-0.06 (-0.18, 0.05)	0.20 (0.43)	-0.23 (-0.40, -0.05)
Thermometer n=	37	31	29	28	27	13	13
Mean (SD/CI)	63.0 (21.3)	64.2 (25.5)	-0.5 (-8.2, 7.1)	61.6 (53.0)	-5.0 (-11.2, 1.2)	59.3 (21.1)	-6.4 (-20.7, 7.7)

Table 7 Patient ALSFRS-R scores.

Scores range from 0 (severe disability) to 48 (no disability). Scores highlighted in bold indicate scores that have changed significantly from baseline.

ALSFRS-R	Baseline Mean (SD)	3 months Mean (SD)	Change from baseline Mean (CI)	6 months Mean (SD)	Change from baseline Mean (CI)	12 months Mean (SD)	Change from baseline Mean (CI)
Telehealth							
	n=18	n=16	n=15	n=16	n=16	n=6	n=6
Mean	31.9 (9.7)	32.1 (10.4)	-0.06 (-2.6, 3.4)	31.1 (9.0)	-0.3 (-2.6, 1.9)	28.7 (7.6)	**-4.7** **(-8.5, -0.81)**
Control							
	n=20	n=15	n=15	n=12	n=12	n=7	n=7
Mean	32.1 (8.0)	29.8 (8.7)	-1.5 (-4.1, 1.0)	29.4 (9.0)	-3.7 (-6.8, -0.5)	25.9 (6.0)	-5.1 (-12, 1.3)
Total							
	n=38	n=31	n=30	n=28	n=28	n=13	n=13
Mean	32.0 (8.7)	30.9 (9.5)	-0.6 (-2.2, 1.0)	31.1 (8.9)	-1.6 (-3.6 – 0.4)	27.9 (9.6)	**-4.9** **(-8.4, -1.4)**

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Figure 4 Mean ALS-FRS-R and standard error .
Scores range from 0 (severe disability) to 48 (no disability). An * indicates scores where the mean change from baseline differs significantly from baseline ($p < 0.05$).
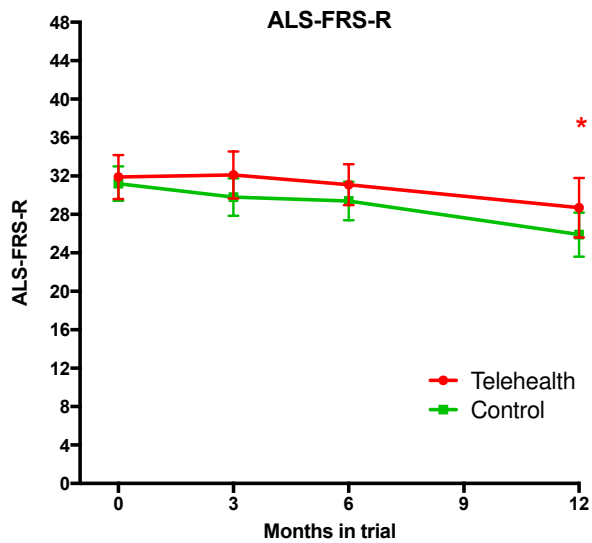
Table 8 Patient HADS Anxiety sub-scores and the number (%) of patients with borderline scores and abnormal scores.

0-7 normal, 8-10 borderline/mild symptoms, 11-21 abnormal: moderate/severe.

HADS	Baseline Mean (SD)	3 months Mean (SD)	3 months Change from baseline Mean (CI)	6 months Mean (SD)	6 months Change from baseline Mean (CI)	12 months Mean (SD)	12 months Change from baseline Mean (CI)
Telehealth Anxiety							
	n=17	n=16	n=16	n=16	n=15	n=6	n=6
Mean (SD/CI)	6.0 (4.0)	5.7 (4.3)	-0.2 (-2.3, 1.9)	4.7 (3.7)	-0.9 (-2.1, 0.4)	5.7 (2.4)	-.0.7 (-3.3, 2.0)
Score ≥8	8 (47%)	4 (25%)	-	3 (19%)	-	1 (6%)	-
Score ≥11	1 (6%)	2 (13%)	-	1 (6%)	-	0 (0%)	-
Control Anxiety							
	n=20	n=15	n=15	n=12	n=12	n=7	n=7
Mean (SD/CI)	4.9 (3.9)	4.6 (4.4)	-0.5 (-2.1, 1.2)	5.1 (5.1)	-.3 (-1.8, 1.3)	6.0 (4.8)	0.9 (4.7)
Score ≥8	3 (15%)	4 (27%)	-	3 (20%)	-	2 (13%)	-
Score ≥11	2 (10%)	3 (20%)	-	2 (13%)	-	1 (7%)	-
Total Anxiety							
	n=37	n=31	n=31	n=28	n=27	n=13	n=13
Mean (SD/CI)	5.4 (4.0)	5.2 (4.3)	-0.3 (-1.6, 0.9)	4.9 (4.3)	-0.6 (-1.5, 0.3)	5.8 (3.8)	0.2 (-2.1, 2.4)
Score ≥8	11 (30%)	8 (26%)	-	6 (19%)	-	3 (10%)	-
Score ≥	3 (8%)	5 (16%)	-	3 (10%)	-	1 (3%)	-

Table 9 Patient HADS Depression sub-scores and the number (%) of patients with borderline scores and abnormal scores.

0-7 normal, 8-10 borderline/mild symptoms, 11-21 abnormal: moderate/severe.

HADS	Baseline	3 months		6 months		12 months	
	Mean (SD)	Mean (SD)	Change from baseline Mean (CI)	Mean (SD)	Change from baseline Mean (CI)	Mean (SD)	Change from baseline Mean (CI)
Telehealth Depression							
	n=20	n=16	n=16	n=16	n=15	n=6	n=6
Mean (SD/CI)	5.9 (2.9)	5.6 (2.7)	-0.3 (-2.1, 1.6)	5.8 (3.0)	0.3 (-1.0, 1.6)	7.5 (4.3)	1.7 (-1.0, 4.4)
Score ≥8	5 (29%)	6 (38%)	-	6 (38%)	-	3 (19%)	-
Score ≥11	0 (0%)	0 (0%)	-	0 (0%)	-	3 (19%)	-
Control Depression							
	n=20	n=15	n=15	n=12	n=12	n=7	n=7
Mean (SD/CI)	3.9 (3.0)	6.1 (3.8)	1.5 (-0.4, 3.3)	5.8 (3.3)	0.8 (-1.7, 3.3)	6.4 (3.6)	0.9 (-3.4, 5.1)
Score ≥8	3 (15%)	4 (27%)	-	3 (20%)	-	3 (20%)	-
Score ≥11	1 (5%)	3 (20%)	-	1 (7%)	-	1 (7%)	-
Total Depression							
	n=37	n=31	n=31	n=28	n=27	n=13	n=13
Mean (SD/CI)	4.8 (3.1)	5.8 (3.2)	0.6 (-0.7, 1.9)	5.8 (3.1)	0.5 (-0.7, 1.7)	6.9 (4.6, 9.2)	1.2 (-1.0, 3.5)
Score ≥8	8 (22%)	10 (32%)	-	9 (29%)	-	6 (19%)	-
Score ≥11	1 (3%)	3 (10%)	-	1 (3%)	-	4 (13%)	-

Table 10 "Current" and "worst" pain scores over previous week.
Rated on a modified Likert score from 0-10.

Pain scores	Base -line Mean (SD)	3 months		6 months		12 months	
		Mean (SD)	Change from baseline Mean (CI)	Mean (SD)	Change from baseline Mean (CI)	Mean (SD)	Change from baseline Mean (CI)
Current pain (0-10)							
Control	20	15	15	13	13	7	7
Mean (SD/CI)	1.4 (1.4)	1.6 (2.0)	0.33 (-0.5, 1.2)	1.4 (2.0)	0.2 (-1.1, 1.4)	2.6 (2.5)	-0.9 (-2.6, 0.9)
Telehealth	17	16	15	15	15	6	6
Mean (SD/CI)	1.7 (1.9)	2.1 (2.4)	0.1 (-1.3, 1.4)	1.8 (2.3)	1.8 (0.7, 2.9)	1.8 (1.6)	0.8 (-1.2, 2.9)
Total	37	31	30	28	28	13	13
Mean (SD/CI)	1.5 (1.7)	1.9 (2.2)	0.2 (-0.5, 0.9)	1.6 (2.2)	1.0 (0.2, 1.9)	2.2 (2.1)	-0.1 (-1.3, 1.1)
Worst pain (0-10)							
Control	20	15	15	13	13	7	7
Mean (SD/CI)	3.2 (2.7)	3.4 (3.1)	-0.1 (-1.3, 1.0)	2.6 (2.7)	-0.2 (-0.8, 0.4)	3.9 (3.1)	0.3 (-1.0, 1.6)
Telehealth	17	16	15	15	15	6	6
Mean (SD/CI)	2.9 (2.8)	3.4 (3.1)	0.1 (-1.2, 1.5)	3.0 (2.8)	3.1 (1.6, 4.7)	3.5 (2.2)	0.3 (-2.4, 2.1)
Total	37	31	30	28	28	13	13
Mean (SD/CI)	3.0 (2.7)	3.2 (2.9)	0.0 (-0.8, 0.8)	2.8 (2.7)	1.6 (0.5, 2.6)	3.7 (2.7)	0.1 (-1.0, 1.1)

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Table 11 CSS-MND saliva severity scores.

Mean, standard deviation and change from baseline (mean, 95% confidence interval). Scores range from 0 (no problems with orophrayngeal secretions) to 36 (severe secretions).

CSS MND	Baseline Mean (SD)	3 months Mean (SD)	Change from baseline Mean (CI)	6 months Mean (SD)	Change from baseline Mean (CI)	12 months Mean (SD)	Change from baseline Mean (CI)
Telehealth	n=17	n=16	n=14	n=16	n=16	n=6	n=6
Mean (SD)	4.2 (6.0)	4.8 (6.4)	1.9 (0.2, 3.5)	2.6 (1.2)	0.0 (-2.8, 2.8)	2.3 (3.2)	0.2 (-1.4, 1.9)
Control	n=20	n=15	n=14	n=12	n=12	n=7	n=6
Mean (SD)	4.1 (5.2)	5.5 (6.2)	1.0 (-1.5, 3.5)	2.8 (1.1)	0.1 (-1.56, 1.7)	3.4 (4.5)	-0.7 (-0.7, 3.4)
Total	n=37	n=31	n=29	n=28	n=28	n=13	n=12
Mean (SD)	4.1 (5.5)	5.1 (6.2)	1.4 (0-2.9)	2.6 (1.1)	0.0 (-1.6, 1.6)	3.4 (4.5)	0.2 (-1.4, 1.9)

Table 12 Carer SF-36 physical and mental sub-scores.
These scores are standardised to a normative reference population in which the mean is 50 and standard deviation is 10.

Carer SF-36	Base-line Mean (SD)	3 months Mean (SD)	Change from baseline Mean (CI)	6 months Mean (SD)	Change from baseline Mean (CI)	12 months Mean (SD)	Change from baseline Mean (CI)
Telehealth							
Physical	n=16	n=14	n=13	n=15	n=14	n=4	n=4
Mean	52.4	49.0	-1.9	51.6	0.10	51.0	-3.6
(SD/CI)	(11.1)	(9.6)	(-8.0, 4.2)	(9.7)	(-4.9, 5.2)	(3.1)	(-13.8,6.6)
Mental	16	14	13	15	14	4	4
Mean	47.9	50.5	3.3	48.6	1.2	45.3	-2.9
(SD/CI)	(13.1)	(14.5)	(-1.1, 7.7)	(14.4)	(-2.8, 5.2)	(14.5)	(-9.6, 3.8)
Control							
Physical	n=18	n=13	n=13	n=11	n=11	n=7	n=7
Mean	52.9	51.9	-3.2	49.1	-4.7	52.2	-3.0
(SD/CI)	(7.7)	(7.0)	(-8.1, 1.8)	(8.8)	(-8.9, -0.4)	(9.6)	(-10.2,4.2)
Mental	n=18	n=13	n=13	n=11	n=11	n=7	n=7
Mean	50.6	51.2	1.7	51.8	0.70	51.7	2.4
(SD/CI)	(10.3)	(8.7)	(-2.2, 5.5)	(10.5)	(-6.8, 8.1)	(10.3)	(-4.5, 9.3)
Total							
Physical	n=34	n=27	n=26	n=26	n=25	n=11	n=11
Mean	52.7	50.4	-2.5	50.1	-2.0	51.8	-3.2
(SD/CI)	(9.3)	(8.4)	(-6.1, 1.1)	(9.2)	(-5.3, 1.3)	(7.6)	(-7.9, 1.5)
Mental	n=34	n=27	n=26	n=26	n=25	n=11	n=11
Mean	49.3	50.8	2.5	49.9	1.0	49.4	0.4
(SD/CI)	(11.6)	(11.8)	(-0.3, 5.2)	(12.8)	(-2.7, 4.6)	(11.7)	(-4.1, 5.0)

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Figure 5 Carer RAND physical component scores (PCS) and mental component scores (MCS).
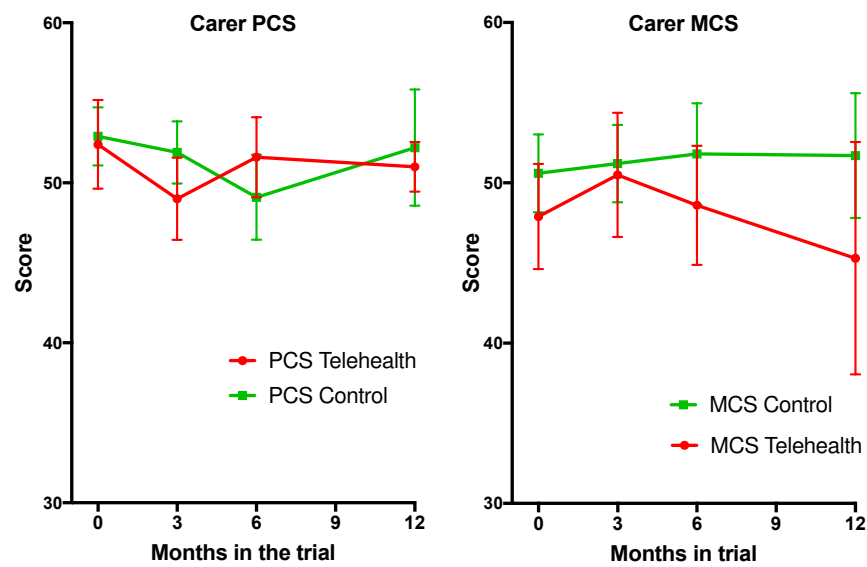
Table 13 Carer HADS depression sub scores and the number (%) of patients with borderline scores or abnormal scores.
Scores 0-7 are normal, 8-10 borderline/mild symptoms, 11-21 abnormal: moderate/severe).

	Baseline	3 months		6 months		12 months	
	Mean (SD)	Mean (SD)	Change from baseline Mean (CI)	Mean (SD)	Change from baseline Mean (CI)	Mean (SD)	Change from baseline Mean (CI)
Telehealth Depression							
	n=16	n=14	n=13	n=15	n=14	n=6	n=6
Mean	4.0	4.6	0.1	4.3	0.1	4.8	1.3
(SD/CI)	(3.2)	(4.1)	(-1.0, 1,2)	(3.9)	(-0.9, 1.0)	(3.5)	(-1.5, 4.1)
Score ≥8	1 (6%)	3 (21%)	-	3 (20%)	-	1 (14%)	-
Score ≥11	1 (6%)	1 (7%)	-	1 (7%)	-	0 (0%)	-
Control Depression							
	n=18	n=14	n=14	n=11	n=11	n=7	n=7
Mean	3.3	4.8	1.4	4.3	2.1	3.4	1.3
(SD/CI)	(2.8)	(4.2)	(0.0, 2.8)	(4.5)	(0.4, 4.6)	(3.4)	(-0.8, 3.4)
Score ≥8	2 (11%)	3 (21%)	-	3 (27%)	-	1 (14%)	-
Score ≥11	1 (6%)	1 (7%)	-	1 (9%)	-	0 (0%)	-
Total Depression							
	n=34	n=28	n=27	n=26	n=25	n=13	n=13
Mean	3.6	4.7	0.8	4.3	1.0	4.1	1.3
(SD/CI)	(3.0)	(4.0)	(-0.1, 1.7)	(4.0)	(-0.2, 2.1)	(3.4)	(-0.2, 2.7)
Score ≥8	2 (6%)	6 (21%)	-	6 (21%)	-	2 (15%)	-
Score ≥11	1 (3%)	2 (7%)	-	2 (7%)	-	0 (0%)	-

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Table 14 Carer HADS anxiety sub scores and the number (%) of patients with borderline scores or abnormal scores.

Scores 0-7 are normal, 8-10 borderline/mild symptoms, 11-21 abnormal: moderate/severe).

	Baseline	3 months		6 months		12 months	
	Mean (SD)	Mean (SD)	Change from baseline Mean (CI)	Mean (SD)	Change from baseline Mean (CI)	Mean (SD)	Change from baseline Mean (CI)
Telehealth Anxiety							
	n=16	n=14	n=13	n=15	n=14	n=6	n=6
Mean (SD/CI)	6.3 (4.6)	7.1 (4.6)	0.0 (-1.8, 1.7)	6.0 (5.1)	-0.8 (-2.9, 1.3)	7.3 (5.0)	0.3 (-1.4, 1.9)
Score ≥8	7 (44%)	3 (21%)	-	5 (33%)	-	3 (43%)	-
Score ≥11	2 (13%)	1 (7%)	-	3 (20%)	-	3 (43%)	-
Control Anxiety							
	n=18	n=14	n=14	n=11	n=11	n=7	n=7
Mean (SD/CI)	5.9 (3.5)	6.2 (4.4)	-0.2 (-1.8, 1.4)	6.4 (4.8)	0.3 (-2.1, 2.7)	5.6 (4.0)	-0.6 (-1.6, 0.5)
Score ≥8	6 (33%)	6 (43%)	-	4 (36%)	-	2 (29%)	-
Score ≥11	2 (11%)	2 (14%)	-	3 (27%)	-	1 (14%)	-
Total Anxiety							
	n=34	n=28	n=27	n=26	n=25	n=13	n=13
Mean (SD/CI)	6.1 (4.0)	7.1 (4.6)	-0.1 (-1.2, 1.0)	6.2 (4.8)	-0.3 (-1.8, 1.1)	6.4 (4.4)	-0.2 (-1.4, 1.9)
Score ≥8	13 (35%)	3 (11%)	-	**9 (31%)**	**-**	**5 (38%)**	-
Score ≥11	4 (11%)	5 (18%)	-	**6 (21%)**	**-**	**4 (31%)**	**-**

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Table 15 The 12-item Zarit Burden Interview scores.

Scores range from 0 (no burden) to 48 (severe burden). A cut-off of scores ≥17 suggests high burden (222).

	Base-line	3 months		6 months		12 months	
	Mean (SD)	Mean (SD)	Change from baseline Mean (CI)	Mean (SD)	Change from baseline Mean (CI)	Mean (SD)	Change from baseline Mean (CI)
Telehealth							
	n=18	n=14	n=14	n=15	n=15	n=6	n=6
Mean (SD/CI)	11.5 (9.9)	12.7 (11.2)	1.6 (-1.6, 4.8)	13.7 (10.7)	2.4 (-1.3, 6.1)	13.8 (12.6)	4.3 (-1.2, 9.9)
Score ≥17	3 (19%)	4 (29%)		4 (27%)		2 (33%)	
Control							
	n=16	n=13	n=13	n=10	n=10	n=6	n=6
Mean (SD/CI)	12.9 (7.9)	15.9 (8.9)	3.0 (-0.6, 6.6)	12.4 (9.5)	2.6 (-0.5, 5.7)	13.5 (9.6)	-0.3 (-7.9, 6.2)
Score ≥17	6 (33%)	4 (31%)	-	2 (20%)		2 (33%)	
Total							
	n=34	n=27	n=27	n=25	n=25	n=12	n=12
Mean (SD/CI)	12.3 (8.8)	14.2 (10.1)	2.6 (0.0-4.5)	13.2 (9.0)	2.5 (0.1, 4.8)	13.7 (10.7)	1.8 (-2.3, 5.8)
Score ≥17	9 (27%)	8 (30%)		6 (24%)		4 (33%)	

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Figure 6 The number of patient-reported MND related healthcare encounters in the three months prior to the study (baseline) and during the study
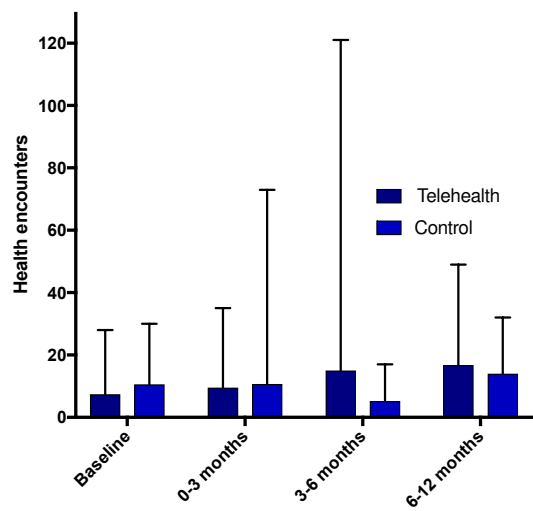Mean and range, n=38.

Figure 7 Patient encounters with healthcare professionals due to MND in the three months prior to the study commencement
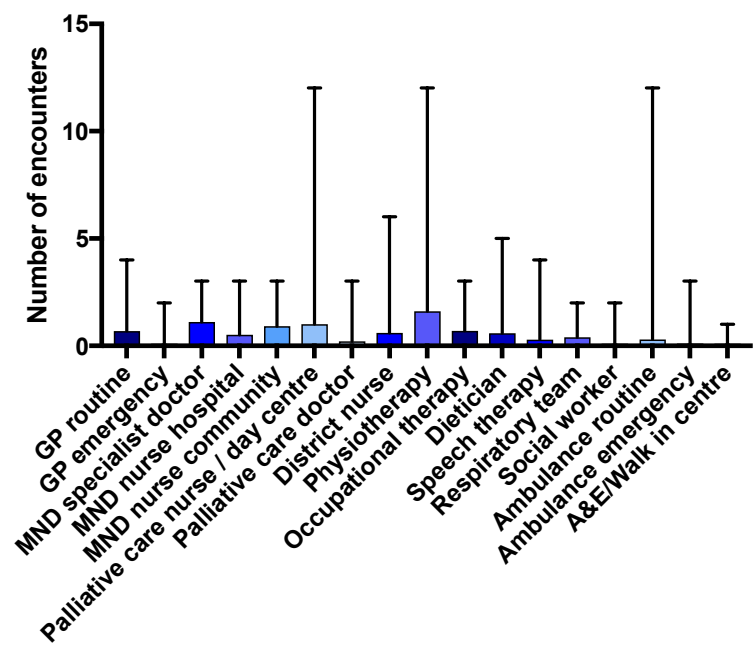Mean and range, n=38.

Figure 8 Patient estimated hours of informal (unpaid) and formal (paid) care received per week.
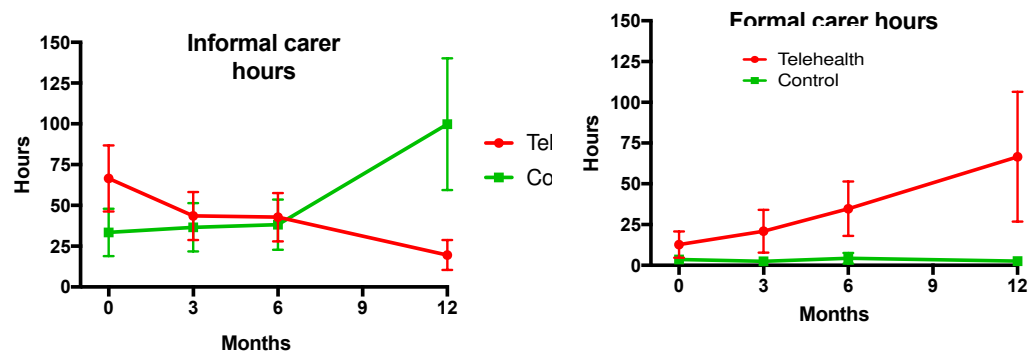
Mean and interquartile range.

Figure 8 Individual patient estimated median hours of informal (unpaid) and formal (paid) care received per week
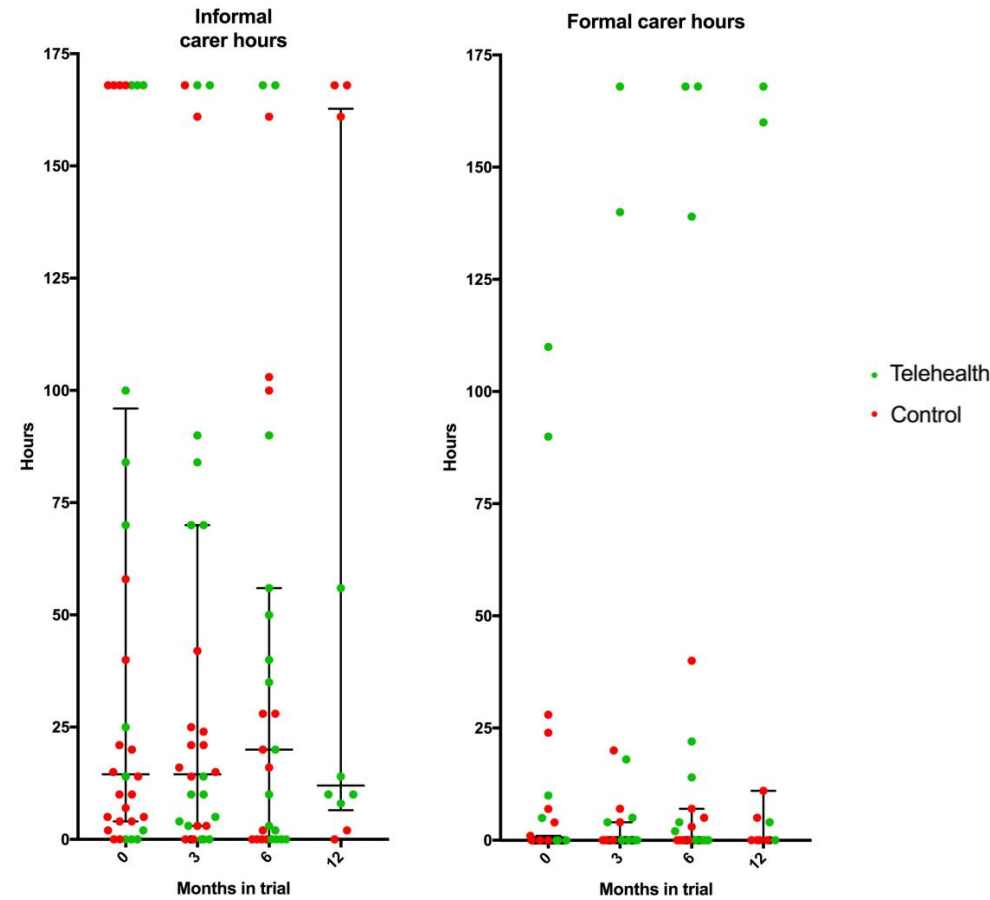
Mean and the interquartile range.

Table 16 Patient estimated hours of paid and unpaid care received per week.

	Baseline	**3 month**	**6 months**	**12 months**
Telehealth				
Paid carer hours	n=17	n=16	n=15	n=5
Mean (SD)	12.7 (33.2)	20.9 (52.4)	34.7 (64.6)	66.6 (89.0)
Median (Range)	0 (0-110)	0 (0-168)	0 (0-168)	5 (0-168)
Unpaid carer hours	n=12	n=16	n=15	n=5
Mean (SD)	66.6 (70.2)	43.5 (58.6)	42.8 (57.4)	19.6 (20.5)
Median (Range)	47.5 (0-168)	10 (0-168)	20 (0-168)	10 (0-168)
Control				
Paid carer hours	n=18	n=13	n=12	n=6
Mean (SD)	3.6 (8.4)	2.4 (5.7)	4.3 (11.4)	2.5 (4.5)
Median (Range)	0 (0-28)	0 (0-20)	0 (0-40)	0 (0-11)
Unpaid carer hours	n=20	n=14	n=12	n=5
Mean (SD)	33.4 (64.9)	36.6 (55.4)	38.2 (53.3)	99.8 (90.2)
Median (Range)	12.0 (0-168)	18.5 (0-168)	18 (0-161)	161 (0-168)
Total				
Paid carer hours	n=35	n=29	n=27	n=11
Mean (SD)	8.0 (24.0)	12.6 (39.7)	21.2 (50.4)	31.6 (65.6)
Median (Range)	0 (0-110)	0 (0-168)	0 (0-168)	0 (0-168)
Unpaid carer hours	n=32	n=30	n=27	n=10
Mean (SD)	52.7 (66.7)	40.3 (56.3)	40.7 (54.6)	59.7 (74.8)
Median (Range)	14.5 (0-168)	14.5 (0-168)	20 (0-168)	12 (0-168)

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Table 17 The adverse events recorded during the trial.

	Telehealth		Control		Total	
	Number of events	Number of patients/carers (%)	Number of events	Number of patients/carers (%)	Number of events	Number of patients/carers (%)
MND related						
Chest infection/ respiratory symptoms	7	7 (35%)	4	4 (20%)	11	11 (55%)
Falls	8	7 (35%)	3	3 (15%)	11	10 (50%)
Musculoskeletal symptoms	3	3 (15%)	0	0 (0%)	3	3 (15%)
Excessive saliva / choking	2	1 (5%)	0	0 (0%)	2	1 (5%)
Elective PEG insertion	2	2 (10%)	1	1 (5%)	3	3 (15%)
PEG site problem	0	0 (0%)	1	1 (5%)	1	1 (5%)
Patient psychological distress	0	0 (0%)	1	1 (5%)	1	1 (3%)
Carer psychological distress	11	5 (29%)	6	5 (26%)	17	10 (27%)
Other adverse events						
Other medical	7	3 (15%)	5	5 (25%)	12	8 (40%)
Other surgical	0	0 (0%)	2	1 (5%)	2	1 (5%)

Table 18 Summary of health encounters for the three months prior to baseline

	Total in 3 months[3]	Total physicians[4]	Total nurses[5]	Total therapists[6]
Telehealth				
Total (n=18)	133	38	43	52
Mean (SD)	7.4 (6.3)	2.1 (2.3)	2.4 (2.6)	2.9 (3.1)
Median	5.5	1	1.5	2
Range	0-28	0-8	0-10	0-11
Control				
Total (n=20)	211	45	72	88
Mean (SD)	10.6 (8.5)	2.3 (2.1)	3.6 (5.1)	4.4 (4.3)
Median	8	2	1	4
Range	1-30	0-10	0-19	0-13
Total				
Total (n=38)	344	83	115	140
Mean (SD)	9.1 (7.7)	2.2 (2.2)	3.0 (4.1)	3.7 (3.8)
Median	7	2	1	2.5
Range	0-30	0-10	0-19	0-13

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[3] Total excluded ambulance journey and unrelated/non-NHS services

[4] Physicians included were MND neurologists, palliative care physicians and general practitioners.

[5] Nurses included district nurses, MND specialist nurses in hospital and community and hospice nurses.

[6] Therapists included speech and language therapists, physiotherapists, occupational therapists, respiratory specialists, dieticians and PEG nurses.

Table 19 Summary of patient reported MND related health-care encounters between months 0-3 of the study.

	Total[7]	Total physicians[8]	Total nurses[9]	Total therapists[10]
Telehealth				
Total (n=16)	152	40	51	61
Mean (SD)	9.5 (9.1)	2.5 (2.3)	3.2 (3.6)	3.8 (4.7)
Median	8	2	2	3
Range	2-35	0-8	0-13	0-18
Control				
Total (n=15)	160	38	55	59
Mean (SD)	10.7 (17.6)	2.5 (4.2)	3.7 (9.6)	3.9 (3.7)
Median	8	1	1	3
Range	0-73	0-17	0-38	0-11
Total				
Total (n=31)	312	78	106	120
Mean (SD)	10.1 (13.6)	2.5 (3.3)	3.4 (7.0)	3.9 (4.2)
Median	6	2	1	3
Range	0-73	0-17	0-38	0-18

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[7] Total excluded ambulance journey and unrelated/non-NHS services

[8] Physicians included MND neurologists, palliative care physicians and general practitioners.

[9] Nurses included district nurses, MND specialist nurses in hospital and community and hospice nurses.

[10] Therapists included speech and language therapists, physiotherapists, occupational therapists, respiratory specialists, dieticians and PEG nurses.

Table 20 Summary of patient reported MND related health-care encounters between months 3-6 of the study.

	Total[11]	Total physicians[12]	Total nurses[13]	Total therapists[14]
Telehealth				
Total (n=16)	241	45	143	53
Mean (SD)	15.1 (29.3)	2.8 (3.0)	8.9 (28.3)	3.3 (4.9)
Median	8	2	1	1.5
Range	0-121	0-12	0-115	0-17
Control				
Total (n=12)	83	16	41	26
Mean (SD)	5.2 (1.5)	1.3 (0.9)	3.4 (4.0)	2.2 (1.6)
Median	4	1	2	2.5
Range	2-17	0-3	0-12	0-4
Total				
Total (n=28)	310	61	184	79
Mean (SD)	11.3 (22.2)	2.1 (2.4)	6.8	2.8 (3.9)
Median	4	2	1	2
Range	0-121	0-12	0-115	0-79

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[11] Total excluded ambulance journey and unrelated/non-NHS services

[12] Physicians included MND neurologists, palliative care physicians and general practitioners.

[13] Nurses included district nurses, MND specialist nurses in hospital and community and hospice nurses.

[14] Therapists included speech and language therapists, physiotherapists, occupational therapists, respiratory specialists, dieticians and PEG nurses.

Table 21 Summary of patient reported MND related health-care encounters for the six months between months 6-12 of the study.

	Total in 6 months[15]	Total physicians[16]	Total nurses[17]	Total therapists[18]
Telehealth				
Total (n=6)	101	18	52	30
Mean (SD)	16.8 (17.2)	3.0 (1.4)	8.8 (13)	5.0 (3.9)
Median	9.5	3	3	4
Range	3-49	1-5	1-35	1-10
Control				
Total (n=7)	98	26	32	40
Mean (SD)	14.0 (10.7)	3.7 (1.8)	4.6 (8.0)	5.7 (6.3)
Median	8	4	1	5
Range	5-32	1-6	0-22	1-19
Total				
Total (n=13)	199	44	87	70
Mean (SD)	15.3 (13.5)	3.4 (1.6)	6.5 (10.5)	5.4 (5.1)
Median	8	4	2	5
Range	3-49	1-6	0-35	1-19

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[15] Total excluded ambulance journey and unrelated/non-NHS services

[16] Physicians included MND neurologists, palliative care physicians and general practitioners.

[17] Nurses included district nurses, MND specialist nurses in hospital and community and hospice nurses.

[18] Therapists included speech and language therapists, physiotherapists, occupational therapists, respiratory specialists, dieticians and PEG nurses.

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Table 22 The number of admissions (and number of patients) and days in hospital reported by patients in the three months prior to recruitment.

	Telehealth (n=18)		Control (n=20)		Total (n=38)	
	Number of admissions (number of patients)	Nights in hospital	Number of admissions (number of patients)	Nights in hospital	Number of admissions (number of patients)	Nights in hospital
Elective						
PEG insertion	0	0	4 (3)	15	4 (3)	15
Diagnosis	1 (1)	1	0	0	1 (1)	1
Total elective	1 (1)	1	4 (3)	15	5 (5)	16
Emergency						
Fall	0	0	1 (1)	9	1 (1)	9
Choking	3 (1)	16	0	0	3 (1)	16
Gastrostomy site infection	0	0	1 (1)	2	1 (1)	2
Total emergency	3 (1)	16	2 (2)	11	5 (3)	27
Unrelated to MND						
Total unrelated admissions	0	0	0	0	0	0

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Table 23 The total number and reason for hospital admissions reported by all participants during the first 12 months of the study and the number of overnights stayed in hospital.

	Telehealth		Control		Total	
	Admissions (patients)	Nights	Admissions (patients)	Nights	Admissions (patients)	Nights
Elective						
PEG insertion	2 (2)	21	1 (1)	6	3 (3)	27
Symptom control	2 (2)	14*	0	0	2 (2)	14*
Total elective	4 (4)	72*	1 (1)	6	5 (5)	41*
Emergency						
Respiratory symptoms	1 (1)	6	2 (2)	15	3 (3)	21
Collapse, poor oral intake	1 (1)	2	0	0	1 (1)	2
Total emergency	2 (2)	8	2 (2)	15	4 (4)	23
Unrelated to MND						
Elective: hip replacement	2 (1)	6	0	0	2 (1)	6
Emergency: lung cancer	0	0	4 (1)	50	4 (1)	50
Emergency: postural hypotension	0	0	1 (1)	3	1 (1)	3
Total unrelated	2 (1)	6	5 (2)	53	7 (3)	59

*It was not possible to establish the number of nights from one patients' admission so these nights are not included.

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Table 24 Participants' motivations to participation in research.

Incentives to participating in trials	
Low burden of the intervention	" Oh I was interested in that because it's so easy to do; it literally takes five minutes from home." Patient 317
Able to participate in trials without leaving home	"My care's here. I can't have anything that takes it away from what I'm doing with P. It's got to be very simple things. I can sit with my iPad and I can fill in a questionnaire. Done, dusted, finished." Carer 184
Clear information about what is involved	"If it was local and we were going anywhere or people were coming here and; I could always look at each one individually but I think I wouldn't want to spend a lot of time away from home. So that would be my main criteria. Patient 408

Motivations to participating in research	
To help find a cure	"If I can be of any help to any research, you know, which'll help try and find a cure." Patient 056
To help other people with MND	"It might come along too later to help me but it will help people who come after me." Patient 122 "Just trying to help other people; if me pressing a few buttons …can help in the future, it's not a problem" Patient 354
In gratitude to the clinicians	"I think that the people at the Hallamshire are just about the best in the, in the, in the game" Patient 062
To do something positive	"… it's that feeling of doing something positive." Carer 402 "I like that idea that moving forward" Patient 423
To learn about research	"I've always been interested in medical science…so I said any research that they're doing I want to get involved in." Patient 423
To help their family, who may be at risk	"Carer: I gave blood as well.. because …we've got the boys … I think that's quite a big thing for me" Carer 381
To have better contact with MND team	"It was good because, it meant, in the first year I was going to the clinic every month." Patient 122
To receive better treatment	"I'm offering my services … but in return … I'm getting a repeating MOT." Patient 313
To find out more about their condition	"That led to the, the obvious question "Well if you find anything wrong will you tell me?"." Patient 313
To increase the chances of them being involved in a treatment trial	"I do believe that if you're not in the loop then if something comes along then you're on the wrong side of the fence. If you're involved with different … then you're more likely to be selected for possible hopeful cures…" Patient 232

Table 25 Participants' attitudes towards recruitment and randomisation in the TiM trial.

Recruitment and randomisation to the TiM trial	
Recruitment process provided sufficient information	*"I think it were all pretty much straight forward, in the letter that you sent out, plus when you came, I think it were all pretty straight forward, yeah." Patient 145*
Patients were willing to be randomised as they understood the research question	*"Q: Was there a particular arm of the study that you wanted..?* *Patient : No, because it's a subject that not very much seems to be known about, so if I can help in any area of it, I will." Patient 166*
Patients would prefer to be in the intervention arm	*"Q: And how did you feel about being assigned to the Telehealth side?* *Patient : Well I've preferred that side of it." Patient 381*
Patients were not demoralized if they were assigned the control arm	*"I should think most people would probably want to have tablet. I think, they'd think "this is alright." But quite frankly it doesn't bother me." Patient 070*
Involving the control arm in interviews avoided resentful demoralization	*"I read the notes. Some would get the interview, some would get the tablet" Carer 070*
Researchers could influence the randomisation process	*"Patient : We thought: they'll put [my sister] on the real drug because they can monitor her for longer.* *Q: Do you think that the study researchers can have an influence on which arm of the study you go in?* *Patient : Probably not, no. Probably it's the drug company who are pulling the strings. They are paying the money aren't they?" Patient 184*

Table 26 Participants' attitudes towards and knowledge of research.

Participants' attitudes towards and knowledge of research	
Patients gain information about research and new treatments through…	
Clinic	*" I like having a chat with you and finding out what's happened, what's new, because all we have is hope, we don't have a lot more"." Patient 134*
Friends and fellow patients	*"It's really just through word of mouth. " Patient 122*
MND Association	*"The MNDA puts posts on about research" Patient 145*
Internet	*"I mean we have found, for instance, a website; you can actually see it on YouTube, called Deanna Protocol" Patient 317*
Social media/ peer networks	*"There's also a long term ALS survivors' website where people, have been diagnosed with it… and been told that you've only got a year left to live, but they've done radical changes, ….and those people have halted it" Patient 317*
Patient seek out, evaluate and use unproven treatments	*"I don't follow regimes as strict as the Deanna protocol but I just pick out certain things that I think would help me, hence the reference to moringa and coconut oil." Patient 232*
Frustration with the speed of drug development	*"I just feel like, after 30 years with millions … of pounds spent we've still got a tablet that [has little evidence]" Patient 184* *"We need to be getting a move on… Some day, we've got to stop messing around with mice." Patient 184* *"I don't hold out too much confidence about the UK system of getting drugs to market and funding them with the likes of NICE posing usual financial constraints." Patient 232*
Time is running out for a cure	*"Once you get to what I always call "frank" stage …I don't think there's any drug that would bring you out of that." Patient 184*
Patients have little to lose	*"We being the patients with MND, have nothing to lose… There's always risk in life." Patient 232*
Learning about research makes patients hopeful	*"[you think] There's got to be things that we can do, come on, we're gonna really give this a hundred percent; and the more we looked the more intrigued we became…. you can see people that have had really good benefits from it." Patient 317* *"We're all kind of pinning our hopes …on GM604" Patient 232*
Patients recognize information may be giving false hope	*"Too much information could fill people with a false hope and you've gotta manage people's expectations" Patient 122*
Putting trust in the doctors to run safe trials in the best interests of the patient	*"Q: Did you consider the downsides, the risks of having a lumbar puncture when you came?* *Patient: No. I just thought, well if that's all I've got to put up with. But if a doctor can't do a lumbar it's a bad job." Patient 184* *"I would have complete faith in [consultants] team saying "Right, lets get some people in now and let's do it" Patient 184*
Wanting to see tangible benefits of treatments which reverse the disease	*"No one will ever convince me that they know [riluzole] works. …How do they know I've had three months more life?...Who would know? .. I can't walk any better, I can't speak any better, I can't do anything any better." Patient 184* *"…it doesn't have to cure you it just has to make things better." Carer 232* *"If there was a magic bullet and I had to sell everything to purchase that bullet, I would." Patient 232*

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Table 27 Barriers to participation in research.

Barriers to participation in research	
Additional burden	*" Well, just another job.... To remember" Carer 217*
Research is time consuming	*"Initially it is a bit overwhelming … we do seem to have signed-up for absolutely everything…" Carer 402* *"It's difficult, … sometimes you get to the stage where you think: you know what? I just don't feel like this, I've just had enough" Carer 402*
Intrusion or disruption of family life	*"Carer: I just don't think; … we, we just try to keep ourself and look after him, look after him and that's it.* *Q: …Have any of those worries been the case during the study?* *Carer: No." Carer 228* *"I don't want the family life to be disrupted, that's really important to us." Patient 408*
Time spent away from home	*"I'd need to know about the, the time that would be needed to be spent, if I needed to spend time away from here, from home" Patient 408*
Research can be tiring	*"On Thursday I went for my research, had the lumbar puncture, the tissue sample, blood samples I think. So then I came home. For two days after that I was more or less housebound." Patient 184*
Travel to hospital is expensive	*"…the train tickets are a bit expensive, so we've driven the last few times. But … we got the free parking and things like that…" Carer 392*
Travel difficult	*"It's gonna be a lot more difficult with a wheelchair" Carer 392*

Table 28 Participant reaction to the TiM research questionnaires.

Were questions acceptable?	
Questions posed in the questionnaire were acceptable	*"No. To be quite frank, doctor, I wouldn't care a monkey's what you ask ...I have no hang-ups about any questions, however personal, the team think it's necessary to ask; I've seen it all, done it all and got the t-shirt." Carer 229* *"Patient : I was fine about doing them." Patient 116*
There was a limit to the number of questions participants were willing to answer	*"Patient : You don't want another one of them hundred and fifty page things to fill out, that were, whatever it was last year." Carer 248*
Questions on emotions were acceptable to those experiencing emotional distress	*"It's more the emotional ones that I have trouble filling in cos I've been depressed for quite a ...and it's, it's just hard admitting that yes, maybe some days it's not great and I know that I'm not great at the moment but. But no, they seemed good. They were really clear, and it wasn't too, too much to do." Patient 408*
Participants wanted questions to cover all potential aspects of MND	*"At the moment I've not got a lot of problems with my legs, but in 18 months I might need a wheelchair, or I might be having to use a breathing machine. So every question is relevant." Patient 070*
Questions about future complications were acceptable because patients were aware of what may occur	*"When you read things about these questions: it brings things home to you. Well yeah, I have deteriorated.... It doesn't really significantly affect me at all because, I like to think I'm a reasonably intelligent man and I know things are deteriorating." Patient 184*
Which questions best reflected the experiences of patients and carers?	
Questions about mood/emotions best reflected their experiences	*"I think the best ones are the ones about how it makes you feel and how it affects your mood etc. That's very important ...." Patient 122*
The carer burden accurately captured the experience of carers	*"It was a strange one cos [the ZBI] was asking you what I feel about spending the time with him, that I don't have time for meself.... Yeah, it is quite a thing cos you're always thinking... "Has he got enough drinks? ... then anything to eat?"... I don't like to be too far away from him, even though I'm in the house ... in case summat happened and he needs me." Carer 091*
Carer strain is linked to patient and carer wellbeing	*"...obviously if strains exist, become too much for the carer, then the patient, to a degree, suffers.." Carer 229*
Mood/emotions affected patients health and functional abilities	*"Feelings of anxiousness can affect my legs, and I know that. I try not to control, try not to get anxious about situations but sometimes it's hard when you know, your are going to move from A to B, you're going to get anxious about it." Patient 076*

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Table 29 Weaknesses with the questionnaires identified.

SF-36 questionnaires failed to reflect the experience of life with MND	
SF-36 questions were too subjective	*"That's sort of looking at question [SF-36], and putting down, you're limited and then you sort of realise; I can't really do that; and you don't think about it all the time do you? Some of them I wanted to put "sometimes", you know… sometimes I have but I've just gone for on the whole" Patient 408*
Patients found it difficult to assess their global health and were unsure whether to include MND in the assessment	*"Patient : It's slightly confusing when they ask about health because it's hard to take the MND out of the equation, I think. Apart from that I would be very healthy." Patient 116 "Patient : My health other than the illness? (Pause) Taking the illness into account I would say poor, but if I ignore the, the illness I would say very good." Patient 137 [referring to SF-36]*
Patients felt "healthy" despite having MND	*" To be honest, I feel great. So does that say I'm excellent. But you know that you're not, so you can't be excellent." Patient 175 [referring to SF-36]*
Carers felt they had no health problems and felt the QoL questions were not relevant	*"I mean this: [reads] "I feel as if I'm slowed down"; it's not because of caring for you but because I'm getting older… I can't do a forward roll over a gatepost anymore!" Carer 137 [referring to SF-36]*
Those with severe disability had few "daily activities" on which to assess the impact of MND	*"Patient : It doesn't affect my work because I don't do any! Q: It's housework as well. Patient : No. I don't do any! I do a little bit." Patient 070 [referring to SF-36]*
Other weaknesses	
Participants found it difficult to quantify the time taken by domestic jobs that are usually shared	*" But there are things now… I'll say "its time for a cup of tea". It will always be me that makes it. I'm not saying I resent it, because P can't do it… But I don't class that as care… Carer 175 [referring to informal care question]*
Questions should better reflect patients' functional abilities and coping strategies	*"It's about monitoring really, and with these questionnaires you are not able to say how you manage. If we know we are going out for a full day, then P knows not to plan anything for the next day because he's gonna be tired." Carer 076*
Answering questions may be difficult if they not want to admit they have problems	*"….It's like C was saying, you've just got to be honest and sometimes that's really hard cos you don't want to admit that maybe you're not as good as you were". Patient 408*

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Table 30 The calculated total sample sizes for the two approaches to calculating the endpoint at different effect sizes.

These were calculated by the trial statistician and based on the parameters stated above.

	Single time point		Longitudinal[19]	
	Unadjusted	**+30% drop-out**	**Unadjusted**	**+30% drop-out**
Effect size				
0.2 SD	n=1052	n=1503	n=396	n=566
0.3 SD	n= 468	n= 669	n=176	n=251
0.4 SD	n= 264	n= 377	n=100	n=143
0.5 SD	n= 170	n= 243	n=64	n=91

[19] Assuming one baseline and four follow-ups with a common correlation of 0.5.