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Associations between adherence to the physical activity and exercise program applied in the LAST-study (Life After STroke) and functional recovery after stroke

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Running Head: The impact of long-term adherence post-stroke

Title: Associations between adherence to the physical activity and exercise program applied in the LAST-study (Life After STroke) and functional recovery after stroke

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Title: Associations between adherence to the physical activity and exercise program applied in the LAST-study (Life After STroke) and functional recovery after stroke

Abstract

Objective: To investigate the associations between participants' adherence to a physical activity and exercise program after stroke and functional recovery 18 months after inclusion.

Design: Secondary analyses of the intervention-arm in the multisite randomized controlled trial Life After STroke (LAST).

Setting: Primary health care services in three Norwegian municipalities.

Participants: Of the 380 participants enrolled, 186 (48.9%) were randomized to the intervention. The study sample comprised community dwelling individuals included three months after stroke, with mean age 71.7 years (SD 11.9) and 82 (44.1%) women. According to National Institutes of Health Stroke Scale (NIHSS), 97.3% were diagnosed with mild (NIHSS <8) and 2.7% with moderate (8 to 16 on NIHSS) stroke.

Intervention: Monthly coaching by physiotherapists encouraging participants to adhere to 30 minutes of daily physical activity and 45-60 minutes of weekly exercise.

Main Outcome Measures: The primary outcome was Motor Assessment Scale (MAS). Secondary outcome measures were Six-minute walk test, Timed Up and Go (TUG), Berg Balance Scale (BBS) and the physical domains of the Stroke Impact Scale (SIS). Adherence was assessed by combining participants' training diaries and physiotherapists' reports.

Results: The relationship between adherence and functional recovery was analyzed with simple and multiple linear regression models. Adjusted for age, sex, dependency and

cognition, results showed statistically significant associations between adherence and functional outcomes after 18-months, as measured by MAS, TUG, BBS and SIS ($p \leq 0.026$).

Conclusions: Increased adherence to physical activity and exercise was associated with improved functional recovery after mild to moderate stroke. This emphasizes the importance of developing adherence-enhancing interventions. Dose-response studies are recommended for future research.

Key words: Stroke rehabilitation, physical activity, exercise, patient adherence.

List of abbreviations:

B, Regression coefficient estimate; BBS, Berg Balance Scale; CI, confidence interval; LAST, Life After STroke; MAS, Motor Assessment Scale; MMSE, Mini-Mental State Examination; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; 6MWT, six-minute walk test; SIS, Stroke Impact Scale; TUG, Timed Up and Go test.

Physical activity and exercise of moderate or high intensities are recommended as a part of comprehensive rehabilitation in the chronic phase after stroke.[1,2] However, a substantial portion of individuals surviving stroke face physical and psychological barriers,[2] which limits their ability and motivation to engage in physical activities over time.[3,4]

Adherence to treatment is proposed to be the key link between an intervention and the achieved outcomes, and degree of adherence is shown to have major influence on findings from clinical research.[5] Hence, neutral results might reflect the lack of adherence to the intervention, rather than the lack of beneficial effects of the intervention.

Previous rehabilitation studies that evaluated how patient outcomes were affected by adherence have provided evidence for a positive dose-response relationship between adherence and functional outcomes after stroke.[6-11] This research was mainly focused on hospital or inpatient rehabilitation within six months after onset of stroke. To our knowledge, no studies have investigated whether these findings are observable in the long-term, or among community-dwelling individuals after stroke.

In the Life After Stroke (LAST) study, a randomized controlled trial, regular individualized coaching over 18 months post-stroke established and maintained increased levels of physical activity and exercise. In spite of this, there were no significant differences in maintenance of motor function between the intervention-arm and the control-arm.[12] Training diaries from LAST revealed large differences in adherence between participants,[13] and therefore, the true effect of the physical activity and exercise program may have been watered down. In a long-term follow-up program after stroke, detailed information from diaries on adherence provides a unique opportunity to study the associations between adherence and functional outcomes.

In the present study, participants in the intervention group who were the most adherent to the physical activity and exercise protocol of LAST were hypothesized to achieve better

functional recovery at follow-up. Hence, the primary aim of the present study was to assess the associations between participants' degree of adherence to physical activity and exercise and motor function 18 months after inclusion. Secondary aims were to evaluate the associations between participants' adherence and walking capacity, balance and self-perceived functional outcomes.

Methods

Study design, setting and participants

LAST was designed as a pragmatic, single-blinded, parallel group, multisite randomized controlled trial.[12] The present study reports secondary analyses of the associations between adherence to the physical activity and exercise program applied in the intervention group and functional outcomes of LAST.

Participants in LAST were recruited from 18 October 2011 to 26 June 2014 at the outpatient clinics at the stroke units of two Norwegian hospitals. Inclusion criteria were: diagnosed with first-ever or recurrent stroke (infarction or intracerebral hemorrhage), aged ≥ 18 years, discharged from hospital or inpatient rehabilitation at inclusion, community dwelling, modified Rankin Scale (mRS) score < 5, and cognitive function by Mini-Mental State Examination (MMSE) > 20 points (> 16 points for participants with aphasia). Exclusion criteria were serious medical comorbidity with short life expectancy, or a condition contraindicating motor training. To ensure safety, in line with good clinical practice and the current Norwegian guidelines,[14] participants underwent a complete medical history and a physical examination by a medical practitioner during screening. Patients with

uncompensated heart failure and/or unstable coronary function were excluded. Consenting participants allocated to the intervention group were followed prospectively every month for 18 months after inclusion.

LAST was approved by the Regional Committee of Medical and Health Research Ethics (REC no. 2011/1427), and registered with ClinicalTrials.gov (no. NCT01467206).

Intervention

Additional to standard care in line with the Norwegian national guidelines,[14] participants randomized to the intervention group received a follow-up program delivered by the primary health care services in three Norwegian municipalities.[15] The intervention comprised individualized coaching on physical activity and exercise by a physiotherapist during 18 consecutive months. The main purpose of coaching was to motivate and encourage the participants to follow an individually adapted training program, with regular meetings between the participant and the physiotherapist once every month. During the first six months, the meetings were planned face-to-face, preferably at the participant's home. During the following six months, every second meeting could be a phone meeting if preferred, while four of the six meetings could be phone meetings in the final six months. In the meetings the physiotherapist would lead the conversation using elements from motivational interviewing technique.[16] Together, physiotherapist and participant reviewed and reassessed the content and progression of the planned training schedule. To reduce the risk of contamination of the intervention to the control group, only the intervention group was encouraged to report detailed information about physical activity and exercise. Setting and regular evaluation of goals were also part of the intervention and emphasized during follow-up.

Participants were encouraged to perform 30 minutes of physical activity seven days a week, in addition to 45-60 minutes of exercise once a week. Based on the individuals' preferences and goals, schedules with at least two alternatives for physical activity and two alternatives for exercise were set every month. Physical activity was defined as any physical movement that causes energy expenditure due to skeletal muscle contraction, in accordance with the World Health Organization's definition.[17] Examples of physical activities were walking, housework or gardening. Exercise was defined as planned, structured, repetitive and purposeful in the sense that its objective was improvement or maintenance of one or more components of physical fitness.[17] Participants were encouraged to aim at high intensity (i.e. a score of 15 to 17 on the 6-20 Borg scale[18]) during exercise. Hiking, swimming or bicycling were examples of exercise.

Baseline assessments

At inclusion, age, sex, living condition, type of stroke and medical history were recorded. Stroke severity was measured by the National Institutes of Health Stroke Scale (NIHSS),[19] functional dependency by mRS,[20] and cognitive function by the MMSE.[21]

Primary outcome

The primary outcome measure was the Motor Assessment Scale (MAS)[22,23] at 18-month follow-up. MAS evaluates functional tasks, scored on a scale from 0 to 48 (max),[24] and covers all basic motor functions, e.g. walking stairs and advanced hand functions.[22]

Secondary outcomes

Walking capacity was measured by the six-minute walk test (6MWT),[25] which quantifies the distance walked (m) during six minutes.[26,27]

Balance was assessed by Timed Up and Go test (TUG) and the Berg Balance Scale (BBS). TUG[28] assesses balance, functional mobility and risk of falling, measuring the time taken to rise from a chair, walk three meters, turn, walk back and sit down.[27] The BBS consists of 14 items, each rated on a five-point ordinal scale ranging from 0 (cannot perform the task) to 4 (independence), making the total scores within a range of 0 to 56.[29-31]

Self-perceived functional outcomes were measured by the Stroke Impact Scale 3.0 (SIS). SIS is a multidimensional self-reported measure, divided into eight subtests or domains, including four related to functional recovery.[26] The four domains included in the composite score were strength, hand function, mobility and activities of daily living/instrumental activities of daily living (ADL/IADL), each rated on a scale from 0 to 100 (max).[32]

Outcome measures were assessed both at inclusion and at 18-month follow-up, except BBS and SIS, which were assessed only at follow-up.

Adherence

Adherence was assessed by self-reports in standardized training diaries, in which participants were encouraged to report amounts of physical activity and exercise immediately after each training session. Additionally, the physiotherapists reported whether the participants had performed the training program in line with the agreement at each appointment, and an overall estimation of adherence was reported by the physiotherapists in standardized separate adherence forms.[13] Combining data from these measures made up the adherence measure.

Statistical analyses

Descriptive statistics included participants' demographics, clinical characteristics and functional outcomes both at inclusion and at 18-month follow-up. Results were presented as n (%) and mean (SD). For instrument scales with less than half of the items missing, the missing values were singly imputed using the expectation–maximization algorithm. The scores of participants who died in advance of the follow-up assessments were imputed as zero on all scales, except mRS (in which a score of 6 indicates death), TUG and the physical domains of SIS. Multiple imputation was used to impute all other missing values, with m=100 imputations as recommended by van Buuren.[12,33]

Participants performing at least 210 minutes of physical activity during a week (e.g. 30 minutes seven days), and at least 45 minutes of exercise, respectively, were defined as adherent to the treatment protocol. Weeks with reported amounts of physical activity or exercise below these limits were defined as non-adherent. Further, number of weeks adherent to physical activity and exercise, respectively, were accumulated as total sums during the follow-up. With four weeks within each month, the number of adherent weeks could possibly range from zero to 72 weeks. For those who died during follow-up or discontinued the intervention, observations until death or discontinuation were included in the further analyses.

Linear regression analyses were carried out with the functional outcome scores of MAS, 6MWT, TUG, BBS and the physical domains of SIS, all measured at 18-month follow-up, as dependent variables, one at a time. Covariates of primary interest were adherence to exercise, adherence to physical activity, and adherence to both. The regression analyses were carried out both unadjusted and adjusted for the following covariates, one at a time and simultaneously: age, sex, stroke severity as measured by mRS at inclusion, MMSE and the corresponding outcome variable score measured at baseline.

Two-sided P-values < 0.05 were considered statistically significant. Ninety-five percent confidence intervals (95% CI) were reported where relevant. Statistical analyses were carried out in IBM SPSS (version 24.0; IBM, Armonk, NY, USA) and Microsoft Excel 2010 for Windows (Microsoft, Redmond, WA, USA).

Results

Of the 380 participants enrolled in LAST, 186 (48.9%) were randomized to the intervention-arm and included in the present study (Figure 1). Forty-two (22.6%) participants discontinued the intervention, including nine (4.8%) participants who died during follow-up. In total, 144 participants received the allocated intervention. All participants were invited to the 18-month follow-up assessments, regardless of whether they had completed the intervention or not. Hence, a total of 153 participants were eligible for follow-up assessments at 18-months after inclusion. At follow-up, some participants did not perform the complete test procedure due to exhaustion, lack of capacity or inability to walk (i.e. n=130 assessed 6MWT, n=148 assessed TUG, n=152 assessed BBS, n=144 assessed SIS).

Mean age (SD) in the study sample was 71.7 (11.9) years and 82 (44.1%) were women (Table 1). Most participants (97.3%) suffered mild stroke with a score < 8 points on the NIHSS. Outcome measure scores at baseline and at 18-month follow-up (Table 2), reflected a relatively high level of functional capacity and recovery.

The mean (SD) number of weeks that participants were adherent to the combination of physical activity and exercise was 24.3 (21.3), ranging from zero to 69 weeks. Adherence to

physical activity was 33.4 (25.3) weeks and adherence to exercise was 36.9 (24.0) weeks, ranging from zero to 72 weeks. Details of participants' degree of adherence are reported elsewhere.[13]

Associations of adherence with primary outcome

Unadjusted, increasing adherence to physical activity and exercise studied both in combination and independently, were associated with increased motor function as measured by MAS ($p \leq 0.007$, Table 3-5). After adjustments for age, sex, mRS, MMSE and MAS score at baseline, the regression coefficient estimates (B) were slightly lower, but the associations between adherence and MAS remained statistically significant (Table 3-5).

Associations of adherence with secondary outcomes

Unadjusted for the covariates, adherence to physical activity and exercise combined was significantly associated with 6MWT, TUG, BBS and the physical domains of SIS (Table 3). When adjusted for the covariates, the estimates were slightly lower. In spite of this, the associations remained statistically significant, except for 6MWT ($p = 0.086$) (Table 3).

Unadjusted, adherence to physical activity and exercise, measured independently, was significantly associated with all of the secondary outcomes ($p \leq 0.007$), except for exercise in relation to SIS ($p = 0.155$) (Table 4, 5). The regression coefficient estimates (B) of adherence to physical activity or exercise were slightly lower after the adjustment of the covariates (Table 4, 5), except a slight increase in the estimates for adherence to exercise and TUG, BBS and SIS (Table 5).

Discussion

In line with the hypothesis, the main results indicated positive associations between adherence to a physical activity and exercise program and functional recovery after stroke. After adjustments for important influencing covariates, increased adherence to the combined measure of physical activity and exercise were significantly associated with improved motor function, balance and self-perceived functional outcomes at 18-month follow-up. Increased adherence to either physical activity or exercise, was also significantly associated with primary and secondary outcomes. A stronger association was found between adherence to physical activity and functional recovery, than between adherence to exercise and functional recovery. The present study is the first to show that better adherence to a physical activity and exercise program was associated with better functional recovery during a follow-up period of 18 months in a large cohort of community-dwelling older individuals after stroke.

The results of the present study support previous research that enhanced adherence is associated with improved stroke outcomes.[34] Duncan et al. (2002) reported that better adherence to post-stroke rehabilitation guidelines was associated with better physical functioning six months after stroke.[6] A comparable study by Micieli et al. (2002) indicated effect on survival and disability.[7] Later studies have confirmed that there is evidence for a dose-dependent relationship between intensity of rehabilitation therapies and functional recovery within the first six months after stroke, especially on walking ability, walking speed and extended ADL.[8-11]

In the present study, the statistically significant associations between adherence to physical activity and exercise and motor function may also be clinically meaningful. A 10% increase of the total MAS-score from baseline appears clinically meaningful, although no minimal clinically important difference of MAS-score is established for chronic stroke.[26] Based on the results of the present study, it would require an average of 26.0 weeks of adherence to physical activity, or an average of 36.3 weeks of adherence to exercise to achieve a clinical meaningful change of MAS-score (i.e. an increase of ≥ 4 points). Actually, only 40.3% of the participants achieved ≥ 26.0 weeks adherence to physical activity, and 55.9% achieved ≥ 36.3 weeks adherence to exercise. Furthermore, a difference in adherence to physical activity and exercise of, for instance, twenty weeks would change the MAS-score by 2.82 points (i.e. 0.141 points/week, table 3). This shows how different degrees of adherence may have large consequences for functional recovery at follow-up.

The associations between adherence to physical activity and functional recovery were stronger than the associations between adherence to exercise and functional recovery. This may be explained by the challenge of achieving high-intensity exercise within this patient population.[35] Previous results showed that only an average of 24% of the reported amount of exercise among participants in the intervention group of LAST reached high intensity as required per protocol.[13] It is to be expected that adherence to the exercise intensity was not sufficient to induce a cardiorespiratory effect that could reduce disability.[36] The low intensity levels may be explained by physical and psychological impairments, such as hemi-paretic gait, reduced balance, increased risk and fear of falling, post-stroke fatigue, lack of

277 motivation, depression or lower self-efficacy for exercise, which are common barriers to
278 vigorous exercise after stroke.[35,37]

279 Despite differences between adherence to physical activity and exercise, the findings support
280 that participants were capable of achieving clinically meaningful improvements in functional
281 recovery with increased levels of adherence over time. Considering that the potential for
282 motor recovery is highest within the first 3 months after stroke,[38] a strength of the present
283 study was that participants were included 10 to 16 weeks after the acute stroke. Consequently,
284 the improvements in function were gained after the phase of spontaneous recovery and early
285 rehabilitation. Nevertheless, a complex combination of factors seem to affect adherence to
286 physical activity and exercise after stroke, in particular in long-term stroke care.[4]
287 Unfortunately, these challenges are still getting little attention, both in research and in clinical
288 work.[5] Future interventions should address the modifiable factors that influence adherence to
289 physical activity and exercise, helping clinicians to identify individual barriers and facilitators
290 to physical activity in patients with stroke.[4]

291

292 **Study Limitations**

293 The design of the study does not allow conclusions about causality. Further, conclusions for
294 individuals with severe stroke cannot be drawn, because the study sample consisted of
295 participants mildly to moderately affected by stroke, and mainly with few limitations of
296 function.

297 Several participants may have reached ceiling effects for some of the functional outcome
298 measures, such as MAS and BBS. In addition, adherence was defined in a conservative way
299 (meaning that physical activity and exercise exceeding the recommendations by the treatment

protocol would be underestimated). This may have resulted in underestimation of the associations of adherence with functional recovery.

Bias related to self-reported data should also be regarded as a limitation,[39,40] although self-reports in training diaries seemed to have enhanced adherence, as predicted in the protocol.[15] It could also be discussed whether it was appropriate to adjust for the corresponding outcome variable scores at baseline. However, when unadjusted and adjusted estimates were similar, this strengthens the findings.

Conclusions

This study indicates evidence for both clinically and statistically significant associations between increased adherence to a physical activity and exercise program and improved functional recovery after mild to moderate stroke in long-term rehabilitation. This impact of adherence on patient outcomes, both in short and long-term follow-up, indicates that the development of interventions to enhance adherence should be given priority within this patient population. Dose-response studies would be needed to determine the relationship between the degree of adherence and to the amounts of physical activity and exercise in long-term rehabilitation after stroke.

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Figure legend:

Figure 1: Flow chart. MMSE, Mini-Mental State Examination; MAS, Motor Assessment Scale.

Table 1. Baseline demographics and clinical characteristics. Data are n (%) or mean (SD).

			Intervention group (N=186)
Demographics			
Age (years)			71.7 (11.9)
		<80	142 (76.3%)
		≥80	44 (23.7%)
Sex			
		Female	82 (44.1%)
		Male	104 (55.9%)
Living condition			
		Living with someone	130 (69.9%)
		Living alone	56 (30.1%)
MMSE			27.8 (2.3)
		≥25	164 (88.2%)
		<25	22 (11.8%)
Stroke characteristics			
Time from stroke (days)			111.3 (24.5)
Stroke type			
		Infarction,	172 (92.5%)
		Haemorrhage	14 (7.5%)
NIHSS			1.5 (2.3)
	Mild stroke	<8	181 (97.3%)
	Moderate stroke	8-16	5 (2.7%)
	Severe stroke	>16	0
mRS			1.45 (1.08)
		mRS=0	34 (18.3%)
		mRS=1	78 (41.9%)
		mRS=2	36 (19.3%)
		mRS=3	32 (17.3%)
		mRS=4	6 (3.2%)
Co-morbidity			
		Previous stroke	29 (15.6%)
		TIA	20 (10.8%)
		Hypertension	90 (48.4%)
		Myocardial infarction	19 (10.2%)
		Heart failure	3 (1.6%)
		Atrial fibrillation	32 (17.2%)
		Diabetes	25 (13.4%)
		Lung diseases	19 (10.2%)

MMSE, Mini-Mental State Examination; NIHSS, The National Institutes of Health Stroke Scale; mRS, Modified Rankin Scale; TIA, transient ischemic attack.

Table 2. Functional outcomes at inclusion and at 18-month follow-up, estimates based on MI (multiple imputation).

	Inclusion		18-month follow-up	
Intervention group	n	Mean (SE)	n	Mean (SE)
Instrument/Domain				
MAS (0-48), total sum	186	41.9 (0.5)	186	39.9 (0.9)
6MWT, distance in meters	186	391.1 (12.5)	186	371.6 (14.4)
TUG, time in seconds	186	12.3 (0.6)	186	19.5 (2.2)
BBS (0-56), total sum	N/A	N/A	186	46.5 (1.2)
SIS Muscle strength (0-100)	N/A	N/A	186	78.1 (3.2)
SIS Activities of daily living (0-100)	N/A	N/A	186	81.0 (2.3)
SIS Mobility (0-100)	N/A	N/A	186	81.0 (2.3)
SIS Hand function (0-100)	N/A	N/A	186	77.8 (3.1)
SIS aggregate physical dimension score (0-100)	N/A	N/A	186	79.5 (2.0)

SE, Standard error; MAS, Motor Assessment Scale; 6MWT, Six-minute walk test; TUG, Timed Up and Go; BBS, Berg Balance Scale; SIS, Stroke Impact Scale. N/A indicates not applicable.

Table 3. Linear regression with functional outcomes as dependent variables and adherence to physical activity and exercise combined as primary covariate, unadjusted and adjusted for additional covariates. Based on MI (multiple imputation).

	MAS score (n=186)			6MWT (n=186)			TUG (n=186)			BBS (n=186)			SIS Physical Domain (n=186)		
Unadjusted	B	CI	P	B	CI	P	B	CI	P	B	CI	P	B	CI	P
Intercept	36.489	33.907 to 39.070	<0.001	333.631	290.205 to 377.056	<0.001	25.674	18.938 to 32.410	<0.001	42.307	38.889 to 45.725	<0.001	74.561	68.061 to 81.062	<0.001
Adherence to physical activity and exercise, weeks	0.141	0.062 to 0.220	<0.001	1.564	0.254 to 2.875	0.019	-0.255	-0.442 to -0.068	0.008	0.172	0.068 to 0.276	0.001	0.203	0.033 to 0.373	0.019
Adjusted separately for															
Age	0.130	0.055 to 0.206	0.001	1.233	0.130 to 2.336	0.028	-0.230	-0.409 to -0.051	0.012	0.152	0.057 to 0.247	0.002	0.175	0.018 to 0.333	0.029
Sex	0.143	0.064 to 0.222	<0.001	1.636	0.356 to 2.916	0.012	-0.259	-0.446 to -0.072	0.007	0.175	0.071 to 0.279	0.001	0.209	0.041 to 0.378	0.015
mRS at baseline	0.134	0.061 to 0.207	<0.001	1.424	0.253 to 2.595	0.017	-0.243	-0.423 to -0.062	0.008	0.163	0.066 to 0.259	0.001	0.186	0.032 to 0.339	0.018
MMSE at baseline	0.143	0.064 to 0.222	<0.001	1.576	0.257 to 2.896	0.019	-0.262	-0.450 to -0.074	0.006	0.175	0.070 to 0.279	0.001	0.205	0.033 to 0.376	0.020
Outcome variable score at baseline	0.112	0.036 to 0.187	0.004	0.794	-0.156 to 1.744	0.101	-0.216	-0.395 to -0.037	0.018	N/A	N/A	N/A	N/A	N/A	N/A
Adjusted for all	0.118	0.045 to 0.190	0.002	0.747	-0.106 to 1.599	0.086	-0.216	-0.391 to -0.041	0.015	0.148	0.057 to 0.239	0.001	0.167	0.021 to 0.314	0.026

B, Regression coefficient for adherence; CI, 95% confidence interval; P, P-value. The dependent variables are MAS, Motor Assessment Scale (0 to 48); 6MWT, Six-minute walk test; TUG, Timed Up and Go; BBS, Berg Balance Scale (0 to 56); SIS, Stroke Impact Scale (0 to 100). N/A indicates not applicable.

Table 4. Linear regression with functional outcomes as dependent variables and adherence to physical activity as primary covariate, unadjusted and adjusted for additional covariates. Based on MI (multiple imputation).

	MAS score (n=186)			6MWT (n=186)			TUG (n=186)			BBS (n=186)			SIS Physical Domain (n=186)		
Unadjusted	B	CI	P	B	CI	P	B	CI	P	B	CI	P	B	CI	P
Intercept	35.400	32.591 to 38.209	<0.001	308.149	261.090 to 355.207	<0.001	27.762	20.392 to 35.132	<0.001	40.693	36.976 to 44.410	<0.001	72.402	65.347 to 79.457	<0.001
Adherence to physical activity, weeks	0.136	0.069 to 0.202	<0.001	1.902	0.807 to 2.997	0.001	-0.248	-0.407 to -0.089	0.002	0.173	0.086 to 0.261	<0.001	0.212	0.069 o 0.356	0.004
Adjusted separately for															
Age[1]	0.129	0.065 to 0.192	<0.001	1.704	0.787 to 2.621	<0.001	-0.233	-0.385 to -0.081	0.003	0.161	0.082 to 0.241	<0.001	0.196	0.062 to 0.329	0.004
Sex[1]	0.138	0.071 to 0.204	<0.001	1.995	0.927 to 3.062	<0.001	-0.254	-0.412 to -0.095	0.002	0.178	0.091 to 0.265	<0.001	0.221	0.078 to 0.363	0.002
mRS at baseline[1]	0.121	0.059 to 0.183	<0.001	1.624	0.639 to 2.608	0.001	-0.224	-0.378 to -0.069	0.005	0.155	0.073 to 0.237	<0.001	0.178	0.047 to 0.308	0.008
MMSE at baseline[1]	0.136	0.069 to 0.202	<0.001	1.902	0.805 to 2.999	0.001	-0.248	-0.408 to -0.089	0.002	0.174	0.086 to 0.261	<0.001	0.212	0.069 to 0.356	0.004
Outcome variable score at baseline[1]	0.105	0.041 to 0.169	0.001	0.788	-0.031 to 1.606	0.059	-0.199	-0.353 to -0.045	0.011	N/A	N/A	N/A	N/A	N/A	N/A
Adjusted for all	0.109	0.048 to 0.171	<0.001	0.905	0.172 to 1.638	0.016	-0.199	-0.349 to -0.049	0.010	0.148	0.072 to 0.225	<0.001	0.171	0.047 to 0.296	0.007

B, Regression coefficient for adherence; CI, 95% confidence interval; P, P-value. The dependent variables are MAS, Motor Assessment Scale (0 to 48); 6MWT, Six-minute walk test; TUG, Timed Up and Go; BBS, Berg Balance Scale (0 to 56); SIS, Stroke Impact Scale (0 to 100). N/A indicates not applicable.

Table 5. Linear regression with functional outcomes as dependent variables and adherence to exercise as primary covariate, unadjusted and adjusted for additional covariates. Based on MI (multiple imputation).

	MAS score (n=186)			6MWT (n=186)			TUG (n=186)			BBS (n=186)			SIS Physical Domain (n=186)		
Unadjusted	B	CI	P	B	CI	P	B	CI	P	B	CI	P	B	CI	P
Intercept	36.255	33.055 to 39.455	<0.001	323.561	270.443 to 376.680	<0.001	26.997	18.512 to 35.482	<0.001	41.367	37.151 to 45.583	<0.001	75.158	66.958 to 83.358	<0.001
Adherence to exercise, weeks	0.100	0.028 to 0.171	0.007	1.303	0.123 to 2.484	0.031	-0.204	-0.379 to -0.028	0.023	0.139	0.044 to 0.233	0.004	0.117	-0.044 to 0.279	0.155
Adjusted separately for															
Age[1]	0.088	0.019 to 0.157	0.012	0.971	-0.057 to 1.970	0.057	-0.179	-0.347 to -0.011	0.037	0.118	0.032 to 0.205	0.007	0.089	-0.062 to 0.240	0.246
Sex[1]	0.099	0.027 to 0.171	0.007	1.274	0.118 to 2.430	0.031	-0.202	-0.378 to -0.027	0.024	0.138	0.043 to 0.232	0.004	0.155	-0.046 to 0.275	0.160
mRS at baseline[1]	0.122	0.058 to 0.189	<0.001	1.739	0.690 to 2.789	0.001	-0.244	-0.413 to -0.075	0.005	0.169	0.082 to 0.256	<0.001	0.171	0.022 to 0.320	0.025
MMSE at baseline[1]	0.100	0.028 to 0.173	0.006	1.309	0.123 to 2.496	0.031	-0.208	-0.384 to -0.032	0.020	0.140	0.046 to 0.235	0.004	0.118	-0.045 to 0.281	0.155
Outcome variable score at baseline[1]	0.106	0.040 to 0.173	0.002	0.846	-0.008 to 1.700	0.052	-0.225	-0.392 to -0.059	0.008	N/A	N/A	N/A	N/A	N/A	N/A
Adjusted for all	0.110	0.045 to 0.175	0.001	0.878	0.100 to 1.656	0.027	-0.225	-0.388 to -0.062	0.007	0.149	0.066 to 0.231	<0.001	0.142	0.000 to 0.285	0.050

B, Regression coefficient for adherence; CI, 95% confidence interval; P, P-value. The dependent variables are MAS, Motor Assessment Scale (0 to 48); 6MWT, Six-minute walk test; TUG, Timed Up and Go; BBS, Berg Balance Scale (0 to 56); SIS, Stroke Impact Scale (0 to 100). N/A indicates not applicable.

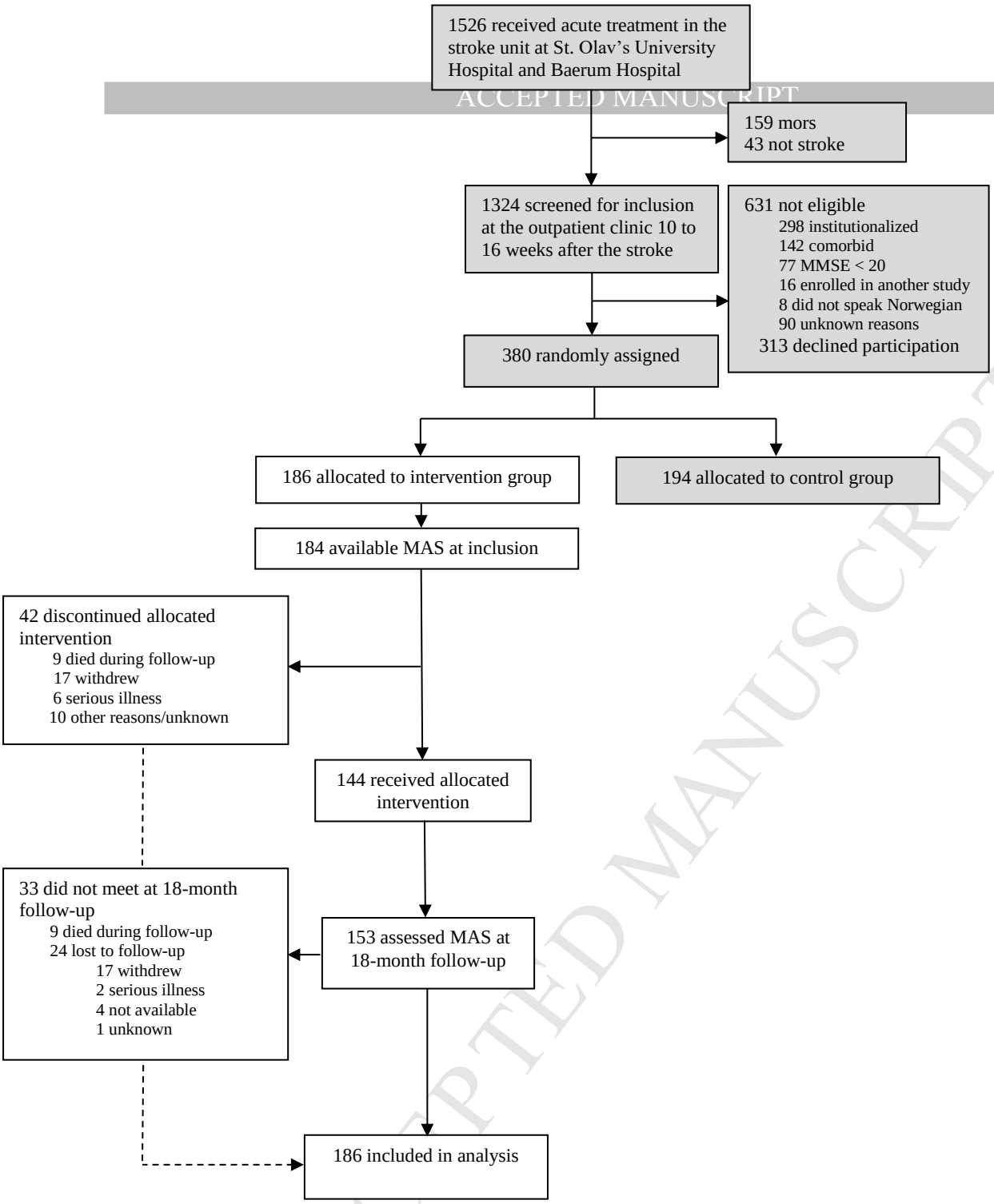

Figure 1: Flow chart