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Factors associated with changes in walking performance in individuals three months after stroke or TIA—secondary analyses from a randomized controlled trial of SMSdelivered training instructions

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1	Factors associated with changes in walking performance in individuals
2	three months after stroke or TIA—secondary analyses from a randomized
3	controlled trial of SMS-delivered training instructions
4	Short title: Predicting changes in walking performance three months after recent stroke and
5	TIA
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Objectives: To identify factors related to changes in walking performance in individuals 3
months after a stroke or TIA.

Design: Cross-sectional study with post-hoc analysis of a randomized controlled study.

Setting: University Hospital, Sweden.

Participants: 79 individuals, 64 (10) years, 37% women, who were acutely hospitalized
because of stroke or TIA between November 2016 and December 2018. Inclusion criteria
were patients aged 18 or above and the major eligibility criteria were the ability to perform
the 6-Minute Walking Test (6MWT, meters).

Intervention: The intervention group received standard care plus daily mobile phone text
messages (SMS) with instructions to perform regular outdoor walking and functional leg
exercises in combination with step counting and training diaries. The control group received
standard care.

Outcome measures: Multivariate analysis was performed and age, sex, group allocation,
comorbidity, baseline 6MWT, BMI, cognition, and chair-stand tests were entered as possible
determinants for changes in 6MWT.

Results: Multiple regression analyses showed that age (Standardized Beta -0.33, 95% CI -3.843to -1.05, P < 0.001), sex (-0.25, 95% CI -68.8 to -10.6, P = 0.008), comorbidity (-0.15, 95%44CI -53.7 to 6.4, P = 0.12), baseline BMI (-0.28, 95% CI -7.8 to -1.6, P = 0.004), baseline456MWT (-0.56, 95% CI -0.5 to -0.3, P < 0.001), and possibly allocation to the SMS group46(0.17, 95% CI -2.0 to 52.1, P = 0.07) were associated with changes in 6MWT three months47after the stroke event. The regression model described 38% of the variance in changes in486MWT

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Conclusions: Post-hoc regression analyses indicated that younger age, male sex, 49 comorbidity, lower BMI, shorter 6MWT at baseline, and allocation to the SMS group 50 contributed to improvement in walking performance at three months in patients with a recent 51 stroke or TIA. These factors may be important when planning SMS or similar rehabilitation 52 services. 53 54 55 Keywords: stroke, risk factors, rehabilitation medicine, clinical trial 56 Clinical Trial Registry: Clinical Trial.gov, number NCT02902367 57 58 STRENGTHS AND LIMITATIONS OF THIS STUDY 59 Study data were drawn from a randomized controlled trial and we used established outcome 60 61 measures. 62 The study design calls for precaution with causal inferences. Our findings cannot be generalized to more disabled community-living individuals after a 63 stroke or to individuals with chronic stroke. 64 The study is relatively small, making the study prone to bias, and all patients are from a 65 66 single center in Sweden, therefore reducing the generalizability of the results. 67 68 69 70

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72	Introduction
73	Approximately three out of four stroke incidents can be attributed to behavioral risk factors-
74	for example, unhealthy diets and sedentary lifestyles (1, 2). Individuals after a stroke are
75	predisposed to functional limitations and a sedentary lifestyle, contributing to the risk of
76	recurrent stroke or cardiovascular complications (1, 3).
77	
78	Outdoor walking is cost-effective and generally easy to perform. A review showed an
79	average of 4000 steps in the chronic phase after stroke, which is far below the recommended
80	10,000 steps a day to meet the guidelines for physical activity (3, 4). In high-functioning
81	individuals with stroke, physical activity including walking is low, although we know that
82	walking after discharge from the hospital is important for secondary prevention, minimizing
83	disability, and promoting long-term metabolic health (5). Actions to increase walking
84	performance soon after a stroke or TIA are needed.
85	
86	In the STROKEWALK study, a previously-reported randomized controlled trial, we found
87	that individuals receiving text messages for three months after stroke and TIA coupled with
88	add-on interventions using a training diary and step counts improved walking and chair-rising
89	performance (6). The present study aims to further study how various baseline characteristics
90	including cardio-metabolic risk markers and group assignment relate to changes in the 6-
91	minute walk test (6MWT), using secondary analyses of data from the STROKEWALK study.
92	
93	Methods

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94 Study design

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This is a post-hoc analysis of the STROKEWALK randomized controlled study performed at
the Uppsala University Hospital in Sweden. Determination of sample size, recruitment, data
collection, and random allocation procedures have been previously described in detail (6).
Ethical approval was obtained from the regional Ethical Review Board of Uppsala University
Hospital, Sweden: Dnr: 2015/550. The present study report follows the Strengthening the
Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting
cross-sectional studies (7) and written consent was obtained from all participants.

Recruitment was initiated in November 2016, and the last three-month follow-up assessment was performed in December 2018. Included were participants aged 18 or above with TIA or verified stroke (infarction or intracerebral hemorrhage with first or recurrent event) with sufficient cognition (Montreal Cognitive Assessment scale, MoCA \geq 26 points), general disability (modified Rankin Scale ≥ 2), and good enough walking performance; i.e., ability to perform the six-minute walking test (with or without a walking aid) (6). The exclusion criteria were known subarachnoid hemorrhage, medical problems such as uncontrolled hypertension, untreated arrhythmias, unstable cardiovascular conditions, a dementia diagnosis, severe aphasia, severe psychiatric problems, or cognitive impairment with difficulties understanding instructions (6).

113 Study outcomes

114 The 6MWT was used to measure the maximal walking distance during 6 minutes over a
115 30 -meter course. Changes are described as differences in walking distance at three
116 months(8). The modified Rankin scale was used to assess general disability and is scored
117 from 0 (no symptoms) to 6 (dead) (9). Cognitive function at baseline was assessed using the

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Montreal Cognitive Assessment scale (0–30 points),(10) with a higher value indicating better function. The Charlson Comorbidity Index (CCI) was used to classify comorbid conditions (11).

For the chair-stand test, the participant was instructed to rise from a seated position without support as quickly as possible five times in a row (12). The tests were performed with standardized instructions from the Short Physical Performance Battery. The 10-meter walk test was used to measure comfortable walking speed (13).

From the patient's medical records, cardio-metabolic biochemical risk factors such as total, LDL, and HDL cholesterol, C-reactive protein (CRP), and triglycerides were analyzed at hospital admission and diagnoses such as diabetes, hypertension, hypercholesterolemia, and cardiac heart failure were registered (14). Biochemical analyses were performed by accredited methods of the Clinical Chemistry Laboratory at the Uppsala University Hospital, Uppsala. Glycated hemoglobin (HbA1C) was analyzed using non-fasting venous blood samples.

The last registration of supine blood pressure was recorded manually before discharge from the hospital. Smoking and education levels were assessed by yes or no answers to the questions: 'Are you a smoker at this time of your life?' and 'Do you have a university degree?' Body mass index was calculated as body weight (kg) divided by height (m) squared. Weight was recorded with participants wearing light indoor clothing. Height was measured to the nearest cm. A hip-mounted pedometer at weeks 1 and 12 was used for daily step count by individuals in the SMS group (Yamax, SW-200).

The SMS intervention group

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The SMS-intervention group received daily text SMS (no cost for the participants) as an addition to standard care with simple instructions on what and how to exercise for three months. The intervention in the SMS-group was comprised of three different strategies: 1) three months of daily SMS-text messages, 2) training diaries, and 3) pedometers for step counts for the first and last week of intervention (6). The text messages gave instructions on how to exercise to increase walking endurance and strength of the lower body, without the possibility to text back for help or advice.

The control group

Patients in the control group were given standard stroke unit care. They had no restrictions
regarding physical activity, exercise, or taking part in rehabilitation services, and were given
standard recommendations. The control group did not use pedometers since it was considered
to be a part of the intervention.

154 Statistics

In the STROKEWALK study, a sample size of 80 individuals (including a possible drop-out rate of 20%) was determined to provide secure power to detect a 34-meter clinically relevant mean difference in the 6-minute walking test (6). An intention-to-treat analysis was applied for all missing values (dropouts), and the change was assumed to be zero. Thus, follow-up data for dropouts were registered with a baseline carry-forward approach. Descriptive data are reported as means (SD) and medians (IQR). According to the histogram, normal Q-Q plots, and the Kolmogorov–Smirnov test, data on changes in 6MWT were normally distributed. Case-wise diagnostics and standardized residuals were used to identify potential outliers. The Chi-square test, Mann-Whitney U-test, and the student's independent test were used to examine baseline differences between those improved at \geq 34 meters or <34 meters in 6MWT.

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2 3 4	166	
5 6	167	In the regression analyses, explanatory variables for changes in 6MWT were first identified
7 8 9	168	by correlation and univariate regression analyses ($P < 0.05$). Correlation strength was
10 11	169	calculated using Spearman's rho or a Pearson correlation. The identified variables were
12 13	170	checked for multi-collinearity by correlation analysis and cross-tabulation and if the
14 15	171	correlation coefficient was 0.80 or more the variable with the lowest r in relation to the
16 17 18	172	dependent variable was omitted from further regression analysis. The baseline 10-meter walk
19 20	173	test was omitted from further analyses due to multi-collinearity. Multiple linear regression
21 22	174	analyses were then conducted with the remaining variables to discover which had the greatest
23 24 25	175	impact on changes in walking performance. The ordinal explanatory variable Charlson
26 27	176	Comorbidity Index was dichotomized and grouped to "no comorbidity" or "one or more than
28 29	177	one comorbidity". The ordinal explanatory variable Montreal Cognitive Assessment scale
30 31 32	178	was dichotomized and grouped to the cutoff score ≥ 26 points. Changes in 6MWT were used
33 34	179	as the dependent variable. We adjusted for age, sex, comorbidity and intervention or control
35 36	180	group allocation. Case-wise diagnostics showed that one individual could be considered an
37 38 39	181	outlier; i.e., with an increase in 6MWT of 365 meters, but were not omitted from further
40 41	182	analysis.
42 43	183	Statistical significance was set at a <i>P</i> value < 0.05. The Statistical Package for the Social
44 45	184	Sciences (SPSS), version 25, was used for the analyses (SPSS Inc., Chicago, IL, U.S.A.).
46 47 48	185	
49 50	186	Results
51 52	187	Seventy-nine patients with a mean age 63.9 (10.4) years, 29 women, mean BMI of 27.5 (4.5)
53 54 55	188	kg/m ² were enrolled and allocated to either SMS intervention ($n = 40$) or control group
56 57	189	(n = 39).(6) Assessments were performed with a median of five (IQR 6) days after stroke or
58 59		
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3 4	190	TIA and after three months. At baseline assessments, seven individuals temporarily used a
5 6 7	191	walking aid.
7 8 9	192	
10 11	193	Table 1 gives the clinical characteristics for all individuals at baseline and changes in 6MWT.
12 13	194	
14 15 16	195	Insert Table 1 about here
17 18	196	
19 20	197	At baseline, 27% of participants had a BMI \geq 30 (obesity), 43% had a BMI between 25 and
21 22 23	198	29.9 (overweight), and 30% had a BMI <25. In this study, all participants could perform the
23 24 25	199	6MWT on both occasions and no adverse advents occurred during testing. The mean 6MWT
26 27	200	was 480 (105) meters. At three months, the mean 6MWT was 523 (104) meters. The mean
28 29 30	201	change in 6MWT was 55 (71) and 33 (80) meters for the SMS and control groups,
30 31 32	202	respectively ($P = 0.2$). On average, the participants in the SMS group walked 6335 steps per
33 34	203	day in the first week of intervention and 8173 steps per day after three months, an increase of
35 36 27	204	29% (n =33).
37 38 39	205	
40 41	206	Linear regression analyses for identification of factors related to change in walking capacity
42 43	207	Table 2 show correlations of possible variables for the regression models.
44 45 46	208	
47 48	209	Insert Table 2 about here
49 50		
51 52 53	210	
54 55	211	The differences in walking performance were significantly associated in a univariate analysis
56 57	212	with baseline BMI and 6MWT at baseline (Table 3). After adjusting for age, sex,
58 59 60	213	comorbidity, and group assignment, the final model still included baseline 6MWT and BMI,

1 2		
3 4	214	which together with age, sex, and group assignment explained 38% of the variance (Table 3).
5 6	215	Younger individuals, men, the SMS intervention group, and those with lower baseline BMI
7 8 9	216	and shorter 6MWT at baseline were more likely to improve their walking performance.
10 11	217	
12 13	218	Insert Table 3 about here
14 15 16	219	
17 18 19	220	Discussion
20 21	221	In this post-hoc study, we showed in regression analyses that younger age, male sex, SMS
22 23	222	assignment, lower baseline BMI, and less distance walked in 6MWT significantly predicted
24 25 26	223	positive change in 6MWT three months after stroke or TIA.
27 28	224	In our study sample, those with higher age improved less in the 6MWT at three months.
29 30	225	Thus, our finding is in line with a general tendency to be less physically active at older ages
31 32 33	226	(14). Age-related physiological changes like reduced oxygen uptake capacity (VO_2 max),
34 35	227	changes in heart and lungs, loss of muscle mass and strength, more comorbidity, and
36 37	228	medications in older age may affect the intensity and ability to perform outdoor walking in
38 39 40	229	the present study(1, 15). However, each individual in this study could find their own
41 42	230	suggested intensity level by using the Borg scale.
43 44	231	
45 46 47	232	In the present study, about 70% of the participants had a BMI above 25. Higher BMI
47 48 49	233	predicted less improvement in walking distance as measured with the 6MWT. It can be
50 51	234	speculated that those with obesity also were sarcopenic; i.e., displayed sarcopenic obesity,
52 53	235	which is known to affect walking performance. However, we did not collect data on muscle
54 55 56	236	mass in this study. In our study sample, we found weight fluctuation in both directions after
57 58	237	three months, which might have affected the results (14). A deterioration in health might be
59 60	238	seen in individuals with high BMI due to difficulties being active in daily living. This study

indicates that individuals after a stroke and with obesity need help initiating lifestyle changesto increase physical activity.

In a longitudinal study of cardiovascular disease secondary prevention, an inverse association between walking speed and mortality was found; with a 53% reduction in mortality risk for those with the highest walking speed (3.8–6.2 km/h). In a longitudinal study of cardiovascular disease secondary prevention, an inverse association between walking speed and mortality was found; with a 53% reduction in mortality risk for those with the highest walking speed (3.8–6.2 km/h) (16). In contrast to the present study, the participants were all women, but they had a similar risk factor profile (16). Another cross-sectional study, using a population three months or longer after stroke found that balance as measured with Berg Balance Scale was a significant predictor of free-living walking activity, and explained 13% of the variance (17). In our selected sample of individuals with high motor functions at baseline, balance was not a major problem (6).

Fini et al. reported a mean of 4078 steps per day, six months or more after stroke.(18) The number of steps we found after the first week of SMS intervention in our sample with recent stroke and TIA is higher than that, averaging 6335 steps per day the first week of intervention and a further increase of 29% after three months. In older adults, a dose-response relationship has been observed for sedentary behavior, as well as between steps per day and mortality(19). Walking speed, steps, and distance can reflect functional status and health and is important for activities and community ambulation in daily life (13). Furthermore, this study sample included more males which could have an impact on the results since male sex was associated with greater improvement in walking performance. In a larger study (AVERT trial) with 2100 participants which examined factors associated with achievement of independent walking at three months after stroke, sex was not an associated factor (20).

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265	The reason why those that walked shorter distances at baseline improved the most is
266	unknown, but regression towards the mean cannot be excluded. Still, in those with the
267	poorest walking performance a smaller increase in steps may be sufficient to have a positive
268	impact on health (21). New epidemiological studies measuring physical activity with
269	accelerometers show that the positive effects of physical activity may have been
270	underestimated (21). A large prospective study indicated that up to 10,000 steps a day was
271	associated with a lower risk of cardiovascular incidence and mortality (21). Additional risk
272	reduction was also found with steps performed at a higher intensity and there was no
273	minimum threshold for the association between increasing steps per day with morbidity and
274	mortality (21). This can be used to motivate the least active individuals to increase their
275	outdoor walking and number of steps per day.
276	Limitations and strengths
277	Limitations and strengths

Limitations and strengths

Some methodological issues need to be addressed in this study. One limitation is that the study design calls for precaution with causal inferences. Another limitation is that our findings cannot be generalized to more disabled community-living individuals after a stroke or to individuals with chronic stroke. However, since we included participants at the hospital with different socio-economic statuses and educational backgrounds, we believe this sample to be representative of the acute stroke and TIA population with fewer motor deficits. Finally, the study is relatively small, making the study prone to bias, and all patients are from a single center in Sweden, therefore reducing the generalizability of the results.

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One strength of the present study is that study data were drawn from a randomized controlled trial and that we used established outcome measures.

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3 4	288	
5 6	289	Conclusion: In summary, younger age, male sex, comorbidity, lower BMI, shorter 6MWT at
7 8 9	290	baseline, and allocation to the SMS group contributed most to improvement in walking
10 11	291	performance in patients with a recent stroke or TIA. These factors may be important to
12 13	292	consider when planning SMS or similar rehabilitation services. Cost-effective and easy
14 15 16	293	delivered interventions for individuals with minor stroke or TIA still requires further targeted
17 18	294	research.
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Table 1. Baseline characteristics of all paratients with < 34 meters increase in the s	six-minute walking test.		<u> </u>	1	1
	Study population	Changes in the 6-m	r uses Enset inute walking fest an		
	Baseline	≥34 m (n=38)	4. Downloaded from tement Superieur (AB ted to text and data n (4. 4. 4. 4. 4. 4. 4. 4. 4. 4. 4. 4. 4. 4	P-value	Missing values, n (%)
Age, mean (SD)	63.9 (10.4)	61.9 (9.1)	65.7 (1 5	0.01	0
Female, n (%)	29 (36.7)	11 (28.9)	18 (4329) 1. 18 (4329) 1.	0.17	0
SMS group, n (%)	40 (50.6)	26 (65.0)	14 (35)	0.002	0
Control group, n (%)	39 (49.4)	12 (30.8)	27 (69 a)		
modified Rankin Scale, 0-2			27 (69%) similar technolog 5 (45.molog	0.47	0
0	11 (13.9)	6 (54.5)	5 (45.13) 1		
1	53 (67.1)	23 (43.4)	<u>ි වි වි</u>		
2	15 (19.0)	9 (60.0)	6 (40.0) g		
Diagnosis, n (%)			ce Bibliographique guidelines xhtml	0.70	0

			₁-2023- yright,		
Cerebral infarction	66 (83.5)	29 (50.9)	4 by copyright, inctuding 28 (491ding 5(55.6)		
Intracerebral hemorrhage	9 (11.4)	4 (44.4)	5(55 6)		
TIA	13 (16.5)	8 (61.5)	5 (38.83) S Ch		
Charlson Comorbidity Index, n (%)			5 (38.5) 4 March Enseignement 2024. Downloaded from 22 (466% and 400 19 (598 data 400 28 30 (57		0
No comorbidity	47 (59.5)	25 (53.2)	22 (468 spinog	0.27	
≥1	32 (40.5)	13 (40.6)	19 (5984 fro		
BMI, mean (SD)	27.5 (4.5)	26.55 (3.77)	28.39 (5 50) 28.39 (5 50)	0.14	0
Diabetes mellitus-2, yes n (%)	12 (15.2)	5 (13.2)		0.63	0
University studies, yes n (%)	40 (62)	16 (42.1)	24 (58) 5. ing	0.14	0
Non-smoking, n (%)	71 (90)	33 (86.8)	38 (92)	0.39	0
Step counts (SMS group), mean (SD)	6335 (2747)	6612 (2741)	5757 (2286)	0.61	3 (7
SGPALS, n (%)			June 14, 2 ar techno		0
Sedentary	11 (13.9)	6 (54.5)	5 (45 g) 225 a	0.47	
Light Physical Activity	53 (67.1)	23 (43.4)	30 (56.6) Agen		
Moderate/High Physical Activity	15 (19.0)	9 (60.0)	6 (40.0) Bibli		
P-HDL cholesterol, (mmol/l), mean (SD)	1.32 (0.39)	1.35 (0.45)	t/guidelines.xhtml	0.44	3 (3

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		BMJ Open	bmjopen-2023 1 by copyright,		
P-LDL cholesterol, (mmol/l), mean (SD)	3.16 (1.09)	3.18 (1.16)	3.13 (1.04)88 3.13 (1.04)88	0.86	3 (3.8)
P-Cholesterol, (mmol/l), mean (SD)	5.13 (1.20)	5.16 (1.30)	5.13 (1 to 2)	0.86	3 (3.8)
P-Triglycerides, (mmol/l), mean (SD)	1.35 (0.63)	1.20 (0.46)		0.03	3 (3.8)
P-HbA1C, mmol/mol), mean (SD)	38.0 (7.54)	37.73 (8.33)	38.26 (66/m D	0.47	3 (3.8)
P-C reactive protein (mg/L), mean (SD)	4.92 (19.40)	6.80 (27.80)		0.20	6 (7.6)
P-Creatinine (mmol/L), mean (SD)	85.12 (25.53)	90.80	78.97 (12,53)	0.11	2 (2.6)
SBP, (mm HG), mean (SD)	130.63 (16.56)	129.8 (16.17)	131.36 (1 3 89)	0.81	4 (5)
DBP, (mm HG), mean (SD)	76.08 (11.0)	79.17 (11.24)	73.23 (10.099	0.02	4 (5)

Abbreviations: BMI, body mass index, CRP, C-reactive protein; DBP, diastolic blood pressure; HbA1C, http://bmjopen.bmj.com/site/about/guidelines.xhtml Abbreviations: BMI, body mass index, CRP, C-reactive protein; DBP, diastolic blood pressure; HbA1C, ydated hemoglobin; HDL, high-

able 2. Correlation of the variables used in the regression models.	Change	P-value
	6-minute	
	walking test	
Age (years)	-0.203	0.07
Sex (female)	-0.127	0.26
Charlson Comorbidity Index (≥1 comorbidity)	-0.198	0.08
Group (SMS/control)	0.237*	0.036
BMI, (kg/m ²)	-225*	0.046
6-minute walking test, baseline (meters)	-0.38**	< 0.001
Chair-stand test, (seconds)	0.194	0.086
Montreal Cognitive Assessment, (≥26 points)	-0.034	0.78
Saltin Grimby Physical Activity Level Scale	Ch.	
Sedentary, light physical activity, moderate/high physical activity	0.078	0.49

BMJ Open Table 3. Univariate and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate and m and age, sex, group allocation, comorbidity, baseline BMI-, chair-stand test-, cognition-, and 6-minute wask test as explanatory variables in March 202 Enseigr pr uses rela individuals after stroke and TIA.

		Univariate	analysis		± ⊻ 0	tivariate analysis	
	Beta	Adjusted R	95% CI	P	ont Superior Beta and Beta and Beta and Beta and Beta and Beta and Beta and Beta and Beta	95% CI	P
	standardized	square					
Age, yrs	-203	0.029	-3.1 to 0.1	0.073		-3.8 to -1.05	< 0.001
Sex, female	-0.121	0.002	-54.4 to 16.4	0.29		-68.8 to -10.6	0.008
CCI, ≥1 comorbidity	-0.19	0.024	-63.8 to 4.9	0.09	e 0.15	-53.7 to 6.4	0.12
Group, SMS	0.145	0.008	-12.1 to 55.9	0.20	0.17 0.17 0.28	-2.0 to 52.1	0.07
BMI, kg/m ²	-0.225	0.038	-7.5 to -0.07	0.046	niar te un	-7.8 to -1.6	0.004
6-minute walk test, meters	-0.38	0.134	-0.4 to -0.1	<0.001	technol 2	-0.5 to -0.3	< 0.001
Abbreviations: CCI, Charlson C The adjusted R square for the m			e service; MoCA, Mo	ontreal Cognit	By e & ssessment Agence Bibliographique de l		

STROBE Statement-checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstrac
		(b) Provide in the abstract an informative and balanced summary of what was done
		and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment,
-		exposure, follow-up, and data collection
Participants	6	(a) Cohort study—Give the eligibility criteria, and the sources and methods of
		selection of participants. Describe methods of follow-up
		Case-control study—Give the eligibility criteria, and the sources and methods of
		case ascertainment and control selection. Give the rationale for the choice of cases
		and controls
		Cross-sectional study—Give the eligibility criteria, and the sources and methods of
		selection of participants
		(b) Cohort study—For matched studies, give matching criteria and number of
		exposed and unexposed
		Case-control study—For matched studies, give matching criteria and the number of
		controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effec
		modifiers. Give diagnostic criteria, if applicable
Data sources/	8*	For each variable of interest, give sources of data and details of methods of
measurement		assessment (measurement). Describe comparability of assessment methods if there
		is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable,
		describe which groupings were chosen and why
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding
		(b) Describe any methods used to examine subgroups and interactions
		(c) Explain how missing data were addressed
		(d) Cohort study—If applicable, explain how loss to follow-up was addressed
		Case-control study—If applicable, explain how matching of cases and controls was
		addressed
		Cross-sectional study—If applicable, describe analytical methods taking account of
		sampling strategy
		(<u>e</u>) Describe any sensitivity analyses
Continued on next page		

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Results		
Participants	13*	(a) Report numbers of individuals at each stage of study-eg numbers potentially eligible,
		examined for eligibility, confirmed eligible, included in the study, completing follow-up, and
		analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information
data		on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) Cohort study—Summarise follow-up time (eg, average and total amount)
Outcome data	15*	Cohort study—Report numbers of outcome events or summary measures over time
		Case-control study-Report numbers in each exposure category, or summary measures of
		exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their
		precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and
		why they were included
		(b) Report category boundaries when continuous variables were categorized
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful
		time period
Other analyses	17	Report other analyses done-eg analyses of subgroups and interactions, and sensitivity
		analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision.
		Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity
		of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other informati	on	
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable,
		for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Factors associated with changes in walking performance in individuals three months after stroke or TIA—secondary analyses from a randomized controlled trial of SMSdelivered training instructions in Sweden

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Primary Subject Heading :	Rehabilitation medicine
Secondary Subject Heading:	Neurology, Geriatric medicine, Public health
Keywords:	Stroke < NEUROLOGY, Risk Factors, REHABILITATION MEDICINE, Clinical Trial

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2 3 4	1	Factors associated with changes in walking performance in individuals
5 6 7	2	three months after stroke or TIA—secondary analyses from a randomized
7 8 9 10	3	controlled trial of SMS-delivered training instructions in Sweden
11 12 13	4	Short title: Predicting changes in walking performance three months after recent stroke and
14 15	5	TIA in Sweden.
16 17 18 19	6 7	Birgit Vahlberg , PhD, RPT, Department of Public Health and Caring Sciences, Geriatrics, Uppsala University, Uppsala.
20 21 22 23	8 9 10	Staffan Eriksson, PhD, RPT, Department of Public Health and Caring Sciences, Geriatrics, Uppsala University, Uppsala; Centre for Clinical Research, Sörmland, Uppsala University, Eskilstuna.
24 25 26	11 12	Ulf Holmbäck, Associate Professor, Nutritionist, Department of Public Health and Caring Sciences, Clinical Nutrition and Metabolism, Uppsala University, Uppsala.
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47 48	23	
49 50	24	
51	25	Word count main text: 3433
52 53	26	
54 55	27	Keywords: stroke, risk factors, rehabilitation medicine, clinical trial
56 57	28	
58 59 60	29	

Objectives: To identify factors related to changes in walking performance in individuals 3
months after a stroke or TIA.

Design: Cross-sectional study with post-hoc analysis of a randomized controlled study.

34 Setting: University Hospital, Sweden.

Participants: 79 individuals, 64 (10) years, 37% women, who were acutely hospitalized
because of stroke or TIA between November 2016 and December 2018. Inclusion criteria
were patients aged 18 or above and the major eligibility criteria were the ability to perform
the 6-minute walking test.

39 Intervention: The intervention group received standard care plus daily mobile phone text
40 messages (SMS) with instructions to perform regular outdoor walking and functional leg
41 exercises in combination with step counting and training diaries. The control group received
42 standard care.

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43 Outcome measures: Multivariate analysis was performed and age, sex, group allocation,
44 comorbidity, baseline 6-minute walk test, BMI, cognition, and chair-stand tests were entered
45 as possible determinants for changes in the 6-minute walk test.

46 Results: Multiple regression analyses showed that age (Standardized Beta -0.33, 95% CI
47 -3.8 to -1.05, P<0.001), sex (-0.24, 95% CI -66.9 to -8.0, P = 0.014), no comorbidity
48 (-0.16, 95% CI -55.5 to 5.4, P = 0.12), baseline BMI (-0.29, 95% CI -8.1 to -1.6, P = 0.004),
49 baseline 6-minute walk test (-0.55, 95% CI -0.5 to -0.3, P <0.001) were associated with
50 changes in 6-minute walk test three months after the stroke event. The regression model

51 described 36% of the variance in changes in the 6-minute walk test.

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3 4	52	Conclusions: Post-hoc regression analyses indicated that younger age, male sex, lower BMI,
5 6 7	53	and shorter 6-minute walk test at baseline and possible no comorbidity contributed to
8 9	54	improvement in walking performance at three months in patients with a recent stroke or TIA.
10 11	55	These factors may be important when planning secondary prevention actions.
12 13 14	56	
15 16	57	Clinical Trial Registry: ClinicalTrial.gov, number NCT02902367
17 18 19	58	
20 21 22	59	STRENGTHS AND LIMITATIONS OF THIS STUDY
23 24	60	Study data were drawn from a randomized controlled trial and we used established outcome
25 26 27	61	measures.
28 29	62	The study design calls for precaution with causal inferences.
30 31 32	63	Our findings cannot be generalized to more disabled community-living individuals after a
33 34 35	64	stroke or to individuals with chronic stroke.
36 37	65	The study is relatively small, making the study prone to bias, and all patients are from a
38 39 40	66	single center in Sweden, therefore reducing the generalizability of the results.
41 42 43	67	
44 45 46	68	
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Introduction

Approximately three out of four stroke incidents can be attributed to behavioral risk factors— for example, unhealthy diets and sedentary lifestyles including low levels of physical activity (PA) (1, 2). Individuals after a stroke are predisposed to functional limitations and a sedentary lifestyle, contributing to the risk of recurrent stroke or cardiovascular complications (1, 3).

Outdoor walking is cost-effective and generally easy to perform. A review showed an average of 4000 steps in the chronic phase after stroke, which is far below the recommended 10,000 steps a day to meet the guidelines for physical activity (3, 4). In high-functioning individuals with stroke, physical activity including walking is low, although we know that walking after discharge from the hospital is important for secondary prevention, minimizing disability, and promoting long-term metabolic health (5, 6). Walking ability and better balance are associated with higher PA levels in everyday life after stroke and lower mood is related to low PA in people with chronic stroke (6, 7). Hence, in the work with secondary prevention, actions to increase walking performance soon after a stroke or TIA are needed, and, in this work knowledge about factors associated with changes in walking distance is important (8). Both stroke and TIA indicate ongoing arteriosclerotic changes in the vessels that can lead to further cardiovascular events and PA is known to decrease the risk of stroke, TIA, and myocardial infarction (9-11). There is a lack of studies investigating changes in walking performance in high-functioning individuals soon after stroke and TIA, and the few studies tend to be conducted months after stroke with a narrow focus on physical functions, overlooking cognition and cardiometabolic risk markers (8, 12).

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In the STROKEWALK study, a previously-reported randomized controlled trial, we found that individuals receiving text messages for three months after stroke and TIA coupled with add-on interventions using a training diary and step counts improved walking distance and chair-rising performance (13). The present study aims to further study how various baseline characteristics including cardio-metabolic risk markers relate to changes in the 6-minute walk test, using secondary analyses of data from the STROKEWALK study.

104 Methods

105 Study design

This is a post-hoc analysis of the STROKEWALK randomized controlled study performed at
the Uppsala University Hospital in Sweden. Determination of sample size, recruitment, data
collection, and random allocation procedures have been previously described in detail (13).
Ethical approval was obtained from the regional Ethical Review Board of Uppsala University
Hospital, Sweden: Dnr: 2015/550. The present study report follows the Strengthening the
Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting
cross-sectional studies (14) and written consent was obtained from all participants.

Recruitment was initiated in November 2016, and the last three-month follow-up assessment was performed in December 2018. Included were participants aged 18 or above with TIA or verified stroke (infarction or intracerebral hemorrhage with first or recurrent event) with sufficient cognition (Montreal Cognitive Assessment scale, MoCA \geq 26 points), general disability (modified Rankin Scale \geq 2), and good enough walking performance; i.e., ability to perform the six-minute walking test (with or without a walking aid) (13). The exclusion criteria were known subarachnoid hemorrhage, medical problems such as uncontrolled Page 7 of 25

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1 2		
3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24	121	hypertension, untreated arrhythmias, unstable cardiovascular conditions, a dementia
	122	diagnosis, severe aphasia, severe psychiatric problems, or cognitive impairment with
	123	difficulties understanding instructions (13).
	124	Study outcomes
	125	The 6-minute walk test was used to measure the maximal walking distance during six
	126	minutes over a 30-meter course. Changes are described as differences in walking distance at
	127	three months (13, 15).
	128	Baseline assessments
25 26 27	129	The modified Rankin scale was used to assess general disability and is scored from 0 (no
28 29	130	symptoms) to 6 (dead) (13, 16).
30 31 32 33	131	Cognitive function at baseline was assessed using the Montreal Cognitive Assessment scale
34 35	132	(0-30 points),(13, 17) with a higher value indicating better function.
33 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60	133	The Charlson Comorbidity Index (CCI) was used to classify comorbid conditions (13, 18).
	134	The last registration of supine blood pressure was recorded manually before discharge from
	135	the hospital. Smoking and education levels were assessed by yes or no answers to the
	136	questions: 'Are you a smoker at this time of your life?' and 'Do you have a university
	137	degree?' For the chair-stand test, the participant was instructed to rise from a seated position
	138	without support as quickly as possible five times in a row (13, 19). The test was performed
	139	with standardized instructions from the Short Physical Performance Battery (13, 20). The
	140	chair-stand test was a measure of lower body strength and the severity of the lower limb
	141	impairment.
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142 The 10-meter walk test was used to measure comfortable walking speed (13, 21).

From the patient's medical records, cardio-metabolic biochemical risk factors such as total,
LDL, and HDL cholesterol, C-reactive protein (CRP), and triglycerides were analyzed at
hospital admission and diagnoses such as diabetes, hypertension, hypercholesterolemia, and
cardiac heart failure were registered (22). Biochemical analyses were performed by
accredited methods of the Clinical Chemistry Laboratory at the Uppsala University Hospital,
Uppsala. Glycated hemoglobin (HbA1C) was analyzed using non-fasting venous blood
samples.

Body mass index was calculated as body weight (kg) divided by height (m) squared. Weight
was recorded with participants wearing light indoor clothing. Height was measured to the
nearest cm. A hip-mounted pedometer at weeks 1 and 12 was used for daily step count by
individuals in the SMS group (Yamax, SW-200).

Ter.

155 The SMS intervention group

The SMS-intervention group received daily text SMS (no cost for the participants) as an addition to standard care with simple instructions on what and how to exercise for three months. The intervention in the SMS group was comprised of three different strategies: 1) three months of daily SMS-text messages, 2) training diaries, and 3) pedometers for step counts for the first and last week of intervention (13). The text messages gave instructions on how to exercise to increase walking endurance and strength of the lower body, without the possibility of texting back for help or advice.

The control group

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Patients in the control group were given standard stroke unit care. They had no restrictions regarding physical activity, exercise, or taking part in rehabilitation services, and were given standard recommendations. The control group did not use pedometers since it was considered to be a part of the intervention.

Patient and Public Involvement Statement: A previous pilot study was conducted to test
the design of the randomized controlled trial. The intervention was designed in collaboration
between individuals with stroke and TIA, healthcare professionals, and researchers.

173 Statistics

In the STROKEWALK study, a sample size of 80 individuals (including a possible drop-out rate of 20%) was determined to provide secure power to detect a 34-meter clinically relevant mean difference in the 6-minute walking test (13). An intention-to-treat analysis was applied for all missing values (dropouts), and the change was assumed to be zero. Thus, follow-up data for dropouts were registered with a baseline carry-forward approach. Descriptive data are reported as means (SD) and medians (IQR). According to the histogram, normal Q-Q plots, and the Kolmogorov-Smirnov test, data on changes in the 6-minute walk test were normally distributed. Case-wise diagnostics and standardized residuals were used to identify potential outliers. Differences in step counts from baseline to three months for the SMS group were calculated with the Student's paired-sample t-test. Baseline differences between those that improved \geq 34 meters or <34 meters in the 6-minute walk test were assessed using the Student's t-test for continuous, normally distributed variables, and the Mann Whitney-U test was applied for ordinal or non-normally distributed variables. The Chi-square test was used for categorical variables. The cut-off of 34 meters was used for power analyses in the original study (13).

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In the regression analyses, baseline explanatory variables for changes in the 6-minute walk test were first identified by correlation and univariate regression analyses (P < 0.05). Correlation strength was calculated using Spearman's rho for non-parametric data or a Pearson correlation for continuous normally distributed variables. The identified variables were checked for multi-collinearity by correlation analysis and cross-tabulation and if the correlation coefficient was 0.80 or more the variable with the lowest r in relation to the dependent variable was omitted from further regression analysis. The baseline 10-meter walk test was omitted from further analyses due to multi-collinearity. Multiple linear regression analyses were then conducted with the remaining variables to discover which had the greatest impact on changes in walking performance. The ordinal explanatory variable Charlson Comorbidity Index was dichotomized and grouped into "no comorbidity" or "one or more than one comorbidity". The ordinal explanatory variable Montreal Cognitive Assessment scale was dichotomized and grouped to the cutoff score ≥ 26 points. Changes in 6MWT were used as the dependent variable. We adjusted for age, sex, and comorbidity. Case-wise diagnostics showed that one individual could be considered an outlier; i.e., with an increase in 6-minute walk test of 365 meters, but were not omitted from further analysis. In this study, a sensitivity analysis with complete case analyses was also carried out. The univariate and multivariate regression analyses were conducted leaving out subjects that dropped out from the study (n=8).

Statistical significance was set at a *P* value <0.05. The Statistical Package for the Social
Sciences (SPSS), version 28, was used for the analyses (SPSS Inc., Chicago, IL, U.S.A.).

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Results

212 Seventy-nine patients with a mean age of 63.9 (10.4) years, 29 women, mean BMI of 27.5 213 (4.5) kg/m² were enrolled and allocated to either SMS intervention (n = 40) or control group

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(n =39) (13). Assessments were performed with a median of five (IQR 6) days after stroke or
TIA and after three months. At baseline assessments, seven individuals temporarily used a
walking aid. A majority of the included individuals did not receive rehabilitation until the
measurement point of three months. Seventy-one individuals remained in the study at three
months and eight individuals had dropped out.

Table 1 gives the clinical characteristics for all individuals at baseline and changes in the 6-minute walk test.

222 ----Insert Table 1 about here---

At baseline, 27% of participants had a BMI \geq 30 (obesity), 43% had a BMI between 25 and 29.9 (overweight), and 30% had a BMI <25. In this study, all participants could perform the 6-minute walk test on both occasions and no adverse advents occurred during testing. At baseline, the median (IQR) 6-minute walk test was 478 (141) meters. At three months, the median 6-minute walk test was 538 (158) meters. The median (IOR) change in the 6-minute walk test after three months was 57 (63) and 23 (73) meters for the SMS and control groups, respectively (P = 0.037) (13). On average, the participants in the SMS group walked 6335 steps per day in the first week of intervention and 8173 steps per day after three months (P < 0.001), an increase of 29% (n = 33). Linear regression analyses for the identification of factors related to changes in walking capacity Table 2 shows correlations of possible variables for the regression models. ---Insert Table 2 about here---

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45 46	25
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49 50 51	25
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239	The differences in walking performance were significantly associated in a univariate analysis
240	with baseline BMI and the 6-minute walk test at baseline (Table 3). After adjusting for age,
241	sex, and comorbidity, the final model still included baseline 6MWT and BMI, which together
242	with age, sex, and no comorbidity explained 36% of the variance (Table 3). Younger
243	individuals, men, and those with no comorbidity, lower baseline BMI, and shorter 6-minute
244	walk test at baseline were more likely to improve their walking performance.
245	
246	Insert Table 3 about here
247	
248	The sensitivity analyses showed that BMI was no longer a strong predictor for changes in the
249	6-minute walk test in the complete case analyses (n=71). Thus, complete case analyses are
250	presented in Table 4.
251	
252	Insert Table 4 about here
253	
254	Discussion
255	In this post hoc study, we showed in regression analyses that younger age, male sex, no
256	comorbidity, lower baseline BMI, and less distance walked in 6-minute walk test
257	significantly predicted positive change in 6-minute walk test three months after stroke or
258	TIA.
259	In our study sample, those with higher age improved less in the 6-minute walk test at three
260	months. Thus, our finding is in line with a general tendency to be less physically active at
261	older ages (14). Age-related physiological changes like reduced oxygen uptake capacity (VO_2
262	max), changes in heart and lungs, loss of muscle mass and strength, more comorbidity, and

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3 4	263	medications in older age may affect the intensity and ability to perform outdoor walking in
5 6 7	264	the present study (1, 23). However, each individual in this study could find their own
7 8 9	265	suggested intensity level by using the Borg scale.
10 11	266	
12 13	267	In the present study, about 70% of the participants had a BMI above 25. Higher BMI
14 15 16	268	predicted less improvement in walking distance as measured with the 6-minute walk test. It
16 17 18	269	can be speculated that those with obesity also were sarcopenic; i.e., displayed sarcopenic
19 20	270	obesity, which is known to affect walking performance (23). In our study sample, we found
21 22	271	weight fluctuation in both directions after three months, which might have affected the results
23 24 25	272	(22). A deterioration in health might be seen in individuals with high BMI due to difficulties
26 27	273	being active in daily living. This study indicates that individuals after a stroke and with
28 29	274	obesity need help initiating lifestyle changes to increase physical activity.
30 31 32	275	In a longitudinal study of cardiovascular disease secondary prevention, an inverse association
33 34	276	between walking speed and mortality was found; with a 53% reduction in mortality risk for
35 36	277	those with the highest walking speed (3.8–6.2 km/h) (24). In contrast to the present study, the
37 38 20	278	participants were all women, but they had a similar risk factor profile (24). Another cross-
39 40 41	279	sectional study, using a population three months or longer after stroke found that balance as
42 43	280	measured with the Berg Balance Scale was a significant predictor of free-living walking
44 45	281	activity, and explained 13% of the variance (12). In our selected sample of individuals with
46 47 48	282	high motor functions at baseline, balance was not a major problem (13).
49 50 51	283	
52 53	284	Fini et al. reported a mean of 4078 steps per day, six months or more after stroke. (25) The
54 55 56	285	number of steps we found after the first week of SMS intervention in our sample with recent
56 57 58	286	stroke and TIA is higher than that, averaging 6335 steps per day the first week of intervention
59 60	287	and a further increase of 29% after three months. In older adults, a dose-response relationship

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has been observed for sedentary behavior, as well as between steps per day and mortality (26). Walking speed, steps, and distance can reflect functional status and health and are important for activities and community ambulation in daily life (21). Furthermore, this study sample included more males which could have an impact on the results since male sex was associated with greater improvement in walking performance. In contrast to this study with individuals walking independently at study start, gender did not affect the outcome of a larger study (AVERT trial) examining factors associated with walking recovery post-stroke (27).

The reason why those who walked shorter distances at baseline improved the most is unknown, but regression toward the mean cannot be excluded. Still, in those with the poorest walking performance, a smaller increase in steps may be sufficient to have a positive impact on health (28). New epidemiological studies measuring physical activity with accelerometers show that the positive effects of physical activity may have been underestimated (28). A large prospective study indicated that up to 10,000 steps a day were associated with a lower risk of cardiovascular incidence and mortality (28). Additional risk reduction was also found with steps performed at a higher intensity and there was no minimum threshold for the association between increasing steps per day with morbidity and mortality (28). This can be used to motivate the least active individuals to increase their outdoor walking and number of steps per day.

Limitations and strengths

Some methodological issues need to be addressed in this study. One limitation is that the study design calls for precaution with causal inferences. Another limitation is that our findings cannot be generalized to more disabled community-living individuals after a stroke

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3 4	312	or to individuals with chronic stroke. However, since we included participants at the hospital
5 6 7	313	with different socio-economic statuses and educational backgrounds, we believe this sample
7 8 9	314	to be representative of the acute stroke and TIA population with fewer motor deficits. Finally,
10 11	315	the study is relatively small, making the study prone to bias, and all patients are from a single
12 13 14	316	center in Sweden, therefore reducing the generalizability of the results.
15 16	317	One strength of the present study is that study data were drawn from a randomized controlled
17 18 19	318	trial and that we used established outcome measures.
20 21	319	
22 23	320	Conclusion: In summary, younger age, male sex, no comorbidity, lower BMI, and shorter 6-
24 25	321	minute walk test at baseline contributed most to improvement in walking performance in
26 27 28	322	patients with a recent stroke or TIA. These factors may be important when planning
29 30	323	secondary prevention actions. Cost-effective and easily delivered interventions for
31 32	324	individuals with minor stroke or TIA to increase walking distance still require further
33 34 35	325	targeted research.
36 37	326	
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University, Sweden. Contributors: This study was conceived, organized, and managed by BV, SE, UH, and EL. BV acts as a guarantor of the study. All authors listed above contributed to the study design and data interpretation. Writing of the first draft of the paper was done by BMV and all authors were involved in the preparation and critique of the manuscript and reviewed the paper before submission. Funding: This study was funded by the Medical Faculty at Uppsala University (grant number N/A), the Swedish National Stroke Association (Strokeförbundet) (grant number N/A), and the Geriatric Funding, Sweden (grant number N/A). Patient consent for publication: Not applicable. **Competing interests**: The author(s) report that there are no competing interests to declare. Ethics approval: This study involves human participants and was approved by the regional Ethical Review Board of Uppsala University Hospital, Sweden: Dnr: 2015/550. Data availability statement: The data set associated with this work is available from the corresponding author upon reasonable request.

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474						
475	Table 1. Baseline character	ristics of all patients in	the study with \geq	34 meters increa	se in the	
476	six-minute walking test at t	meters increase in	n the six-			
477	minute walking test. The St	tudent's t-test was use	d for continuous,	normally distrib	uted	
478	variables, and the Mann Wl	hitney-U test was app	lied for ordinal or	non-normally di	stributed	
479	variables. The Chi-square to	est was used for categ	orical variables.			
480						Missin
		Study	Changes in	the 6-minute		
		population	walki	ng test		
		6				Missin
		Baseline	≥34 m	<34 m		values
			(n=38)	(n=41)	P-value	values n (%)
-	mean (SD)	63.9 (10.4)	61.9 (9.1)	65.7 (11.2)	0.01	0
Femal	le, n (%)	29 (36.7)	11 (28.9)	18 (43.9)	0.17	0
SMS	group, n (%)	40 (50.6)	26 (65.0)	14 (35.0)	0.002	0
Contr	ol group, n (%)	39 (49.4)	12 (30.8)	27 (69.2)		
modif	ied Rankin Scale, 0-2				0.47	0
0		11 (13.9)	6 (54.5)	5 (45.5)		
1		53 (67.1)	23 (43.4)	30 (56.6)		
2		15 (19.0)	9 (60.0)	6 (40.0)		
Diagn	osis, n (%)				0.70	0
Ce	rebral infarction	66 (83.5)	29 (50.9)	28 (49.1)		
	racerebral hemorrhage	9 (11.4)	4 (44.4)	5(55.6)		
TL	Α	13 (16.5)	8 (61.5)	5 (38.5)		

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	Charlson Comorbidity Index, n (%)					
	No comorbidity	47 (59.5)	25 (53.2)	22 (46.8)	0.27	
	≥1	32 (40.5)	13 (40.6)	19 (59.4)		
-	BMI, mean (SD)	27.5 (4.5)	26.55 (3.77)	28.39 (5.03)	0.14	0
_	Diabetes mellitus-2, yes n (%)	12 (15.2)	5 (13.2)	7 (17.1)	0.63	0
	University studies, yes n (%)	40 (62)	16 (42.1)	24 (58.5)	0.14	0
_	Non-smoking, n (%)	71 (90)	33 (86.8)	38 (92.7)	0.39	0
_	Step counts (SMS group), mean (SD)	6335 (2747)	6612 (2741)	5757 (2786)	0.61	3 (7.5)
	SGPALS, n (%)	5			0.47	0 0 3 (7.5) 0
	Sedentary	11 (13.9)	6 (54.5)	5 (45.5)		
	Light Physical Activity	53 (67.1)	23 (43.4)	30 (56.6)		
	Moderate/High Physical Activity	15 (19.0)	9 (60.0)	6 (40.0)		
	P-HDL cholesterol, (mmol/l),	1.32 (0.39)	1.35 (0.45)	1.26 (0.32)	0.44	3 (3.8)
	mean (SD)		~			
	P-LDL cholesterol, (mmol/l), mean	3.16 (1.09)	3.18 (1.16)	3.13 (1.04)	0.86	3 (3.8)
	(SD)		L C			
	P-Cholesterol, (mmol/l), mean (SD)	5.13 (1.20)	5.16 (1.30)	5.13 (1.12)	0.86	3 (3.8)
_	P-Triglycerides, (mmol/l), mean (SD)	1.35 (0.63)	1.20 (0.46)	1.50 (0.74)	0.03	3 (3.8)
	P-HbA1C, mmol/mol), mean (SD)	38.0 (7.54)	37.73 (8.33)	38.26 (6.77)	0.47	3 (3.8)
	P-C reactive protein (mg/L), mean (SD)	4.92 (19.40)	6.80 (27.80)	3.20 (3.95)	0.20	6 (7.6)
	P-Creatinine (mmol/L), mean (SD)	85.12 (25.53)	90.80	78.97 (17.83)	0.11	2 (2.6)
	SBP, (mm HG), mean (SD)	130.63(16.56)	129.80 (16.17)	131.36 (17.09)	0.81	2 (2.6) 4 (5)
	DBP, (mm HG), mean (SD)	76.08 (11.0)	79.17 (11.24)	73.23 (10.09)	0.02	4 (5)

lipoprotein; SGPALS, Saltin Grimby Physical Activity Scale; SMS, short message service group; SBP, systolic blood pressure

Table 2. Correlation of the variables used in the regression models and changes in walking

performance. Correlation strength was calculated using Spearman's rho for non-parametric

data or Pearson correlation for continuous normally distributed variables.

	Change 6-minute walking test,	
	r	P-value
Age (years)	-0.39	< 0.001
Sex (female)	-0.13	0.26
CCI (≥1 comorbidity)	-0.20	0.08
BMI, (kg/m ²)	-0.23	0.046
6-minute walking test, baseline (meters)	-0.38	< 0.001
Chair-stand test, (seconds)	0.19	0.086
Montreal Cognitive Assessment scale, (≥26 points),	0.014	0.91
Saltin Grimby Physical Activity Level Scale		
(Sedentary, light physical activity, moderate/high physical activity)	0.078	0.49
Abbreviations: BMI, Body Mass Index; CCI, Charlson Comorbidity Index		

BMJ Open Table 3. Univariate and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate and m

and age, sex, comorbidity, baseline BMI-, and baseline 6-minute walk test as independent variables in indeviduals after stroke and TIA. An 4 March 202 Enseigr pr uses rela

493	intention-to-treat analysis was	performed with	n drop-outs included	(n=8).
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		Univariate analysis				Multivariate analysis		
	Beta	Adjusted	95% CI	Р	Beta	whipaded from to -1.0 text and data mining	Р	
	standardized	R square			standardized	ed from leur (Al d data		
Age, yrs	-20	0.029	-3.1 to 0.1	0.073	-0.33	mining	< 0.00	
Sex, female	-0.12	0.002	-54.4 to 16.4	0.29	-0.24	≥66 <u>∋</u> to -8.0	0.014	
CCI, ≥1 comorbidity	-0.19	0.024	-63.8 to 4.9	0.09	-0.16	ining, to 5.4	0.12	
BMI, kg/m ²	-0.23	0.038	-7.5 to -0.07	0.046	-0.29	a 8. 6 to -1.6	0.004	
6-minute walk test, meters	-0.38	0.134	-0.4 to -0.1	< 0.001	-0.55	similar to -0.3	< 0.00	
Abbreviations: BMI, Body M	Mass Index; CCI,	Charlson Corr	orbidity Index			e 14, chno		
The adjusted R square for th	e multivariate an	alysis is 0.36.				ıne 14, 2025 a technologies		
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BMJ Open **Table 4.** Sensitivity analysis: Univariate and multivariate regression analyses with changes in walking performance (6-minute walking test) as the dependent variable and age, sex, comorbidity, baseline BMI-, and baseline 6-minute walk test as independent variables in individuals after

stroke and TIA. In the sensitivity analysis, individuals with missing data at three months were not analyzed =8) relig

						464	
		Univariate	analysis		Mult	analysis	
	Beta	Adjusted	95% CI	Р	Beta	S I S I S I S I S I S I S I S I S I S I	Р
	standardized	R square			standardized	Superior Superior Superior (ABE) (AB	
Age, yrs	-0.25	0.05	-3.9 to -0.2	0.03	-0.33	1. 🛎	0.002
Sex, female	-0.11	-0.002	-57.5 to 20.8	0.35	-0.24	2.7 to -7.1	0.01
CCI, ≥1 comorbidity	-0.18	0.018	-66.6 to 9.7	0.14	-0.22	-67.4 to -2.6	0.03
BMI, kg/m ²	-0.21	0.031	-8.1 to 0.43	0.08		com/ op.56 to -0.26 -5.56 to -0.26 14, 2025 a	
6-minute walk test, meters	-0.42	0.16	-0.47 to -0.15	< 0.001	-0.55	-0.56 to -0.26	<0.00
Abbreviations: BMI, Body Mas	s Index; CCI, Cha	rlson Comort	oidity Index			- 14, J	
The adjusted R square for the m	ultivariate analysi	is is 0.34.				2025 at Agence Bibliographique de l	

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CONSORT CHECKLIST

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Section and Topic	ltem No.	Checklist Item	Reported on Page No
Title and abstract	110.	oneonist nem	ragenic
	1a	Identification as a randomized trial in the title	
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	
	2b	Specific objectives or hypotheses	
Methods Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	
That doolgin	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	
Participants	4a	Eligibility criteria for participants	
	4b	Settings and locations where the data were collected	
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	
Outcomes	6a	Completely defined prespecified primary and secondary outcome measures, including how and when they were assessed	
	6b	Any changes to trial outcomes after the trial commenced, with reasons	
Sample size	7a	How sample size was determined	
	7b	When applicable, explanation of any interim analyses and stopping guidelines	
Randomization			
Sequence generation	8a	Method used to generate the random allocation sequence	
	8b	Type of randomization; details of any restriction (such as blocking and block size)	
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	
Results Participant flow (a diagram is strongly	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analyzed for the primary outcome	
recommended)	13b	For each group, losses and exclusions after randomization, together with reasons	
Recruitment	14a	Dates defining the periods of recruitment and follow-up	
	14b	Why the trial ended or was stopped	
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	
Numbers analyzed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing prespecified from exploratory	
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	
Comment			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	
Generalizability	21	Generalizability (external validity, applicability) of the trial findings	
Interpretation Other information	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	
Registration	23	Registration number and name of trial registry	
Protocol	24	Where the full trial protocol can be accessed, if available	
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	
recommend reading CONSOF	RT extensi	atement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If rele ons for cluster randomized trials, noninferiority and equivalence trials, nonpharmacological treatments, herbal interventions, and pr for those and for up-to-date references relevant to this checklist, see http://www.consort-statement.org.	

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Factors associated with changes in walking performance in individuals three months after stroke or TIA—secondary analyses from a randomized controlled trial of SMSdelivered training instructions in Sweden

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2 3		
4 5	1	Factors associated with changes in walking performance in individuals
6 7	2	three months after stroke or TIA—secondary analyses from a randomized
8 9 10	3	controlled trial of SMS-delivered training instructions in Sweden
11 12 13	4	Short title: Predicting changes in walking performance three months after recent stroke and
14 15	5	TIA in Sweden.
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54 55 56	27	Keywords: stroke, risk factors, rehabilitation medicine, clinical trial
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59 60	29	

Objectives: To identify factors related to changes in walking performance in individuals 3
months after a stroke or TIA.

Design: Cross-sectional study with post-hoc analysis of a randomized controlled study.

34 Setting: University Hospital, Sweden.

Participants: 79 individuals, 64 (10) years, 37% women, who were acutely hospitalized
because of stroke or TIA between November 2016 and December 2018. Inclusion criteria
were patients aged 18 or above and the major eligibility criterion was the ability to perform
the 6-minute walking test.

39 Intervention: The intervention group received standard care plus daily mobile phone text
40 messages (SMS) with instructions to perform regular outdoor walking and functional leg
41 exercises in combination with step counting and training diaries. The control group received
42 standard care.

Outcome measures: Multivariate analysis was performed and age, sex, group allocation,
comorbidity, baseline 6-minute walk test, BMI, cognition, and chair-stand tests were entered
as possible determinants for changes in the 6-minute walk test.

46 Results: Multiple regression analyses showed that age (Standardized Beta -0.33, 95% CI
47 -3.8 to -1.05, P<0.001), sex (-0.24, 95% CI -66.9 to -8.0, P = 0.014), no comorbidity
48 (-0.16, 95% CI -55.5 to 5.4, P = 0.11), baseline BMI (-0.29, 95% CI -8.1 to -1.6, P = 0.004),

49 baseline 6-minute walk test (-0.55, 95% CI -0.5 to -0.3, P < 0.001) were associated with

50 changes in 6-minute walk test three months after the stroke event. The regression model

51 described 36% of the variance in changes in the 6-minute walk test.

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2 3 4	52	Conclusions: Post-hoc regression analyses indicated that younger age, male sex, lower BMI,
5 6 7	53	and shorter 6-minute walk test at baseline and possible no comorbidity contributed to
7 8 9	54	improvement in walking performance at three months in patients with a recent stroke or TIA.
10 11	55	These factors may be important when planning secondary prevention actions.
12 13 14	56	
15 16	57	Clinical Trial Registry: ClinicalTrial.gov, number NCT02902367
17 18 19	58	
20 21 22	59	STRENGTHS AND LIMITATIONS OF THIS STUDY
23 24	60	Study data were drawn from a randomized controlled trial and we used established outcome
25 26 27	61	measures.
28 29	62	The study design calls for precaution with causal inferences.
30 31 32	63	Our findings cannot be generalized to more disabled community-living individuals after a
33 34 35	64	stroke or to individuals with chronic stroke.
36 37	65	The study is relatively small, making the study prone to bias, and all patients are from a
38 39 40	66	single center in Sweden, reducing the generalizability of the results.
41 42 43	67	
44 45 46	68	
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73 Introduction

Approximately three out of four stroke incidents can be attributed to behavioral risk factors for example, unhealthy diets and low levels of physical activity (1, 2). Both stroke and TIA indicate ongoing arteriosclerotic changes in the vessels that can lead to further cardiovascular events (1, 2). Physical activity is known to decrease the risk of stroke, TIA, and myocardial infarction (3-5).

After a stroke, individuals are often predisposed to functional limitations, contributing to a further risk of recurrent stroke or cardiovascular complications (1, 6). Individuals who have suffered from a stroke take an average of 4000 steps a day in the chronic phase after stroke, which is far below the recommended 10,000 steps to meet the guidelines for physical activity (6, 7). Also, individuals with high function after a stroke limit their activity. Still, we know that even low-intensity physical activity, such as walking, is important for minimizing disability and promoting long-term metabolic health (8, 9). Outdoor walking is generally easy to perform. It is a cost-effective measure to address sedentary lifestyles and increase physical activity after stroke.

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Research demonstrates that the ability to walk longer distances and good balance correlates
with higher physical activity levels following a stroke (9, 10). Thus, interventions for
enhancing walking performance are of crucial importance for secondary prevention (11).
Metrics such as walking distance can be utilized as an indicator of the level of physical
activity after a stroke or TIA. In addition, understanding factors associated with improved
walking is also essential for developing targeted interventions.

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There is a lack of studies investigating changes in walking performance shortly following a stroke and TIA (11, 12). In the STROKEWALK study, a previously-reported randomized controlled trial, we found that individuals receiving text messages for three months after stroke and TIA coupled with add-on interventions using a training diary and step counts improved walking distance and chair-rising performance (13). The present study aims to further study how various baseline characteristics including cardio-metabolic risk markers relate to changes in the 6-minute walk test, using secondary analyses of data from the STROKEWALK study.

106 Methods

107 Study design

This is a post-hoc analysis of the STROKEWALK randomized controlled study performed at
the Uppsala University Hospital in Sweden. Determination of sample size, recruitment, data
collection, and random allocation procedures have been previously described in detail (13).
Ethical approval was obtained from the regional Ethical Review Board of Uppsala University
Hospital, Sweden: Dnr: 2015/550. The present study report follows the Strengthening the
Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting
cross-sectional studies (14) and written consent was obtained from all participants.

116 Recruitment was initiated in November 2016, and the last three-month follow-up assessment 117 was performed in December 2018. Included were participants aged 18 or above with TIA or 118 verified stroke (infarction or intracerebral hemorrhage with first or recurrent event) with 119 sufficient cognition (Montreal Cognitive Assessment scale, MoCA \geq 26 points), general 120 disability (modified Rankin Scale \geq 2), and good enough walking performance; i.e., ability to

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3 4	121	perform the six-minute walking test (with or without a walking aid) (13). The exclusion
5 6	122	criteria were known subarachnoid hemorrhage, medical problems such as uncontrolled
7 8	123	hypertension, untreated arrhythmias, unstable cardiovascular conditions, a dementia
9 10 11	124	diagnosis, severe aphasia, severe psychiatric problems, or cognitive impairment with
12 13	125	difficulties understanding instructions (13).
14 15	126	
16 17	120	
18 19 20	127	Study outcomes
21 22	128	The 6-minute walk test was used to measure the maximal walking distance during six
23	120	The o-minute wark test was used to measure the maximal warking distance during six
24 25	129	minutes over a 30-meter course. Changes are described as differences in walking distance at
26 27	130	three months (13, 15). All baseline data were collected on one occasion while the patients
28 29	131	were still treated at the hospital or the first days after discharge and after three months close
30 31 22	132	to the end of interventions.
32 33		
34 35	133	
36 37		
38 39	134	Baseline assessments
40		
41 42	135	All baseline data were collected on one occasion while the patients were still treated at the
43 44	136	hospital or the first days after discharge.
45 46		
47 48	137	The modified Rankin scale was used to assess general disability and is scored from 0 (no
49 50	138	symptoms) to 6 (dead) (13, 16).
51 52		
53 54	139	Cognitive function at baseline was assessed using the Montreal Cognitive Assessment scale
55 56	140	(0-30 points),(13, 17) with a higher value indicating better function.
57 58		
59 60	141	The Charlson Comorbidity Index (CCI) was used to classify comorbid conditions (13, 18).
50		

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The last registration of supine blood pressure was recorded manually before discharge from the hospital. Smoking and education levels were assessed by yes or no answers to the questions: 'Are you a smoker at this time of your life?' and 'Do you have a university degree?' For the chair-stand test, the participant was instructed to rise from a seated position without support as quickly as possible five times in a row (13, 19). The test was performed with standardized instructions from the Short Physical Performance Battery (13, 20). The chair-stand test was a measure of lower body strength and the severity of the lower limb impairment. The 10-meter walk test was used to measure comfortable walking speed (13, 21). From the patient's medical records, cardio-metabolic biochemical risk factors such as total, LDL, and HDL cholesterol, C-reactive protein (CRP), and triglycerides were analyzed at hospital admission and diagnoses such as diabetes, hypertension, hypercholesterolemia, and cardiac heart failure were registered (22). Biochemical analyses were performed by accredited methods of the Clinical Chemistry Laboratory at the Uppsala University Hospital, Uppsala. Glycated hemoglobin (HbA1C) was analyzed using non-fasting venous blood samples. Body mass index was calculated as body weight (kg) divided by height (m) squared. Weight was recorded with participants wearing light indoor clothing. Height was measured to the nearest cm. A hip-mounted pedometer at weeks 1 and 12 was used for daily step count by individuals in the SMS group (Yamax, SW-200). The SMS intervention group

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The SMS-intervention group received daily text SMS (no cost for the participants) as an addition to standard care with simple instructions on what and how to exercise for three months. The intervention in the SMS group was comprised of three different strategies: 1) three months of daily SMS-text messages, 2) training diaries, and 3) pedometers for step counts for the first and last week of intervention (13). The text messages gave instructions on how to exercise to increase walking endurance and strength of the lower body, without the possibility of texting back for help or advice. The control group Patients in the control group were given standard stroke unit care. They had no restrictions regarding physical activity, exercise, or taking part in rehabilitation services, and were given standard recommendations. The control group did not use pedometers since it was considered to be a part of the intervention. The number of individuals that were taking part in rehabilitation services during the study was not recorded. Patient and Public Involvement Statement: A previous pilot study was conducted to test the design of the randomized controlled trial. The intervention was designed in collaboration between individuals with stroke and TIA, healthcare professionals, and researchers. **Statistics** In the STROKEWALK study, a sample size of 80 individuals (including a possible drop-out rate of 20%) was determined to provide secure power to detect a 34-meter clinically relevant mean difference in the 6-minute walking test (13). An intention-to-treat analysis was applied for all missing values (dropouts), and the change was assumed to be zero. Thus, follow-up

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data for dropouts were registered with a baseline carry-forward approach. Descriptive data

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are reported as means (SD) and medians (IQR). According to the histogram, normal Q-Q plots, and the Kolmogorov-Smirnov test, data on changes in the 6-minute walk test were normally distributed. Case-wise diagnostics and standardized residuals were used to identify potential outliers. Differences in step counts from baseline to three months for the SMS group were calculated with the Student's paired-sample t-test. Baseline differences between those that improved \geq 34 meters or <34 meters in the 6-minute walk test were assessed using the Student's t-test for continuous, normally distributed variables, and the Mann Whitney-U test was applied for ordinal or non-normally distributed variables. The Chi-square test was used for categorical variables. The cut-off of 34 meters was used for power analyses in the original study (13). In the regression analyses, baseline explanatory variables for changes in the 6-minute walk test were first identified by correlation and univariate regression analyses (P < 0.05). Correlation strength was calculated using Spearman's rho for non-parametric data or a Pearson correlation for continuous normally distributed variables. The identified variables were checked for multi-collinearity by correlation analysis and cross-tabulation and if the correlation coefficient was 0.80 or more the variable with the lowest r in relation to the

dependent variable was omitted from further regression analysis. The baseline 10-meter walk test was omitted from further analyses due to multi-collinearity. Multiple linear regression analyses were then conducted with the remaining variables to discover which had the greatest impact on changes in walking performance. The ordinal explanatory variable Charlson Comorbidity Index was dichotomized and grouped into "no comorbidity" or "one or more than one comorbidity". The ordinal explanatory variable Montreal Cognitive Assessment scale was dichotomized and grouped to the cutoff score ≥ 26 points. Changes in the 6-minute walk test were used as the dependent variable. We adjusted for age, sex, and comorbidity. Case-wise diagnostics showed that one individual could be considered an outlier; i.e., with an

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3 4	214	increase in the 6-minute walk test of 365 meters, but were not omitted from further analysis.
5 6 7	215	In this study, a sensitivity analysis with complete case analyses was also carried out. The
, 8 9	216	univariate and multivariate regression analyses were conducted leaving out subjects that
10 11	217	dropped out from the study (n=8).
12 13 14	218	Statistical significance was set at a <i>P</i> value <0.05. The Statistical Package for the Social
15 16	219	Sciences (SPSS), version 28, was used for the analyses (SPSS Inc., Chicago, IL, U.S.A.).
17 18 10	220	
19 20 21	221	Results
22 23	222	Seventy-nine patients with a mean age of 63.9 (10.4) years, 29 women, mean BMI of 27.5
24 25 26	223	(4.5) kg/m ² were enrolled and allocated to either SMS intervention ($n = 40$) or control group
20 27 28	224	(n = 39) (13). Assessments were performed with a median of five (IQR 6) days after stroke or
29 30	225	TIA and after three months. At baseline assessments, seven individuals temporarily used a
31 32 33	226	walking aid. Seventy-one individuals remained in the study at three months and eight
34 35	227	individuals had dropped out.
36 37	228	Table 1 gives the clinical characteristics for all individuals at baseline and changes in the 6-
38 39	229	minute walk test.
40 41 42	230	
42 43 44	231	Insert Table 1 about here
45 46	232	
47 48 40	233	At baseline, 27% of participants had a BMI \geq 30 (obesity), 43% had a BMI between 25 and
49 50 51	234	29.9 (overweight), and 30% had a BMI <25. In this study, all participants could perform the
52 53	235	6-minute walk test on both occasions and no adverse advents occurred during testing. At
54 55 56	236	baseline, the median (IQR) 6-minute walk test was 478 (141) meters. At three months, the
57 58	237	median 6-minute walk test was 538 (158) meters. The median (IQR) change in the 6-minute
59 60	238	walk test after three months was 57 (63) and 23 (73) meters for the SMS and control groups,

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respectively and the SMS group showed a significantly greater increase in walking distance compared to the control group (P = 0.037) (13). On average, the participants in the SMS group walked 6335 steps per day in the first week of intervention and 8173 steps per day after three months (P < 0.001), an increase of 22.5% (n = 33). Linear regression analyses for the identification of factors related to changes in walking capacity Table 2 shows correlations of possible variables for the regression models. ---Insert Table 2 about here---The differences in walking performance were significantly associated in univariate analysis with baseline BMI and the 6-minute walk test at baseline (Table 3). After adjusting for age, sex, and comorbidity, the final model still included a baseline 6-minute walk test and BMI, which together with age, sex, and no comorbidity explained 36% of the variance (Table 3). Younger individuals, men, and those with no comorbidity, lower baseline BMI, and shorter 6-minute walk tests at baseline were more likely to improve their walking performance. ---Insert Table 3 about here---The sensitivity analyses showed that BMI was no longer a strong predictor for changes in the 6-minute walk test in the complete case analyses (n=71). Thus, complete case analyses are presented in Table 4.

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263 ----Insert Table 4 about here----

3 4	263	Insert Table 4 about here
5 6 7	264	
8 9 10 11 12 13 14 15 16 17 18 19 20 21	265	Discussion
	266	In this post hoc study, we showed in regression analyses that younger age, male sex, no
	267	comorbidity, lower baseline BMI, and less distance walked in 6-minute walk test
	268	significantly predicted positive change in 6-minute walk test three months after stroke or
	269	TIA.
	270	In our study sample, those with higher age improved less in the 6-minute walk test at three
22 23	271	months. Thus, our finding is in line with a general tendency to be less physically active at
24 25 26	272	older ages (14). Age-related physiological changes like reduced oxygen uptake capacity (VO_2
27 28 29 30 31 32 33 34 35	273	max), changes in heart and lungs, loss of muscle mass and strength, more comorbidity, and
	274	medications in older age may affect the intensity and ability to perform outdoor walking in
	275	the present study (1, 23). However, each individual in this study could find their own
	276	suggested intensity level by using the Borg scale.
36 37	277	
38 39 40 41 42	278	In the present study, about 70% of the participants had a BMI above 25. Higher BMI
	279	predicted less improvement in walking distance as measured with the 6-minute walk test. It
43 44	280	can be speculated that those with obesity also were sarcopenic; i.e., displayed sarcopenic
45 46 47	281	obesity, which is known to affect walking performance (23). In our study sample, we found
47 48 49	282	weight fluctuation in both directions after three months, which might have affected the results
50 51	283	(22). A deterioration in health might be seen in individuals with high BMI due to difficulties
52 53 54	284	being active in daily living. This study indicates that individuals after a stroke and with
54 55 56	285	obesity need help initiating lifestyle changes to increase physical activity.
57 58	286	In a longitudinal study of cardiovascular disease secondary prevention, an inverse association
59 60	287	between walking speed and mortality was found; with a 53% reduction in mortality risk for

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those with the highest walking speed (3.8–6.2 km/h) (24). In contrast to the present study, the participants were all women, but they had a similar risk factor profile (24). Another cross-sectional study, using a population three months or longer after stroke found that balance as measured with the Berg Balance Scale was a significant predictor of free-living walking activity, and explained 13% of the variance (12). In our selected sample of individuals with high motor functions at baseline, balance was not a major problem (13).

Fini et al. reported a mean of 4078 steps per day, six months or more after stroke. (25) The number of steps we found after the first week of SMS intervention in our sample with recent stroke and TIA is higher than that, averaging 6335 steps per day the first week of intervention and a further increase of 29% after three months. In older adults, a dose-response relationship has been observed for sedentary behavior, as well as between steps per day and mortality (26). Walking speed, steps, and distance can reflect functional status and health and are important for activities and community ambulation in daily life (21). Furthermore, this study sample included more males which could have an impact on the results since male sex was associated with greater improvement in walking performance. In contrast to this study with individuals walking independently at the study start, gender did not affect the outcome of a larger study (AVERT trial) examining factors associated with walking recovery post-stroke (27).

The reason why those who walked shorter distances at baseline improved the most is
unknown, but regression toward the mean cannot be excluded. Still, in those with the poorest
walking performance, a smaller increase in steps may be sufficient to have a positive impact
on health (28). New epidemiological studies measuring physical activity with accelerometers

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show that the positive effects of physical activity may have been underestimated (28). A large prospective study indicated that up to 10,000 steps a day were associated with a lower risk of cardiovascular incidence and mortality (28). Additional risk reduction was also found with steps performed at a higher intensity and there was no minimum threshold for the association between increasing steps per day with morbidity and mortality (28). This can be used to motivate the least active individuals to increase their outdoor walking and number of steps per day.

Limitations and strengths

Some methodological issues need to be addressed in this study. One limitation is that the study design calls for precaution with causal inferences. Another limitation is that our findings cannot be generalized to more disabled community-living individuals after a stroke or to individuals with chronic stroke. However, since we included participants at the hospital with different socio-economic statuses and educational backgrounds, we believe this sample to be representative of the acute stroke and TIA population with fewer motor deficits. Finally, the study is relatively small, making the study prone to bias, and all patients are from a single center in Sweden, therefore reducing the generalizability of the results.

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One strength of the present study is that study data were drawn from a randomized controlledtrial and that we used established outcome measures.

Conclusion: In summary, younger age, male sex, no comorbidity, lower BMI, and shorter 6minute walk test at baseline contributed most to improvement in walking performance in
patients with a recent stroke or TIA. These factors may be important when planning
secondary prevention actions. Cost-effective and easily delivered interventions for

2 3	226	
3 4	336	individuals with minor stroke or TIA to increase walking distance still require further
5 6 7	337	targeted research.
7 8 9	338	
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37 38 39	349	
40 41	350	Contributors: This study was conceived, organized, and managed by BV, SE, UH, and EL.
42 43	351	BV acts as a guarantor of the study. All authors listed above contributed to the study design
44 45 46	352	and data interpretation. Writing of the first draft of the paper was done by BV and all authors
40 47 48	353	were involved in the preparation and critique of the manuscript and reviewed the paper before
49 50 51	354	submission.
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27 28 29	366	
30 31 32	367	Data availability statement: The data set associated with this work is available from the
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49 50 51	374	EL: <u>http://orcid.org/0000-0002-5313-9052</u>
52 53 54	375	
55 56 57	376	Figure: None.
58 59 60	377	

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470 Table 1. Baseline characterist	tics of all patients in th	the study with ≥ 34 m	neters increase i	n the	
471 six-minute walking test at thr	ee months versus pati	ents with < 34 met	ers increase in th	e six-	
472 minute walking test.					
	Study	Changes in t	he 6-minute		
	population	walkir	ng test		Missin
	R				
	Baseline	≥34 m	<34 m		
		(n=38)	(n=41)	Р-	values
				value	n (%)
Age, mean (SD) ^b	63.9 (10.4)	61.9 (9.1)	65.7 (11.2)	0.01	0
Female, n (%) °	29 (36.7)	11 (28.9)	18 (43.9)	0.17	0
SMS group, n (%) °	40 (50.6)	26 (68.4)	14 (34.1)	0.002	0
Control group, n (%) ^c	39 (49.4)	12 (31.6)	27 (65.9)		
modified Rankin Scale, 0-2 ^c				0.47	0
0	11 (13.9)	6 (15.8)	5 (12.2)		
1	53 (67.1)	23 (60.5)	30 (73.2)		
2	15 (19.0)	9 (23.7)	6 (14.6)		
Diagnosis, n (%) °				0.70	0
Cerebral infarction	57 (83.5)	28 (73.7)	29 (70.7)		
Intracerebral hemorrhage	9 (11.4)	5 (13.2)	4 (9.8)		
TIA	13 (16.5)	5 (13.2)	8 (19.5)		

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Charlson Comorbidity Index, n (%) °					0
No comorbidity	47 (59.5)	25 (65.8)	22 (53.7)	0.27	
≥1	32 (40.5)	13 (34.2)	19 (46.3)		
BMI, mean (SD) ^a	27.51 (4.5)	26.56 (3.77)	28.39 (5.03)	0.07	0
Diabetes mellitus-2, yes n (%) ^c	12 (15.2)	5 (13.2)	7 (17.1)	0.63	0
University studies, yes n (%) ^c	40 (50.6)	16 (42.1)	24 (58.5)	0.14	0
Non-smoking, n (%) ^c	71 (89.9)	33 (86.8)	38 (92.7)	0.39	0 0 3 0 3 (3.8
Step counts (SMS group), mean (SD) ^a	6335 (2747)	6612 (2741)	5757 (2786)	0.38	3
SGPALS, n (%) °				0.47	0
Sedentary	11 (13.9)	6 (15.8)	5 (12.2)		
Light Physical Activity	53 (67.1)	23 (60.5)	30 (73.2)		
Moderate/High Physical Activity	15 (19.0)	9 (23.7)	6 (14.6)		
P-HDL cholesterol, (mmol/l), mean (SD) ^b	1.32 (0.39)	1.35 (0.45)	1.28 (0.34)	0.44	3 (3.8
P-LDL cholesterol, (mmol/l), mean (SD) ^b	3.16 (1.09)	3.18 (1.16)	3.13 (1.03)	0.86	3 (3.8)
P-Cholesterol, (mmol/l), mean (SD) ^b	5.13 (1.20)	5.13 (1.30)	5.13 (1.12)	0.86	3 (3 8
P-Triglycerides, (mmol/l), mean (SD) ^b	1.35 (0.63)	1.20 (0.46)	1.49 (0.73)	0.03	3 (3.8
P-HbA1C, mmol/mol), mean (SD) ^b	38.0 (7.54)	37.74 (8.33)	38.26 (6.77)	0.47	3 (3.8
P-C reactive protein (mg/L), mean (SD) ^b	4.92 (19.40)	6.80 (27.80)	3.20 (3.95)	0.20	3 (3.8 6 (7.6
P-Creatinine (mmol/L), mean (SD) ^a	85.12 (25.53)	78.97 (17.83)	90.80 (30.14)	0.042	2 (2 6
SBP, (mm HG), mean (SD) ^a	130.63(16.56)	129.83 (16.17)	131.36 (17.09)	0.69	4 (5)
DBP, (mm HG), mean (SD) ^b	76.08 (11.0)	79.17 (11.24)	73.23 (10.09)	0.02	4 (5)
473 Abbreviations: BMI, body mass in	ndex, CRP, C-rea	ctive protein; DBF	, diastolic blood		
474 pressure; HbA1C, glycated hemog	globin; HDL, higł	n-density lipoprote	in; LDL, low-den	sity	

⁵⁹₆₀ 476 group; SBP, systolic blood pressure.

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477	^a The Student's t-test was	used for continuous	, normally distributed variables.	
+//	The Student's t-test was	used for continuous,	, normany distributed variables.	

^b The Mann Whitney-U test was applied for ordinal or non-normally distributed variables.

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479 ^c The Chi-square test was used for categorical variables.

Table 2. Correlation of the variables used in the regression models and changes in walking

503 performance.

		Change 6- minute	P-	
		walking	value	
		test, r		
	Age (years) ^b	-0.39	< 0.00	
	Sex (female) ^b	-0.13	0.26	
	CCI (≥ 1 comorbidity) ^b	-0.20	0.08	
	BMI, (kg/m ²) ^a	-0.23	0.046	
	6-minute walking test, baseline (meters) ^a	-0.38	< 0.00	
	Chair-stand test, (seconds) ^a	0.10	0.39	
	Montreal Cognitive Assessment scale, (≥26 points), ^b	0.014	0.91	
	Saltin Grimby Physical Activity Level Scale ^b			
	(Sedentary, light physical activity, moderate/high physical activity) Abbreviations: BMI, Body Mass Index; CCI, Charlson Comorbidity Ind	0.078	0.49	
505 506	^a Correlation strength was calculated using Spearman's rho for ordinal a distributed variables	and non-norr	nally	
507	^b Correlation strength was calculated using Pearson correlation for conti	inuous and n	ormally	
508	distributed variables			
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BMJ Open Table 3. Univariate and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate and multivariate regression analyses with changes in walking performance (6-minutegrave and multivariate and m

and age, sex, comorbidity, baseline BMI-, and baseline 6-minute walk test as independent variables in indeviduals after stroke and TIA. An 4 March 202 Enseigr pr uses rela

513	intention-to-treat anal	ysis was performe	ed with drop-outs in	ncluded (n=8).
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		Univariate	analysis	Mult	ivanjate analysi	S	
	Beta	Adjusted	95% CI	P	Beta	text text text text text text text text	Р
	standardized	R square			standardized	while add from to -1.0 t Seperieur (ABES) .	
Age, yrs	-0.20	0.029	-3.1 to 0.1	0.073	-0.33	mining.	<0.00
Sex, female	-0.12	0.002	-54.4 to 16.4	0.29	-0.24	≥66 3 9 to -8.0	0.014
CCI, ≥1 comorbidity	-0.19	0.024	-63.8 to 4.9	0.09	-0.16	trainin5555 to 5.4 and 8.6 to -1.6	0.11
BMI, kg/m ²	-0.23	0.038	-7.5 to -0.07	0.046	-0.29	and 8.00 to -1.6	0.004
6-minute walk test, meters	-0.38	0.134	-0.4 to -0.1	< 0.001	-0.55	similar tec	< 0.00
Abbreviations: BMI, Body	Mass Index; CCI,	Charlson Com	orbidity Index			e 14, chnc	
The adjusted R square for t	he multivariate an	alysis is 0.36.				2025 plogie	
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BMJ Open **Table 4.** Sensitivity analysis: Univariate and multivariate regression analyses with changes in walking performance (6-minute walking test) as the dependent variable and age, sex, comorbidity, baseline BMI-, and baseline 6-minute walk test as independent variables in individuals after

stroke and TIA. In the sensitivity analysis, individuals with missing data at three months were not analyzed =8) relig

	Univariate analysis				Mult	in the analysis	
	Beta standardized	Adjusted R square	95% CI	P	Beta standardized	t Superieur (ABI	Р
Age, yrs	-0.25	0.05	-3.9 to -0.2	0.03	-0.33	5 10 - 1.1	0.00
Sex, female	-0.11	-0.002	-57.5 to 20.8	0.35	-0.24	2.7 to -7.1	0.01
CCI, ≥1 comorbidity	-0.18	0.018	-66.6 to 9.7	0.14	-0.22	-67.4 to -2.6	0.03
BMI, kg/m ²	-0.21	0.031	-8.1 to 0.43	0.08		and si	
6-minute walk test, meters	-0.42	0.16	-0.47 to -0.15	< 0.001	-0.55	-0.56 to -0.26	<0.0
Abbreviations: BMI, Body Mas The adjusted R square for the m			oidity Index			com/ op.56 to -0.26 -0.000 -0.000 at Agence Bibliographique de l	
			2			nique d	

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CONSORT CHECKLIST

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Section and Topic	ltem No.	Checklist Item	Reporte on Page No
Fitle and abstract	-		
	1a	Identification as a randomized trial in the title	
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	
ntroduction	_		
Background and objectives	2a	Scientific background and explanation of rationale	
	2b	Specific objectives or hypotheses	
Nethods Trial design	За	Description of trial design (such as parallel, factorial) including allocation ratio	
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	
Participants	4a	Eligibility criteria for participants	
	4b	Settings and locations where the data were collected	
nterventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	
Dutcomes	6a	Completely defined prespecified primary and secondary outcome measures, including how and when they were assessed	
	6b	Any changes to trial outcomes after the trial commenced, with reasons	
Sample size	7a	How sample size was determined	
	7b	When applicable, explanation of any interim analyses and stopping guidelines	
Randomization			
Sequence generation	8a	Method used to generate the random allocation sequence	
5	8b	Type of randomization; details of any restriction (such as blocking and block size)	
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	
Statistical	12a	Statistical methods used to compare groups for primary and secondary outcomes	
methods	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	
Results Participant flow (a diagram is strongly	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analyzed for the primary outcome	
recommended)	13b	For each group, losses and exclusions after randomization, together with reasons	
Recruitment	14a	Dates defining the periods of recruitment and follow-up	
	14b	Why the trial ended or was stopped	
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	
Numbers analyzed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing prespecified from exploratory	
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	
Comment Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	
Generalizability	21	Generalizability (external validity, applicability) of the trial findings	
nterpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	
Other information Registration	23	Registration number and name of trial registry	
Protocol	24	Where the full trial protocol can be accessed, if available	
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	

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 STROBE Statement—checklist of items that should be included in reports of observational studies

No 1	Recommendation (a) Indicate the study's design with a commonly used term in the title or the abstract
	(b) Provide in the abstract an informative and balanced summary of what was done
	and what was found
2	Explain the scientific background and rationale for the investigation being reported
3	State specific objectives, including any prespecified hypotheses
4	Present key elements of study design early in the paper
5	Describe the setting, locations, and relevant dates, including periods of recruitment
	exposure, follow-up, and data collection
6	(a) Cohort study—Give the eligibility criteria, and the sources and methods of
	selection of participants. Describe methods of follow-up
	Case-control study—Give the eligibility criteria, and the sources and methods of
	case ascertainment and control selection. Give the rationale for the choice of cases
	and controls
	Cross-sectional study—Give the eligibility criteria, and the sources and methods or
	selection of participants
	(b) Cohort study—For matched studies, give matching criteria and number of
	exposed and unexposed
	Case-control study—For matched studies, give matching criteria and the number o
	controls per case
7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect
	modifiers. Give diagnostic criteria, if applicable
8*	For each variable of interest, give sources of data and details of methods of
	assessment (measurement). Describe comparability of assessment methods if there
	is more than one group
9	Describe any efforts to address potential sources of bias
10	Explain how the study size was arrived at
11	Explain how quantitative variables were handled in the analyses. If applicable,
	describe which groupings were chosen and why
12	(a) Describe all statistical methods, including those used to control for confounding
	(b) Describe any methods used to examine subgroups and interactions
	(c) Explain how missing data were addressed
	(d) Cohort study—If applicable, explain how loss to follow-up was addressed
	Case-control study—If applicable, explain how matching of cases and controls was
	addressed
	Cross-sectional study-If applicable, describe analytical methods taking account o
	sampling strategy
	(<u>e</u>) Describe any sensitivity analyses
	3 4 5 6 7 7 8* 9 10 11

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Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and
		analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information
data		on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) Cohort study—Summarise follow-up time (eg, average and total amount)
Outcome data	15*	Cohort study—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of
		exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their
		precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and
		why they were included
		(b) Report category boundaries when continuous variables were categorized
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful
		time period
Other analyses	17	Report other analyses done-eg analyses of subgroups and interactions, and sensitivity
		analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision.
		Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity
		of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other informati	ion	
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable,
		for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.