eRehabilitation after stroke: the interplay between the effectiveness, the implementation and the context

Brouns, B.

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The effect of a comprehensive eRehabilitation intervention alongside conventional stroke rehabilitation, on disability and health-related quality of life: a pre-post comparison

Berber Brouns | Leti van Bodegom-Vos | Arend. J. de Kloet | Sietske J. Tamminga
Gerard Volker | Monique A.M. Berger |Marta Fiocco | Paulien. H. Goossens
Thea P.M. Vliet Vlieland | Jorit J.L. Meesters

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ABSTRACT

Objective: This study compared the effect of conventional rehabilitation (control group; CG) with an individualized, tailored eRehabilitation intervention alongside conventional rehabilitation (Fast@home; intervention group; IG) on disability and quality of life, in people with stroke.

Method: Pre-post design. The intervention comprised cognitive (Braingymmer®) and physical (Telerevalidatie®/Physitrack®) exercises, activity-tracking (Activ8®) and psycho education. Assessments were done at admission (T0) and after 3 (T3) and 6 months (T6). The primary outcome concerned disability (Stroke Impact Scale, SIS) and secondary outcomes measures of health-related quality of life, fatigue, self-management, participation and physical activity. Change scores between T0-T3, T3-T6 and T0-T6 were compared by analysis of variance and linear mixed models.

Results: 153 and 165 people with stroke were included in CG/IG, respectively. In the IG, 82 (50%) people received the intervention, of whom 54 (66%) used it. Between T3-T6, the change scores of the SIS subscales Communication (CG/IG; -1.7/-0.3) and Physical strength (-5.7/3.3) were significantly greater in the total IG (all mean differences < minimally clinically important differences). No significant differences for other SIS subscales or secondary outcomes, nor between T0-T3 and T0-T6 were seen.

Conclusion: eRehabilitation alongside conventional stroke rehabilitation had a small effect on communication and physical strength on the longer term.

INTRODUCTION

Worldwide, about 9 million people experience a stroke each year, in many leading to a broad range of long-term disabilities with a major impact on multiple areas of life [1]. More than half of the people with stroke suffer from physical, mental and/or cognitive impairments six months post-stroke [2,3]. In order to enhance recovery of limitations, people with stroke may be referred to inpatient or outpatient specialized rehabilitation facilities offering multidisciplinary treatment [4]. In the Netherlands, about 10% of the people with stroke are admitted to such facilities, mostly those with severe disability and the potential for recovery [5].

During the last decade there is an increasing interest in the use of digital technologies to deliver rehabilitation, addressed as eRehabilitation, in specialized rehabilitation facilities. Examples of eRehabilitation applications relevant for stroke rehabilitation are virtual reality [6], online communication and consultation [7,8] and applications for the delivery of specific physical or cognitive exercises [9]. A number of systematic reviews on eRehabilitation in stroke, published in the past 10 years, assessed their effectiveness within the first six months after stroke, and concluded that these applications may result in increased access to care [9] and time spent on therapy related activities [6]. Moreover, improved healthcare outcomes, like walking speed, balance and mobility [6], cognition and mood [8] and health-related quality of life [7], were found.

So far, most studies on eRehabilitation in stroke focused on interventions targeting only one domain of rehabilitation treatment [9]. In daily practice however, people with stroke face multiple and distinct problems. Therefore, different applications may be useful at the same time. Yet, making an appropriate selection and handling different ways of access are only two of the many challenges people with stroke and healthcare professionals are facing in the use of eRehabilitation. Integrating a selection of various eRehabilitation applications within one combined intervention would greatly increase their user-friendliness, especially if the selection made appropriately addresses the needs of the individual patient [10].

Evidence on the effectiveness of such comprehensive eRehabilitation interventions, combining eRehabilitation applications covering more than one domain of early rehabilitation treatment, is scarces. Three controlled clinical trials combined multiple applications in one intervention, i.e. online exercise programs with activity tracking or stroke-related education [11-13]. All three studies compared a comprehensive eRehabilitation intervention with conventional rehabilitation, showing equal effect with respect to improvement of motor function and knowledge about stroke [11-13]. However, none of these studies included people with stroke admitted to a specialized rehabilitation facility [14], nor did they explore the effects of eRehabilitation when integrated in conventional rehabilitation service delivery. The latter is striking, as it is suggested that eRehabilitation should preferably be offered alongside conventional stroke rehabilitation to achieve its full potential [15].

Therefore, the present study aimed to compare the effect of a comprehensive eRehabilitation intervention, Fit After STroke @home (Fast@home), consisting of different components offered in addition to conventional stroke rehabilitation in a specialized rehabilitation facility on disability and health-related quality of life.

METHOD

1. Design and setting

This pre-post test controlled pragmatic clinical trial was conducted at two rehabilitation centres, Basalt The Hague/Leiden, The Netherlands. Two groups were compared; the control group (CG; May 2016 – April 2017) receiving only conventional stroke rehabilitation and the intervention group (IG; May 2017 – April 2018) receiving Fast@Home alongside conventional rehabilitation. Data were gathered in an ongoing, observational study, Stroke Cohort Outcomes of REhabilitation (SCORE; Dutch Trial Register no. 4293). Assessments were done at admission (T0), and three (T3) and six months (T6) after admission and the assessors were not blinded.

The SCORE-study was approved by the Medical Ethics Review Committee (protocol NL46531.058.13) of the Leiden University Medical Center. All participants gave written informed consent. Details and results of SCORE are published elsewhere [16-19]. Reporting of the current study was done according to the STROBE Checklist [20], the description of the intervention was done according to the TIDieR Checklist [21].

2. Participants

Inclusion criteria were: age above 18 years and first ever/recurrent stroke less than six months ago. Exclusion criteria were severe psychiatric conditions; unable to communicate in Dutch; concurrent acquired brain injury and/or drug or alcohol abuse. At admission, the treating rehabilitation physician checked the criteria. Eligible people with stroke were informed by the research team within two weeks. All people included in the SCORE-study between May 2016 and April 2018 were considered eligible for the current analysis on the effect of eRehabilitation. From May 2017, the intervention was implemented in conventional rehabilitation. In rare cases, Fast@Home had already started before inclusion in the study was accomplished. People were excluded if they used the intervention seven or more days before T0.

2.1 Conventional Rehabilitation

During the control and intervention periods, people with stroke received conventional rehabilitation according to a national guideline [22]. Treatment was provided by a multidisciplinary team including a rehabilitation physician (RP), physical therapist (PT), occupational therapist (OT), speech therapist, psychologist and social worker. Rehabilitation treatment could focus on improving motor, cognitive/psychological function, speech, or participation. Conditional on the severity of impairments and living situation, inpatient or outpatient rehabilitation was provided [23].

Box 1: The Fast@home intervention

Fast@home is a web-based eRehabilitation intervention developed to support stroke patients, their informal caregivers and healthcare professionals during inpatient and outpatient rehabilitation and after discharge, and is developed in co-creation with patients, informal caregivers and healthcare professionals (10,24). The mobile application was field tested among a small number of patients before the study started, resulting in a small number of practical adaptations.

Fast@home included the following commercially available eRehabiliation applications (see also figure):

- Physical exercise program, offered by Telerevalidatie (Roessingh Research & Development, Enschede, Netherlands, www.telerevalidatie.nl, used in Basalt Leiden) or Physitrack (Physitrack Limited, London, Great Britain, www.physitrack.com, used in Basalt Den Haag). Exercises for all parts of the body were available and aimed to improve strength, balance, coordination, mobility, stability, speech or aerobic capacity. The exercises were explained by videos within the physical exercise program. A tailored day-to-day schedule for each participating patient could be compiled by the treating physical and/or occupational therapist including a selection of one or more exercises.

- Cognitive exercise program, offered by Braingymmer (Dezzel Media, Almere, Netherlands). Every day, each patient could perform three exercises of 300 seconds, on the domains concentration, logic, perception, memory and velocity.

- Physical activity tracker (Activ8 consumer, 2M Engineering, Valkenswaard, Netherlands, www.activ8all.com). This tracker was worn inside a pocket of jeans and measured the time spent on laying, sitting, standing, walking, cycling or running in minutes. Data could be uploaded with a personal login and viewed in the dashboard of Fast@home.

In addition to the applications, a stroke-related information module was accessible (Kennisbank, upper right of figure). This module was based on the information given by the Dutch patient association (www.hersenstichting.nl) and included information about stroke, consequences of stroke and stories of other patients and informal caregiver. Pictograms were used to increase ease of use and understanding.

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2.2 eRehabilitation Intervention

During the intervention period, all people with stroke had free access to the intervention Fast@home (Box 1), that comprised several commercially available applications for cognitive and physical exercises, activity-tracking and stroke-related psycho education. The intervention was accessible on smartphone, laptop/PC or tablet. Some applications could be used with, some without the support/interference of a healthcare professional.

A tailored strategy, based on barriers and facilitators identified in preceding studies [10,24] was used to implement the intervention. Implementation included among others: structured integration in the healthcare process, providing education and information to

healthcare professionals, people with stroke and their caregivers, providing a helpdesk/ support for all users. Implementation activities were mostly executed as planned and supplemented with instructional activities. Of the 49 healthcare professionals who were invited for the instructional session (RPs, OTs and PTs only), 47 (95.9%) attended. Of those professionals trained to deliver the intervention, 75.8% actually delivered it. Main areas for improvement of the implementation of eRehabilitation are found to be related to healthcare professionals' perceptions of the intervention, integration of eRehabilitation into conventional rehabilitation and technical and organizational contextual factors. More information about the implementation strategy, including fidelity and adaptations and details about the training provided for the healthcare professionals, is published elsewhere.

The intervention was delivered as follows:

1. All people with stroke were registered as user in Fast@Home by the research team. Login credentials for people with stroke were logged in the electronic patient record, and forwarded to the patient by email.
    - Every registered patient had access to the psycho education module.
    - The delivery of applications for cognitive exercises, physical exercises and/or the activity tracker was tailored to individual peoples' needs and goals. For the selected applications, treating therapists compiled an individualised program.
2. People with stroke could access the eRehabilitation intervention for 16 weeks. Its precise composition was defined for each individual patient. All people with stroke were encouraged to use it on a regular basis (multiple times per week), with the intended dose depending on the nature of the intervention. For the cognitive exercise program a dose of 300 seconds of use every day was advised, for the physical exercise program the recommended intensity and frequency could vary, depending on the individual patients' situation and nature of exercises (at least 2- 3 days of the week). With every training session people with stroke needed to sign in only once, and were automatically linked to the different applications showing their individualised program. A training session could be performed at any location with enough space and internet access, mostly at home or in the rehabilitation facility. People with stroke could receive reminders to use the intervention by email or text message. An email/telephone helpdesk was available during work hours.
3. Healthcare professionals received reports on the number/repetitions of exercises performed, to support the patient during conventional consultations and/or adapt the program if necessary.

3. Assessments

Stroke and personal characteristics were derived from medical files and health outcomes were collected with questionnaires. Questionnaires were available digitally and on paper, with reminders by telephone after two and four weeks. Use of the intervention was also recorded. Appendix 1 shows an overview of the timing and content of assessments.

3.1 Sociodemographic and clinical characteristics

From the medical records, stroke type (ischemic/haemorrhagic) and localization (right/left/other) were derived, and information on time between stroke and admission to rehabilitation (days), use of inpatient and/or outpatient rehabilitation and length of rehabilitation (days) was retrieved.

The admission questionnaire included living situation (alone or living with spouse/partner/ children), educational level (low: up to and including lower technical and vocational training; medium: up to and including secondary technical and vocational training; high: up to and including higher technical and vocational training and university) and paid employment before stroke (yes/no). Depression and anxiety were measured by the Hospital Anxiety and Depression Scale (HADS [25]), including 7 items each on anxiety and depression (four-point Likert scale 0–3 points), yielding 2 subscale scores ranging from 0-21 (a higher score indicates a higher level of depression or anxiety).

3.2 Use of the intervention Fast@home

The actual use of the applications was routinely recorded by each application and included: date, starting time and duration per exercise, type of exercise and per exercise the number of repetitions. For the activity tracker, the number of uploads was recorded. For an upload, the patient had to connect the activity tracker to a computer, after which the newly recorded activities were shown. A patient was defined as a user of the intervention if he/she had performed at least one exercise or one upload from the activity tracker. People with stroke who were registered and/or offered the intervention but did not login any of the applications were defined as non-user.

3.3 Primary outcomes

The primary outcome was the Stroke Impact Scale (SIS), which included the following subscales: Physical Strength (4 items, minimal clinical important difference (MCID) 9.2 [26]), Memory (7 items), Feelings & emotion (9 items), Communication (7 items), Activities of Daily Living (ADL, 10 items, MCID 5.9), Mobility (9 items, MCID 4.5) and Meaningful Activities (T3 and T6 only, 8 items). The item scores range from 0 (very difficult) – 5 (not difficult), and the subscale scores from 0-100, with lower scores indicating more impact. The SIS has shown excellent internal consistency and good test-retest reliability [27]. The subscale Hand function was originally included in this study, but because of an error during the collection process, data were only gathered in a subgroup of patient, and were thus omitted from the analyses.

3.4 Secondary outcomes

The EuroQol-5D-3L (EQ5D) measures health-related quality of life (QoL) and consists of five subscales; mobility, self-care, usual activities, pain/discomfort and anxiety/depression [28]. Each dimension had 3 possible answer options: no problems, some problems, extreme problems. Utilities were calculated from the 5 subscales and the VAS scale, using the Dutch tariff [28]. A utility of 1 reflects complete health, -0.239 reflects death.

The 12-item Short-Form Health Survey (SF-12) was used at T3 and T6 to measure mental and physical health. Mental and physical scores can be computed, both scores ranging from 0-100 and higher scores indicating better QoL [29] .

Fatigue was measured using the 9-items Fatigue Severity Scale (FSS), yielding a total score being the mean of the 9 items (item scores and total score range 0-7), with higher scores indicating more fatigue [30]. The FSS has good internal consistency, test re-test reliability and discriminative validity [31].

The Patient Activation Measure Short Form 13 (PAM-13) was used to assess peoples' knowledge, skills and confidence for self-management (item scores 0 (totally disagree) - 5 (totally agree)), yielding a continuous total scale (0-100), higher scores indicating higher levels of patient activation. The shortened 13-item version is found both reliable and valid [32].

Participation was measured with the Utrecht Scale for Evaluation of Rehabilitation-Participation (USER-P) [33], consisting of 3 scales (all range 0-100); Frequency of Activities (11 items), Restrictions (11 items), and Satisfaction with participation (10 items). The internal consistency and test-retest reliability in the rehabilitation population were satisfactory [33].

Physical activity was measured with the 7-items International Physical Activity Questionnaire Short Form (IPAQ-SF), about time spent on physical activities and sedentary time (days/hours/minutes) during the last week [34].

4. Analyses

The target sample size was based on the ability to detect a change score of 5 points on the SIS subscale mobility, with a standard deviation of 14 points [35]. With an alpha of 0.05, two-sided testing, power of 80%, and a drop-out rate of 20%, 296 people with stroke in total were needed to detect a significant difference.

Patient characteristics were described using means and SD, median with interquartile range (IQR) or numbers and percentages, depending on type and distribution of the data. Normal distribution was checked by visual inspection and Kolmogorov-Smirnov tests. Characteristics of participants who did and did not complete the study, and characteristics of people with stroke in the CG and IG were compared by means of independent-samples t-tests, Mann-Whitney U tests, or Fisher's exact tests.

Data were analysed on an intention-to-treat basis (ITT), meaning that all participants were included in the analysis. For the IG group, all people with stroke were considered, regardless whether they received and/or used the intervention. In addition, all analyses were repeated comparing all people in the CG with only those people in the IG who actually used the intervention (per-protocol analysis; PP).

Primary and secondary outcomes were compared between T0-T3 and T3-T6 within and between the CG/IG. The periods T0-T3 and T3-T6 were analysed separately, since those periods differ from each other in clinical activity; during the first period, people with stroke receive rehabilitation, where during the second period most people finished rehabilitation. Within group analysis comprised paired t-tests, Wilcoxon Signed Rank tests or McNemar tests, where appropriate.

Change scores between T0-T3 and T3-T6 were compared between the IG and CG by means of Multivariate Analysis of Covariance (MANCOVA), while adjusting for baseline characteristics that significantly differed between the groups (age and type of rehabilitation). For both T0-T3 and T3-T6, two separate MANCOVAs were performed; one with seven subscales of the SIS and one with all secondary outcome measures. Besides, differences in changes scores between ITT and PP were calculated.

To investigate differences over time, Linear Mixed Models (LMM) were estimated for every primary and secondary outcome. These models take into account the correlation structure present in the data due to repeated measures within each patient, while accommodating for missing observations. The primary and secondary outcomes were entered in the model as dependent continuous variables, time as continuous variable and age (continuous) and type of rehabilitation (inpatient/outpatient/both) as control variables. Due to skewed distributions, power (squared) transformation were performed with EQ5D subscales (without VAS-score) and logarithmic (log natural) transformation were performed with IPAQ-scores. A model with a random slope and with unstructured covariance structure was estimated. For the USER-P, a model with only a random intercept was used since a random slope model did not converge. Since not all outcome variables were normally distributed, LMM with bootstrapping was performed to obtain more accurate confidence intervals and to check whether results about significance groups difference and change over time could be confirmed.

Data were entered and stored using Microsoft Access 2016 and analyses were performed using SPSS 25.0. P-values were considered significant if <0.05.

RESULTS

During the study period, in total 568 people with stroke met the inclusion criteria, of whom 318 (55.9%) gave informed consent and returned the baseline questionnaire (Figure 1); 153 people with stroke in the control period and 164 in the intervention period. Of those people, 306 completed the three-month follow-up (96.2% completion rate), 281 completed the six-month follow-up (88.3% completion rate). Participation was similar in the CG and IG. Baseline characteristics of people with stroke who completed the study and those lost to follow-up did not significantly differ (results not shown).

Apart from significant differences with respect to age (mean CG 58.6 (SD12.4); IG 62.6(SD 10.5) years, p=0.020), no significant differences were found in the baseline characteristics nor length of stay between people with stroke in the CG and IG (Table 1). Compared to the CG, people with stroke who used the intervention more often had a combination of inpatient and outpatient rehabilitation (Table 1, CG n=55, 35.9%; Users n=30, 55.6%).

Use of the intervention in the IG

In this pragmatic trail, healthcare professionals delivered the intervention to 82 participants in the IG (50.0%), of whom 54 (65.8%) used it. Of the 54 users, 36 used the physical exercise applications, 19 the cognitive exercise application and 15 the activity tracker. The median number of cognitive exercises performed was 14 (IQR 2-37), the median number of physical exercises was 10 for both applications (IQR Telerehabilitation 4-23, IQR Physitrack 3-51). The median number of uploads of the data of the activity tracker was 4 times (IQR 1-15). Figure 2 shows that most users (85.2%) stopped using the intervention before T3. More details about the amount of use of the applications in the intervention and the influence of several implementation activities on this use is published elsewhere.

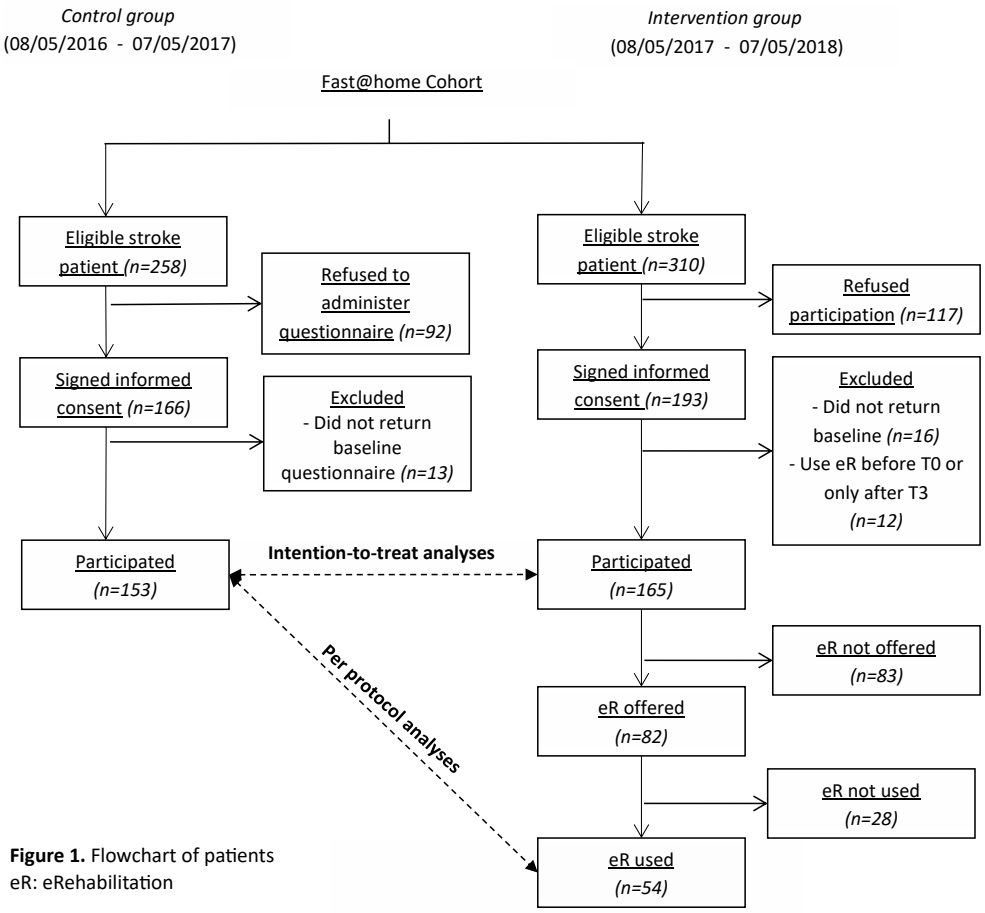

Figure 1. Flowchart of patients
eR: eRehabilitation

Table 1. Characteristics of 318 stroke patients admitted to a rehabilitation centre in a period where conventional rehabilitation was offered (control group) or eRehabilitation was offered in addition (intervention group)

	Control group		Intervention group			
	Total (n =153)	**Missing in %**	**Total (n =165)**	**Missing in %**	**Users (n=54)**	**Missing in %**
Age in years, mean (SD)	58.6 (12.4)	0	**62.6 (10.5)**	0	59.2 (10.4)	**0**
Gender, male n (%)	97 (63.4)	0	103 (62.2)	0	34 (62.9)	0
Stroke type, n haemorrhage (%)	31 (20.3)	1.3	24 (14.5)	1.2	9 (16.7)	0
Location of stroke		9.8		14.5		7.4
Hemisphere, n left (%)	59 (38.6)	.	73 (44.2)	.	29 (53.7)	.
Hemisphere, n right (%)	75 (44.8)	.	64 (38.8)	.	19 (35.2)	.
Other, n (%)	4 (2.6)	.	4 (2.4)	.	2 (3.7)	.
Living status, n living alone (%)	43 (28.1)	1.3	45 (27.3)	2.4	12 (22.2)	3.7
Education level		3.6		3.6		5.6
Low, n (%)	60 (39.2)	.	67 (40.6)	.	17 (31.5)	.
Middle, n (%)	47 (30.7)	.	44 (26.7)	.	19 (35.2)	.
High, n (%)	44 (28.8)	.	48 (29.1)	.	15 (27.8)	.
Employment, n. paid job age <65 (%)	83 (80.6)	0	59 (69.4)	3.6	24 (68.6)	3.7
HADS-A (0-21, low-high depression), mean (SD)	5.1 (3.8)	9.2	4.7 (3.8)	10.3	4.6 (3.9)	7.4
HADS-D (0-21, low-high anxiety), mean (SD)	5.2 (3.9)	9.2	5.2 (3.5)	9.7	4.8 (3.5)	5.6
Time between stroke and start rehabilitation, median, (IQR)	13 (8-30)	0	11 (7.27)	0	11 (7.14)	0
Type of rehabilitation		0		0		0
Inpatient, n (%)	**52 (33.9)**	**.**	**60 (36.4)**	**.**	**18 (33.3)**	**.**
Outpatient, n (%)	**46 (30.1)**	**.**	**37 (22.4)**	**.**	**6 (11.1)**	**.**
In and outpatient, n (%)	**55 (35.9)**	**.**	**68 (41.2)**	**.**	**30 (55.6)**	**.**
Days of inpatient rehabilitation, median, (IQR)	42 (29-77)	5.7	34 (24-47)	11.6	36 (24-47)	0
Days of outpatient rehabilitation, mean (SD)	84 (44-124)	2.1	106 (56-175)	5.4	123 (70-159)	16.6
Days of in- plus outpatient rehabilitation, median, (IQR)	178 (99-244)	5.4	135 (83-196)	13.2	131 (97-181)	13.3
Time between stroke and start rehabilitation, median, (IQR)	13 (8-30)	0	11 (7-27)	0	11 (7-14)	0

In Bold, significant difference with control group ($p<0.05$)
SD; standard deviation, Educational level; low: up to and including lower technical and vocational training/ medium: up to and including secondary technical and vocational training/ high: up to and including higher technical and vocational training and university, HADS-A; Hospital Anxiety and Depression Scale – Anxiety, HADS-D; Hospital Anxiety and Depression Scale – Depression, IQR; Inter quartile range.

Effect on primary outcomes

Regarding the changes within groups, the largest improvements occurred between start of rehabilitation and T3, both for the CG and IG (Table 2a). Between T0-T3, significant improvements of the SIS subscales, except for Feelings & emotion, were seen within both groups. Between T3-T6, significant improvements were only seen within the IG, (SIS subscales Memory and Meaningful activities). All mean changes score between T0-T3 of both the IG and CG were below MCID.

Regarding groups differences, no significant differences between the IG and CG were seen between T0-T3. However, between T3-T6, the improvements were significantly greater in the IG than the CG for the SIS subscales Communication and Physical strength. Taking into account all time points, no significant differences were seen between CG and IG. All mean changes score between T3-T6 of both the IG and CG were below MCID.

Effect on secondary outcomes

Within groups, between T0-T3, the EQ5D total score improved and the USER-P deteriorated significantly and the FSS improved significantly in the IG only (Table 2a). All other secondary outcomes showed no significant within group changes. Between T3-T6 only the USER-P Restriction and Satisfaction scores improved significantly within both groups. None of the between group differences reached significance between T0-T3, nor T3-T6 or T0-T6.

Per-protocol analysis

The PP-analysis overall yielded in similar results as the ITT-analysis (Table 2b). No group differences were found between T0-T3. Between T3-T6, significantly greater improvements on the SIS subscales Communication and Physical strength were seen in the IG as compared to the CG. In addition, differences in the changes scores of the SIS subscales Memory and Meaningful activities reached significance as well. All mean changes score of the PP-analyses, of both IG and CG and between T0-T3 and T3-T6, were below MCID.

To compare the results of the ITT-analyses with the PP-analyses, differences in change scores between ITT and PP were calculated (Appendix 2). The magnitude of improvements over time was larger for the users group (PP) as compared to the total IG (ITT), both between T0-T3 (for 8 of the 12 outcome measures) as well as between T3-T6 (for 13 of the 17 outcome measures).

DISCUSSION

This quasi-experimental pragmatic clinical study found that with a comprehensive eRehabilitation intervention combining multiple applications, offered alongside conventional stroke rehabilitation, some improvements were better maintained on the longer term than with conventional rehabilitation only. Whereas people with stroke in both the control and intervention groups improved significantly during the first three months after admission on various domains of health, no significant differences between the groups were seen. In the second three-month period however, although further improvements within the groups were small, significant differences in favour of the intervention group were found in some of the outcome measures. These differences were even more pronounced if only the people with stroke actually using the intervention were taken into account, suggesting that the longer term differences may be attributed to the intervention.

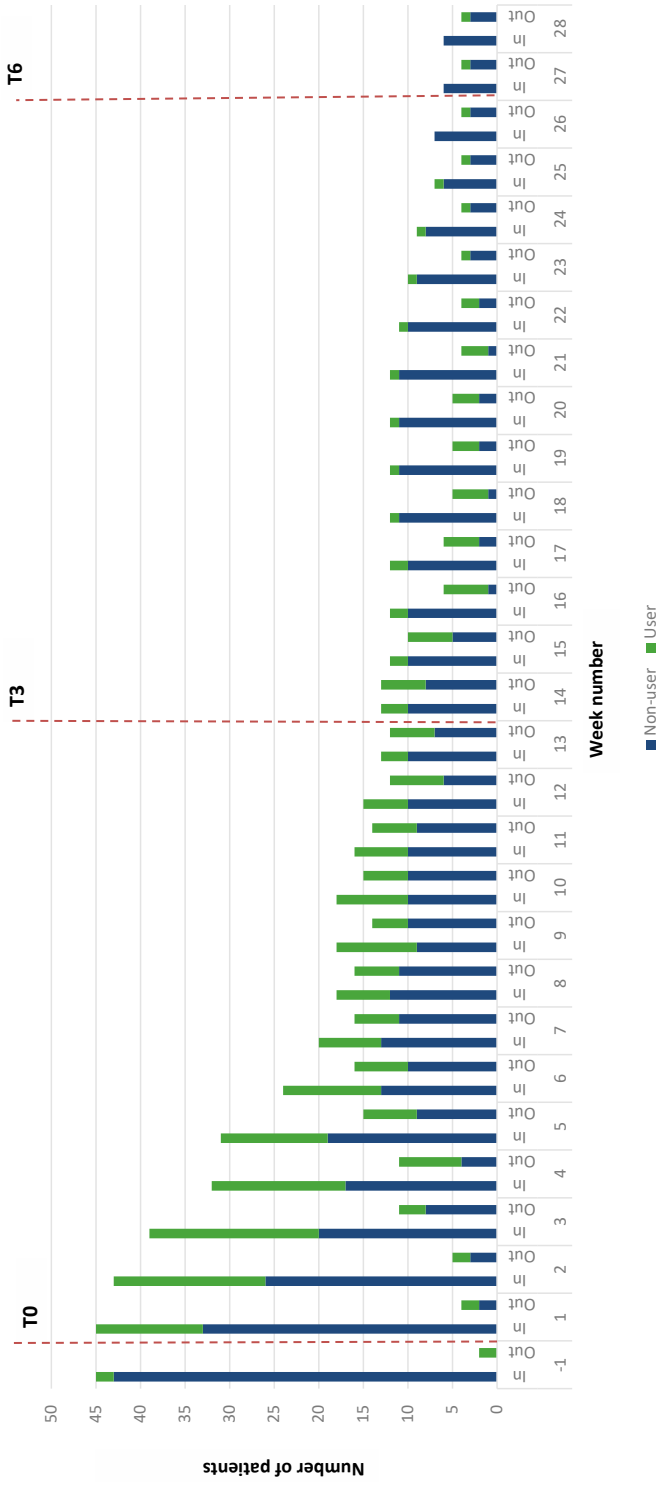

Figure 2. Use of Fast@home over time, for both in patients (in) and out patients (out). Number of non-users (blue) and users (green) of Fast@home over time, with measurement moments at T0 (start of rehabilitation), T3 (3 months after admissions) and T6 (six months after admission)

Table 2a. Intention to treat analysis, comparing the control group (n=153) with the intervention group (n=165). Baseline scores and change score in mean difference (SD) for T0-T3 and T3-T6 and Linear mixed models (LMM) for the whole period (T0-T6)

	T0 baseline		T0-T3 change scores			T3-T6 change scores			LMM (T0-T6)
			Within group		Between groups	Within group		Between groups	Between groups
	Control group	Interven-tion group	Control group	Interven-tion group	p	Control group	Interven-tion group	p	p (95%CI)
SIS (0-100, high-low impact)									
Communication	85.6 (16.1)	85.7 (15.5)	3.5 (13.4)*	2.5 (11.8)*	.13	-1.7 (8.9)	-0.3 (10.5)	**.026**	0.70 (-1.9 - 1.3)
Memory	78.9 (19.0)	80.4 (19.9)	4.5 (14.6)*	3.6 (14.9*	.30	-1.3 (10.3)	2.1 (9.9)*	.65	0.97 (-2.0 - 1.9)
Mobility	72.6 (29.3)	75.5 (24.3)	12.2 (20.0)*	9.4 (19.3)*	.23	-0.8 (10.8)	1.1 (7.9)	.11	0.80 (-2.9 - 2.3)
Feelings & emotion	75.7 (15.8)	75.8 (14.6)	0.6 (14.2)	-1.2 (15.4)	.47	0.5 (11.4)	0.4 (11.2)	.88	0.17 (-3.3 - 0.5)
Activity of Daily Living	75.0 (23.9)	74.8 (21.1)	9.6 (14.5)*	8.8 (18.1)*	.062	0.2 (9.8)	0.7 (6.5)	.30	0.96 (-2.2 - 2.2)
Physical Strength	58.0 (27.6)	55.8 (25.2)	15.3 (33.9)*	9.3 (25.4)*	.066	-5.7 (22.4)	3.3 (11.7)	**.010**	0.48 (-3.2 - 6.8)
Meaningful activities	.	.	.	.	.	1.6 (19.2)	9.1 (18.0)*	.12	.
EQ5D (0-1, low-high HRQoL)	0.71 (0.3)	0.69 (0.2)	0.07 (0.2)*	0.07 (0.2)*	.19	-0.01 (0.2)	0.01 (0.2)	.38	0.50 (0.0 - 0.1)
FSS (0-7, low-high fatigue)	4.5 (1.52)	4.3 (1.5)	.0.1 (1.5)	0.3 (1.5)*	.059	0.2 (1.29)	-0.2 (1.1)*	.11	0.33 (-0.1 - 0.3)
PAM(0-100, low-high self-management)	58.3 (13.9)	60.3 (14.9)	3.2 (16.0)	0.8 (17.4)	.064	2.2 (16.7)	1.3 (14.9)	.47	0.05 (-4.8 - 0.0)
SF-12 (0-100, low-high HRQoL)									
Physical	.	.	.	.	.	1.1 (8.7)	1.1 (6.3)	.98	.
Mental	.	.	.	.	.	0.6 (7.0)	1.7 (7.8)	.48	.
USER-P (0-100, low-high participation)									
Frequency**	35.4 (13.3)	35.0 (12.5)	.5.5 (14.8)*	.6.6 (11.9)*	.41	-4.4 (11.6)	1.9 (10.1)	.46	0.81 (-1.7 - 1.4)
Restriction	.	.	.	.	.	6.4 (18.5)*	5.4 (14.6)*	.24	.
Satisfaction	.	.	.	.	.	3.6 (16.7)*	5.5 (12.0)*	.088	.
IPAQ-SF (minutes physical activity)	754 (1132)	757 (1015)	154 (1620)	102 (1271)	.27	2.8 (674)	60 (666)	.77	0.53 (-0.2 - 0.1)

* Significant within group difference (p<0.05), in bold significant between group difference (p<0.05), LMM; linear mixed models with random slope model, **LMM with random intercept model; HRQoL; Health-related quality of life

Paired t-test for within group comparison, MANCOVA and Linear Mixed Models for between group comparison. Within group differences unadjusted, between group difference and LMM adjusted for age and type of rehabilitation

Table 2b. Per-protocol analyses, comparing the control group (n=153) with the users of eRehabilitation (n=54). Baseline score and change score in mean difference (SD) for T0-T3 and T3-T6 and Linear mixed models (LMM) for the whole period (T0-T6)

	T0 baseline		T0-T3 change scores			T3-T6 change scores			LMM (T0-T6)
			Within group		Between groups	Within group		Between groups	Between groups
	Control group	Interven-tion group	Control group	Interven-tion group	p	Control group	Interven-tion group	p	P (95%CI)
SIS (0-100, high-low impact)									
Communication	85.6 (16.1)	85.7 (17.6)	3.5 (13.4)	0.6 (11.1)	.41	-1.7 (8.9)	2.6 (12.1)	**.019**	.47 (-1.4 - 3.1)
Memory	78.9 (19.0)	79.8 (21.6)	4.5 (14.6)*	3.7 (14.1)	.87	-1.3 (10.3)	4.2 (11.5)*	**.031**	.42 (-1.7 – 4.0)
Mobility	72.6 (29.3)	71.8 (25.5)	12.2 (20.0)*	11.4 (19.5)*	.46	-0.8 (10.8)	1.7 (6.4)	.33	.36 (-2.1 - 5.9)
Feelings & emotion	75.7 (15.8)	75.2 (14.9)	0.6 (14.2)	1.1 (12.5)	.82	0.5 (11.4)	-0.3 (12.1)	.95	.63 (-3.2 - 2.0)
Activity of Daily Living	75.0 (23.9)	70.1 (20.8)	9.6 (14.5)*	11.4 (16.7)*	.053	0.2 (9.8)	3.1 (6.1)*	.20	.06 (-0.1 - 6.3)
Physical Strength	58.0 (27.6)	52.6 (26.0)	15.3 (33.9)*	10.6 (23.3)*	.087	-5.7 (22.4)	6.0 (10.4)*	**.008**	.05 (-0.1 - 13.0)
Meaningful activities	.	.	.	.	.	1.6 (19.2)	16.2 (17.2)*	**.040**	.
EQ5D (0-1, low-high HRQoL)	0.71 (0.3)	0.69 (0.22)	0.06 (0.25)*	0.07 (0.20)*	.21	0.00 (0.2)	0.00 (0.18)	.32	.32 (0.0 - 0.1)
FSS (0-7, low-high fatigue)	4.5 (1.52)	4.6 (1.4)	-0.1 (1.5)	0.0 (1.74)	.31	0.2 (1.29)	-0.3 (1.0)	.13	.50 (-0.4 - 0.2)
PAM (0-100, low-high self-management)	58.3 (13.9)	60.6 (14.2)	3.2 (16.0)	-1.6 (12.2)	.071	2.2 (16.7)	3.6 (10.3)*	.87	.09 (-5.5 - 0.4)
SF-12 (0-100, low – high HRQoL)									
Physical	.	.	.	.	.	1.1 (8.7)	4.1 (.4)	.75	.
Mental	.	.	.	.	.	0.6 (7.0)	-0.2 (9.0)	.41	.
USER-P (0-100, low – high participation)									
Frequency**	35.4 (13.3)	35.1 (12.1)	-5.5 (14.8)*	-6.0 (11.8)*	.88	-4.4 (11.6)	-4.3 (10.0)*	.65	.68 (.1.7 . 2.7)
Restriction	.	.	.	.	.	6.4 (18.5)*	8.2 (15.9)*	.42	.
Satisfaction	.	.	.	.	.	3.6 (16.7)	8.9 (12.5)*	.57	.
IPAQ-SF (minutes physical activity)	754 (1132)	670 (775)	154 (1620)	270 (874)	.67	2.8 (674)	141 (864)	.43	.90 (-0.2 - 0.3)

* Significant within group difference (p<0.05), In bold significant values (p<0.05), CG; control group, IG; intervention group, LMM; linear mixed models with random slope model, **LMM with random intercept model; HRQoL; Health-related quality of life

Paired t-test for within group comparison, MANCOVA and Linear Mixed Models for between group comparison, Within group differences unadjusted, between group difference and LMM adjusted for age and type of rehabilitation

The absence of an effect of eRehabilitation in the first three months after stroke is in line with the results of previous studies [11,13], concluding that those who received eRehabilitation reported additional exercise practice, but this did not directly translate into significant difference in the primary outcomes. The lack of short-term effect is probably related to the intensity of conventional rehabilitation in the first phase after stroke, with limited opportunities for further optimization of care. Moreover, irrespective of the treatment offered, in people with stroke the largest improvements are seen during the first three months following stroke [3,36]. Thus, the added value of the intervention might be under the threshold for clinical significance in that period.

In contrast to other studies, we also collected data during a follow-up period until six months after stroke, when institutional rehabilitation was finished for most people with stroke. Although improvements between three and six months were smaller compared to the first three months in both groups, there appeared to be an overall benefit of the intervention. This is striking, given the disappointingly low rates of participants being offered and using the intervention. Yet, as the differences were greater when only participants actually using the intervention were taken into account, it is not unlikely that the effect was indeed related to the eRehabilitation intervention. Although most participants stopped with the use of the applications after discharge, they were probably more likely to continue doing exercises at home and thereby maintaining or slightly improving the functional gains of the first three months. Although on the longer term some statistically significant differences were seen between the intervention and control groups, their clinical relevance remains uncertain. Overall, the mean change scores were relatively small. For the Physical Strength subscale, the one subscale with significant between group differences and of which an MCID is known, the observed statistically significant difference did not exceed the MCID.

The overall improvements of people with stroke over time and the observed differences between the control and intervention groups were mainly seen for the SIS. The SIS appears to be a valuable instrument, reflecting the heterogeneity of the consequences of stroke on the individual patient. Nevertheless, problems of people with stroke vary widely and evaluating cognitive, physical and mental health in all of them independent of the presence of such problem, may probably dilute the differences between patient groups. Future research should therefore probably also include patient specific outcome measures such as the COPM [37]. Moreover, since the consequences of a stroke are so heterogeneous, more detailed analyses to evaluate changes in relevant domains (e.g. cognitive, motor, aphasia) for a specific subgroup of people with stroke are recommended. Unfortunately the different subgroups in the current study would be too small for such investigations.

The relatively low proportion of people with stroke who received the intervention suggests that although the implementation activities were employed as intended, this may not have led to the change that was predicted. A process evaluation, investigating which components of the implementation strategy actually worked and why with the implementation of the eRehabilitation intervention is currently underway. In this, we found that healthcare professionals did not deliver the eRehabilitation intervention to all patients, most likely due to physical, mental or cognitive limitations of the patients hampering engagement. Moreover, not all patients who received the intervention proceeded. This could

be possibly explained by the fact that those patients did not see added value of continuation of usage after rehabilitation was finished because they had already sufficiently recovered. Although the relatively low use can be seen as an important drawback of the study, our study reflects the situation in usual care, and in that respect the rates of people with stroke who were actively offered the intervention may not be considered that unfavourable.

Although this study suggests the potential of eRehabilitation offered alongside conventional rehabilitation, the results must be interpreted with care, as it has several limitations. First, this study did not have a randomised, controlled design and people with stroke nor healthcare professionals were blinded regarding whether or not they had access to the intervention. Therefore, it cannot be ruled out that their awareness influenced the results, or that other, unknown developments in the rehabilitation centre occurring over time had an impact on the findings. Second, as mentioned previously, the numbers of people with stroke that were offered and actually used eRehabilitation were relatively low. Although the total number of people with stroke included met de requirements of the sample size calculation, this was not true if in the intervention group only people with stroke actually using the intervention were considered. Future studies investigating the effect of the use of eRehabilitation should develop a clear decision algorithm underling the clinical decisions whether or not to deliver the intervention to a patient. Besides, reasons for (non-) use of patient should be registered as well as what (both applications as exercises within an application) is prescribed and performed, which is necessary to calculate adherence. Third, due to data collection errors, we could not use the data of the SIS hand function. However, this study was performed in the clinical setting, reflecting the situation in which eRehabilitation will be used most.

CONCLUSION

In conclusion, this study indicates that a comprehensive eRehabilitation intervention combing multiple applications and offered alongside conventional stroke rehabilitation is beneficial regarding the maintenance of some of the improvements obtained directly after stroke. Future studies need to investigate the effect of a comprehensive eRehabilitation intervention using a parallel group design, and a better monitoring of the delivery and use of the intervention. It would also be of interest to study partial replacement of conventional stroke rehabilitation by eRehabilitation applications instead of offering it on top.

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Appendix 1

Table 1. Time points of assessments

Domain	Outcome	Short	T0	T3	T6
Sociodemographic and clinical characteristics					
Sociodemographic	Sociodemographic characteristics	-	x	.	.
Clinical	Stroke characteristics	-	x	.	.
Depression and anxiety	Hospital Anxiety and Depression Scale	HADS	x	x	x
Primary and secondary outcomes					
Disease impact	Stroke Impact scale	SIS	x	x	x
Generic health	EuroQoL-5D	EQ5D-3L	x	x	x
Fatigue	Fatigue Severity Scale	FSS	x	x	x
Self-management	Patient Activation Measure	PAM-13	x	x	x
Quality of life	Short Form 12	SF-12	.	x	x
Participation	Utrechtse Schaal voor Evaluatie van Revalidatie	USER-P	x	x	x
Physical activity	International Physical Activity Questionnaires	IPAQ-SF	x	x	x

T0; admission, T3; three months after admission, T6; 6 months after admission

Appendix 2

Table 1. Comparison between intention-to-treat (ITT) and per-protocol (PP) analyses; mean change scores for control group (CG, n=153), complete intervention group (IG total, n=164) and users (IG users, n=53) and the mean differences in change scores between the ITT and the PP

	T0-T3				T3-T6			
	ΔCG	**ΔIG Total**	**ΔIG Users**	**Difference IG Total/ IG Users**	**ΔCG**	**ΔIG Total**	**ΔIG User**	**Difference IG Total/ IG Users**
SIS (0-100, high – low impact)								
Communication	3.5	2.5	0.6	-1.9	-1.7	**-0.3**	**2.6**	2.9
Memory	4.5	3.6	3.7	0.1	-1.3	2.1	**4.2**	2.1
Mobility	12.2	9.4	11.4	2.0	-0.8	1.1	1.7	0.6
Feelings & emotion	0.6	-1.2	1.1	2.3	0.5	0.4	-0.3	-0.7
Activity of Daily Living	9.6	8.8	11.4	2.6	0.2	0.7	3.1	2.4
Physical Strength	15.3	9.3	10.6	1.3	-5.7	**3.3**	**6**	2.7
Meaningful activities	-	-	-	-	1.6	9.1	**16.2**	7.1
EQ5D (0-1, low-high HRQoL)	0.07	0.07	0.07	0.0	-0.01	0.01	0.0	-0.01
FSS (0-7, low – high fatigue)	-0.1	0.3	0.0	-0.3	0.2	-0.2	-0.3	.01
PAM-13 (0 – 100, low- high self-management)	3.2	0.8	-1.6	-2.4	2.2	1.3	3.6	2.0
SF-12 (0-100, low-high HRQoL)								
Physical	-	-	-	-	1.1	1.1	4.1	3.0
Mental	-	-	-	-	0.6	1.7	-0.2	-1.9
USER-P (0-100, low – high participation)								
Frequency	-5.5	-6.6	-6.0	-0.6	-4.4	1.9	-4.3	-6.2
Restriction	-	-	-	-	6.4	5.4	8.2	2.8
Satisfaction	-	-	-	-	3.6	5.5	8.9	3.4
IPAQ-SF (minutes physical activity)	154	102	270	168	2.8	60	141	81

In bold; differs significant from control group ($p<0.05$), HRQoL; Health-related quality of life